SPARK THERAPEUTICS, INC.

FORM 10-K
(Annual Report)

Filed 02/27/18 for the Period Ending 12/31/17

Address 3737 MARKET STREET
         SUITE 1300
         PHILADELPHIA, PA, 19104
Telephone 888-772-7560
CIK 0001609351
Symbol ONCE
SIC Code 2836 - Biological Products, (No Diagnostic Substances)
Industry Biotechnology & Medical Research
Sector Healthcare
Fiscal Year 12/31
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

(Mark One)
☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2017

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from ______ to ______

Commission File Number: 001-36819

Spark Therapeutics, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of Incorporation or Organization)

46-2654405
(IRS Employer Identification No.)

3737 Market Street
Suite 1300
Philadelphia, PA
(Address of Principal Executive Offices)

19104
(Zip Code)

(888) 772-7560
(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class
Common Stock, $0.001 par value per share

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐
Table of Contents

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).  Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant’s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.  ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer”, “accelerated filer”, “smaller reporting company”, and "emerging growth company” in Rule 12b-2 of the Exchange Act. (Check one):

<table>
<thead>
<tr>
<th>Large accelerated filer</th>
<th>☒</th>
<th>Accelerated filer</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-accelerated filer</td>
<td>☐</td>
<td>(Do not check if a smaller reporting company)</td>
<td>☐</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smaller reporting company</td>
<td>☐</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emerging growth company</td>
<td>☐</td>
</tr>
</tbody>
</table>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.  ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).  Yes ☐ No ☒

As of June 30, 2017, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the common stock held by non-affiliates of the registrant was approximately $1,486,720,000, based upon the closing price of the registrant's common stock on June 30, 2017.

As of February 22, 2018, there were 37,217,493 shares of the registrant’s common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2018 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.
# Table of Contents

**TABLE OF CONTENTS**

**PART I**
- Item 1. Business .................................................. 5
- Item 1A. Risk Factors .............................................. 32
- Item 1B. Unresolved Staff Comments ..................... 72
- Item 2. Properties .................................................. 72
- Item 3. Legal Proceedings ..................................... 73
- Item 4. Mine Safety Disclosures ............................ 73

**PART II**
- Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities 74
- Item 6. Selected Financial Data ............................. 77
- Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations 79
- Item 7A. Quantitative and Qualitative Disclosures About Market Risk .......................................... 90
- Item 8. Financial Statements and Supplementary Data ................................................................. 90
- Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure 90
- Item 9A. Controls and Procedures .......................... 90
- Item 9B. Other Information .................................... 91

**PART III**
- Item 10. Directors, Executive Officers and Corporate Governance ................................................. 92
- Item 11. Executive Compensation ........................... 92
- Item 13. Certain Relationships and Related Transactions, and Director Independence ................... 92
- Item 14. Principal Accountant Fees and Services ................................................................. 92

**PART IV**
- Item 15. Exhibits, Financial Statement Schedules ........ 93
- Item 16. Form 10-K Summary ............................... 93

**SIGNATURES**

**CERTIFICATIONS**
Forward-looking statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. The words “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our timing and expectations to commercially launch LUXTURNA™ (voretigene neparvovec) and our plans to develop and commercialize our product candidates;
- the timing, scope or likelihood of regulatory filings and approvals, including the timing of European Medicines Agency, or EMA, approval, if any, for our marketing authorization application, or MAA, of LUXTURNA;
- our ability to enter into agreements involving outcomes-based rebates and innovative contracting models with payers for LUXTURNA;
- the timing, progress and results of clinical trials for SPK-7001, SPK-9001, SPK-8011 and our other product candidates, including statements regarding the timing of initiation and completion of clinical trials, dosing of subjects and the period during which the results of the trials will become available;
- our estimates regarding the potential market opportunity for LUXTURNA and our product candidates;
- the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs for our other product candidates;
- our ability to achieve milestones and receive payments under our collaborations;
- our commercialization, medical affairs, marketing and manufacturing capabilities and strategy;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scalability and commercial viability of our proprietary manufacturing processes;
- our expectations about the rate and degree of market acceptance and clinical utility of LUXTURNA and our product candidates, in particular, and gene therapy in general;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;
- our expectations related to our use of our capital resources;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.
PART I.

Item 1. Business

Overview

We are a leader in the field of gene therapy, seeking to transform the lives of patients suffering from debilitating genetic diseases by developing potentially one-time, life-altering treatments. The goal of gene therapy is to overcome the effects of a malfunctioning, disease-causing gene. Gene therapies have the potential to provide long-lasting effects, dramatically and positively changing the lives of patients with conditions where no, or only palliative, therapies exist. We have built a pipeline of gene therapy product candidates that are directed to the retina, the liver and the central nervous system, or CNS.

In December 2017, the U.S. Food and Drug Administration, or FDA, approved LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with viable retinal cells and confirmed biallelic RPE65 mutation-associated retinal dystrophy, a genetic blinding condition caused by mutations in the RPE65 gene. LUXTURNA is the first FDA-approved gene therapy for a genetic disease, the first and only pharmacological treatment for an inherited retinal disease, or IRD, and the first adeno-associated virus, or AAV, vector gene therapy approved in the United States. LUXTURNA will be manufactured at our manufacturing facility located in Philadelphia, which is the first licensed manufacturing facility in the United States for a gene therapy treating an inherited disease. LUXTURNA has received orphan product designation and, upon approval, we received a rare pediatric disease priority review voucher. In January 2018, we entered into a license and commercialization agreement with Novartis Pharma AG, or Novartis, for the development and commercialization of investigational voretigene neparvovec outside the United States.

We are supporting the appropriate use of LUXTURNA in the United States through small, targeted commercial and medical affairs groups to build and promote access to the product. LUXTURNA will be administered by leading retinal surgeons at selected treatment centers in the United States that specialize in treating IRDs. In January 2018, we announced two novel payer programs to help ensure eligible patients in the United States have access to LUXTURNA: (i) an innovative contracting model; and (ii) an outcomes-based rebate arrangement with a short-term efficacy measure and a long-term durability measure.

Our clinical pipeline includes: (i) an ocular program consisting of SPK-7001, our product candidate targeting choroideremia, or CHM, currently in Phase 1/2 clinical trial, and (ii) our hemophilia programs consisting of SPK-9001, our lead product candidate in the SPK-FIX program for hemophilia B and SPK-8011, our lead product candidate in the SPK-FVIII program for hemophilia A, both currently in Phase 1/2 clinical trials. We retain global rights to all of our clinical-stage product candidates other than SPK-FIX product candidates, which we licensed to Pfizer Inc., or Pfizer.

SPK-7001 is our lead product candidate for the treatment of CHM, an IRD caused by mutations in the REP-1 gene. We have completed enrollment of ten participants in two dose cohorts of our Phase 1/2 trial for SPK-7001 and continue to follow subjects in the trial. In July 2017, we completed enrollment of five additional subjects in the trial who are at an earlier stage of disease. To date, SPK-7001 has been well tolerated and we have not observed any product candidate-related serious adverse events, or SAEs, in this trial. We have received orphan product designation for SPK-7001 for the treatment of CHM in both the United States and the European Union.

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B. In July 2016, FDA granted breakthrough therapy designation to SPK-9001, the lead product candidate in our SPK-FIX program.

Throughout 2017, Pfizer and we provided periodic updates at medical meetings on the progress of the ongoing Phase 1/2 trial of SPK-9001. Most recently, in December 2017 at the American Society of Hematology, or ASH, Annual Meeting, we presented the following interim data, as of the November 29, 2017 cutoff date, on the first eleven subjects in the trial each of whom received a single administration of 5 x 10¹¹ vector genomes per kilogram of body weight:

• With a cumulative follow-up of more than 13 patient years of observation, all 11 participants had discontinued routine infusions of factor IX concentrates and had shown sustained steady-state factor IX activity levels;

• Based on individual participant history for the year prior to the study, the overall annualized bleeding rate, or ABR, was reduced by 97% (calculated based on data after week four) to a mean of 0.3 annual bleeds, compared to a mean of 10.5 bleeds annually before SPK-9001 administration;

• Overall annualized infusion rate, or AIR, was reduced 99% (calculated based on data after week four) to a mean of 0.8 annual infusions, compared to a mean of 62.5 infusions per year before SPK-9001 administration; and

• No participants developed factor IX inhibitors and no SAEs or thromboembolic events were reported.
In February 2018, we entered into a supply agreement with Pfizer for production of one batch of SPK-9001 drug substance.

In our SPK-FVIII program for the treatment of hemophilia A, we initiated a dose-escalating Phase 1/2 clinical trial for our lead product candidate, SPK-8011 in 2017. In February 2018, FDA granted breakthrough therapy designation to SPK-8011. We retain global commercialization rights to the SPK-FVIII program.

In December 2017 at the ASH Annual Meeting, we presented the following interim data, as of the December 6, 2017 cutoff date, on the first four subjects in the Phase 1/2 clinical trial, each of whom had been followed at least 12 weeks and received a single administration of $5 \times 10^{11}$ or $1 \times 10^{12}$ vector genomes per kilogram of body weight:

- Based on individual participant history for the year prior to the study, overall ABR was reduced by 100% (calculated based on data after week four) to a mean of zero annualized bleeds compared to a mean of 5.5 annualized bleeds before administration of SPK-8011;
- Overall AIR was reduced approximately 98% (calculated based on data after week four) to a mean of 1.2 annualized infusions, compared to a mean of 57.8 annualized infusions before SPK-8011 administration; and
- No participants developed factor IX inhibitors and no SAEs or thromboembolic events were reported.

We have several product candidates in various stages of preclinical development. The RPE65 and CHM genes are two of more than 220 genes that have been identified to cause IRDs. We have several preclinical programs targeting other IRDs. We are developing other liver-directed gene therapies, including SPK-GAA, for Pompe disease, an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen in cells. We are developing neurodegenerative disease product candidates that are intended to address TPP1 deficiency, which is a form of Batten disease, and Huntington's disease, among others. We have received orphan product designation in the United States for SPK-TPP1 for the treatment of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

Our product candidates

The following table summarizes information regarding our product candidates and development programs:

<table>
<thead>
<tr>
<th>Preclinical</th>
<th>Phase 1/2</th>
<th>Phase 3</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RETINA-DIRECTED GENE THERAPIES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUXTURNA (voretigene neparvovec): IRD due to biallelic RPE65 mutations (EU)*</td>
<td></td>
<td></td>
<td>Novartis</td>
</tr>
<tr>
<td>SPK-7001: Choroideremia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LHON</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LIVER-DIRECTED GENE THERAPIES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPK-9001: Hemophilia B</td>
<td></td>
<td></td>
<td>Pfizer</td>
</tr>
<tr>
<td>SPK-8011: Hemophilia A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPK-GAA: Pompe disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CNS-DIRECTED GENE THERAPIES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLN2 disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huntington’s disease</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(1) Leber hereditary optic neuropathy
Table of Contents

Retina-directed gene therapies

Biallelic IRD due to RPE65 mutations

Background

Mutations in the RPE65 gene lead to IRD characterized by a range of visual impairments, notably night blindness, or nyctalopia. The RPE65 gene encodes a protein that helps convert the light entering the eye into electrical signals that are transmitted to the brain, enabling sight. Without the properly functioning protein encoded by the RPE65 gene, the visual cycle is disrupted, resulting in debilitating visual impairments, progressing to blindness. The RPE65 gene is expressed in the retinal pigment epithelium, or RPE, layer of the retina.

RPE65-mediated IRD

RPE65-mediated IRD historically has been clinically diagnosed based on clinical presentation and findings and has been characterized most frequently as a form of Leber congenital amaurosis, or LCA, or retinitis pigmentosa, or RP, among over 20 other clinical classifications. We estimate that LCA affects approximately one in every 81,000 individuals and RP affects approximately one in every 4,500 individuals. Because there are no current pharmacologic treatments for IRDs and there are known to be over 220 different genes causing IRDs, there are limited epidemiology data from which to derive population estimates. Additionally, epidemiology estimates vary based on geography. We are aware of studies that estimate the prevalence of RPE65 mutations within the LCA population from approximately 6% to 16% and within the RP population from approximately 1% to 3%. Based on our own assessment of the epidemiology data, we believe the prevalent population is up to approximately 6,000 individuals with RPE65 mutations in the United States, Europe and select additional markets in the Americas and Asia/Pacific. We estimate the United States prevalent population at approximately 1,000 to 2,000 individuals.

LUXTURNA (voretigene neparvovec)

In December 2017, FDA approved LUXTURNA (voretigene neparvovec-rzyl) for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy and viable retinal cells. LUXTURNA is the first FDA-approved gene therapy for a genetic disease, the first and only pharmacological treatment for an IRD and the first AAV vector gene therapy approved in the United States. LUXTURNA will be manufactured at our manufacturing facility located in Philadelphia, which is the first licensed manufacturing facility in the United States for a gene therapy treating an inherited disease. LUXTURNA has received orphan product designation. In January 2018, we entered into a license and commercialization agreement with Novartis for the development and commercialization of investigational voretigene neparvovec outside the United States.

In October 2015, we announced positive top-line results from our pivotal Phase 3 clinical trial of LUXTURNA, the first successfully completed randomized controlled Phase 3 trial of a gene therapy for genetic disease in the United States. The Phase 3 trial demonstrated a statistically significant improvement of functional vision in subjects that were progressing toward complete blindness.

LUXTURNA continues to demonstrate durable effects as measured by both the multi-luminance mobility test, or MLMT, and full-field light sensitivity threshold testing, or FST. In October 2017, we announced that in the continuation of the Phase 3 trial, the original intervention group (n = 20) that received LUXTURNA demonstrated sustained benefit three years post-treatment as measured by the bilateral MLMT and FST. Further, we announced positive two-year follow-up data from the Phase 3 trial on the nine control subjects that crossed over after one year and received LUXTURNA.

We are supporting the appropriate use of LUXTURNA in the United States through small, targeted commercial and medical affairs groups to build and promote access to the product. LUXTURNA will be administered by leading retinal surgeons at selected treatment centers in the United States that specialize in treating IRDs.

In January 2018, we announced two novel payer programs to help ensure eligible patients in the United States have access to LUXTURNA: (i) an innovative contracting model; and (ii) an outcomes-based rebate arrangement with a short-term efficacy measure and a long-term durability measure. Traditionally, specialty medications administered by physicians in hospitals in the United States are purchased by the institution where the patient is treated. The institution then bills the payer, typically including a mark-up on the product. With higher-value, higher-cost therapies, this traditional “buy and bill” model may represent a significant financial burden and risk to the institution and may create substantial additional costs to the payer. Under our innovative contracting model, we enter into an agreement with the commercial payer under which the payer, or a designated specialty pharmacy, purchases LUXTURNA. As a part of this agreement, the payer agrees to provide coverage for its members consistent with FDA labeling of LUXTURNA, expedite benefits processing and cap patient out-of-pocket amounts at in-network limits. Further, we will share risk with certain health insurers by paying rebates if patient outcomes fail to meet specified thresholds, thereby linking the payment for LUXTURNA to both short-term efficacy (30-90 days) and longer-term
durability (30 months) measures that are unique to this one-time gene therapy. The short-term and long-term measures will be based on FST testing scores, with a baseline to be established for each eligible patient before administration of LUXTURN.

We have established Spark Therapeutics Generation Patient Services SM to support commercially insured patients and their caregivers in the United States through the treatment experience. Through this program, we will assist eligible and enrolled commercially insured patients in navigating the insurance process, and will provide options to support their travel and accommodation logistics and costs to and from treatment centers, as well as assistance with other out-of-pocket costs directly related to the treatment.

**SPK-7001 for the treatment of choroideremia**

*Overview*

Choroideremia is an IRD linked to the X-chromosome. Clinically, CHM manifests in affected males in childhood as night blindness and a reduction of visual field, followed by progressive constriction of visual fields. CHM is characterized by deletions or mutations in the CHM gene, resulting in defective or absent Rab escort protein-1, which is the encoded protein of the CHM gene. We estimate prevalence of CHM is between approximately one in 50,000 and one in 100,000 people, implying a total population of up to approximately 12,500 males in the United States and the five major European markets.

**SPK-7001**

Our SPK-CHM program is technically similar to our LUXTURN program, including use of the same vector, targeting the same types of RPE cells and utilizing the same route of administration through sub-retinal injection. SPK-7001 is our investigational product candidate for the treatment of IRD caused by CHM gene mutations. We have received orphan product designation for SPK-7001 in both the United States and the European Union.

**Phase 1/2 clinical trial**

We have completed enrollment of ten participants in two dose cohorts of our Phase 1/2 trial for SPK-7001 and continue to follow subjects in the trial. In July we completed enrollment of five additional subjects in the trial who are at an earlier stage of disease. To date, SPK-7001 has been well tolerated and we have not observed any product candidate-related SAEs in this trial. We will evaluate efficacy primarily by assessing functional vision, as measured by standard ophthalmic tests. Subjects who are administered SPK-7001 will be followed clinically for safety outcomes for 15 years after injection.

**Other IRDs**

The RPE65 and CHM genes are two of more than 220 genes that have been identified to cause IRDs. We have several preclinical programs targeting other IRDs.

**Liver-directed gene therapies**

Our product development portfolio includes product candidates targeting expression of genes in the liver, with a focus on hemophilia and lysosomal storage disorders.

**Hemophilia B**

*Background*

Hemophilia B is a serious and rare inherited disease characterized by insufficient blood clotting that results from the lack of functional FIX, a blood clotting factor normally produced by cells located in the liver. Hemophilia B is caused by mutations in the gene that encodes the coagulation FIX protein. The condition can lead to repeated and sometimes life-threatening episodes of spontaneous bleeding. According to the 2016 World Federation of Hemophilia Annual Global Survey, approximately 30,000 people worldwide suffer from hemophilia B.

The severity of hemophilia B is determined by the circulating levels of FIX. Severe hemophilia B is classified as a level of FIX in the blood of less than 1% of normal. People with severe hemophilia B experience frequent spontaneous bleeding episodes, often into their joints and muscles. Moderate hemophilia B is classified as a level of FIX in the blood equal to or greater than 1% of normal but less than 5% of normal. People with moderate hemophilia B may have bleeds following trauma, or may have spontaneous bleeding episodes, but these will occur less frequently than in those with severe hemophilia B.

The current standard of care for hemophilia B is either prophylactic or on-demand FIX protein replacement therapy, in which frequent intravenous administrations of recombinant FIX are required to stop or prevent bleeding. Prophylactic therapy for hemophilia B, which has been shown to lead to the best outcomes, is practiced only by some adult patients in the United
States due to the significant expense, patient inconvenience and concern about lifetime insurance caps. A gene therapy treatment could offer patients the benefits of prophylaxis without the need for frequent factor infusion.

**SPK-9001**, our lead SPK-FIX product candidate for the treatment of hemophilia B

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of product candidates in our SPK-FIX program for the treatment of hemophilia B. Under this collaboration, we maintain responsibility for the clinical development of SPK-FIX product candidates through the completion of Phase 1/2 trials. Thereafter, Pfizer has responsibility for further clinical development, regulatory approvals and commercialization.

Pfizer and we initiated a Phase 1/2, open label dose-escalation clinical trial of this next-generation hemophilia B product candidate in 2015. In July 2016, FDA granted breakthrough designation to SPK-9001. Throughout 2017, Pfizer and we provided periodic updates at medical meetings on the progress of the ongoing Phase 1/2 trial of SPK-9001.

Most recently, in December 2017 at the ASH Annual Meeting, we presented the following interim data, as of the November 29, 2017 cutoff date, on the first eleven subjects in the trial who received a single administration of 5 x 10^{11} vector genomes per kilogram of body weight:

- With a cumulative follow-up of more than 13 patient years of observation, all 11 participants had discontinued routine infusions of factor IX concentrates and had shown sustained steady-state factor IX activity levels;
- Based on individual participant history for the year prior to the study, the overall ABR was reduced by 97% (calculated based on data after week four) to a mean of 0.3 annual bleeds, compared to a mean of 10.5 bleeds annually before SPK-9001 administration;
- Overall AIR was reduced 99% (calculated based on data after week four) to a mean of 0.8 annual infusions, compared to a mean of 62.5 infusions per year before SPK-9001 administration; and
- No participants developed factor IX inhibitors and no SAEs or thromboembolic events have been reported.

**Hemophilia A**

**Background**

Hemophilia A is a serious and rare inherited disease characterized by insufficient blood clotting that results from the lack of functional factor VIII, a blood clotting factor normally produced by cells located in the liver. Hemophilia A is caused by mutations in the gene that encodes the coagulation factor VIII protein. The condition can lead to repeated and sometimes life-
threatening episodes of spontaneous bleeding. According to the 2016 World Federation of Hemophilia Annual Global Survey, approximately 150,000 people worldwide suffer from hemophilia A.

The severity of hemophilia A is determined by the circulating levels of factor VIII. Severe hemophilia A is classified as a level of factor VIII in the blood of less than 1% of normal. People with severe hemophilia A experience frequent spontaneous bleeding episodes, often into their joints and muscles. Moderate hemophilia A is classified as a level of factor VIII in the blood equal to or greater than 1% of normal but less than 5% of normal. People with moderate hemophilia A may have bleeds following trauma, or may have spontaneous bleeding episodes, but these will occur less frequently than in those with severe hemophilia A.

The current standard of care for hemophilia A is either prophylactic or on-demand factor VIII protein replacement therapy, in which frequent intravenous administrations of recombinant factor VIII are required to stop or prevent bleeding. Prophylactic therapy for hemophilia A, which has been shown to lead to the best outcomes, is practiced only by some adult patients in the United States due to the significant expense, patient inconvenience and concern about lifetime insurance caps. A gene therapy treatment could offer patients the benefits of prophylaxis without the need for frequent factor infusion.

**Table of Contents**

SPK-8011, our lead SPK-FVIII product candidate for the treatment of hemophilia A

We initiated a dose-escalating Phase 1/2 clinical trial for our lead product candidate, SPK-8011, in 2017. In February 2018, FDA granted breakthrough designation to SPK-8011. We retain global commercialization rights to the SPK-FVIII program.

In December 2017, at the ASH Annual Meeting, we presented the following interim data, as of the December 6, 2017 cutoff date, on the first four subjects who had been followed at least 12 weeks and who received a single administration of 5 x 10^{11} or 1 x 10^{12} vector genomes per kilogram of body weight:

- Based on individual participant history for the year prior to the study, overall ABR was reduced by 100% (calculated based on data after week four) to a mean of zero annualized bleeds compared to a mean of 5.5 annualized bleeds before administration of SPK-8011;
- Overall AIR was reduced approximately 98% (calculated based on data after week four) to a mean of 1.2 annualized infusions, compared to a mean of 57.8 annualized infusions before SPK-8011 administration; and
- No participants developed factor VIII inhibitors and no SAEs or thromboembolic events have been reported.

**Participants 1 and 3 each received an infusion of factor for dental extraction procedures.**

**SPK-GAA for the treatment of Pompe disease**

We are developing other liver-directed gene therapies, including SPK-GAA, for Pompe disease. Pompe disease is an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen in cells. Pompe disease is a progressive condition that can lead to muscle weakness making walking, breathing and simple activities difficult.
CNS-directed gene therapies

We are developing neurodegenerative disease product candidates that are intended to address TPP1 deficiency, which is a form of Batten disease, and Huntington's disease, among others. We have received orphan product designation in the United States for SPK-TPPI for the treatment of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

TPP1 deficiency is a form of Batten disease that causes severe childhood neurodegenerative disorders that result in motor and mental decline, seizures and visual deficits appearing between ages two and four and that is fatal by ages ten to twelve in a majority of cases.

Huntington's disease is a hereditary genetic disorder with negative physical, emotional, behavioral and cognitive effects.

We have other neurodegenerative disease programs in preclinical development.

Our manufacturing platform

Using a chemical method we refer to as transfection, we insert many copies of DNA plasmids encoding the specific therapeutic gene sequence, or transgene, into human embryonic kidney cells that have already been grown to high density. During an incubation period following transfection, each cell produces vectors through biosynthesis using the natural machinery available within the cell. At the end of the incubation period, the newly generated vectors are collected from the cells that have been broken apart or, alternatively, from the cell culture medium.

We have made significant investments in developing optimized manufacturing processes and believe that our processes and methods provide the most comprehensive manufacturing process developed to date for AAV-based vector therapies, including:

- sufficient scale to support commercial manufacturing requirements for LUXTURNA and many of our product candidates, including those for IRDs;
- stable manufactured AAV vectors with sufficient longevity so that a small number of initial batches will likely provide adequate commercial supply for multiple years;
- proprietary AAV vector manufacturing processes and techniques that produce a highly purified product candidate, as evidenced by the approximately 25- to 30-fold reduction in non-infectious vector related impurities as compared to vectors used in many previous clinical trials;
- approximately 30 assays to accurately characterize our process and the AAV vectors we produce; and
- a series of high-efficiency purification processes, adapted and customized for multiple different AAV capsids, which allow us to produce higher purity AAV vector solutions, with higher concentrations of active vectors and that are essentially free of empty capsids.

We believe these improvements, and our continued investment in our manufacturing platform, will enable us to develop best-in-class, next-generation gene therapy products. For example, we recently demonstrated proof-of-concept in scaling from the current adherent process to a suspension process. This capability will be important in addressing disease indications with a large target population, such as hemophilia A.

In 2017, we received FDA current good manufacturing practices, or cGMP, validation of our facility in Philadelphia to produce commercial supply of LUXTURNA. Our facility in Philadelphia is the first licensed manufacturing facility in the United States for a gene therapy treating an inherited disease.

Intellectual property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy. Additionally, we intend to rely on regulatory protection afforded through orphan drug designations, data exclusivity and market exclusivity as well as patent term extensions, where available.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these
With respect to both our owned and licensed intellectual property, we cannot be sure that patents will issue with respect to any of the pending patent applications to which we license rights or with respect to any patent applications that we or our licensors may file in the future, nor can we be sure that any of our licensed patents or any patents that may be issued in the future to us or our licensors will be commercially useful in protecting our product candidates and methods of manufacturing the same. Moreover, we have not sought, and may be unable to obtain, patent protection for certain of our product candidates generally, including SPK-CHM, as well as with respect to certain indications. See “Risk factors—Risks related to our intellectual property” for a more comprehensive description of risks related to our intellectual property.

We have licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to our product candidates. Our proprietary intellectual property, including patent and non-patent intellectual property, generally is directed to AAV vectors, methods of treatment of clinical indications important for our development programs, transferring genetic material into cells, inhibiting antibody responses to gene therapies, processes to manufacture and purify our AAV- and lentiviral-based product candidates and other proprietary technologies and processes related to our lead product candidates. We are heavily dependent on the patented or proprietary technologies that we license from third parties. We anticipate that we will require additional licenses to third-party intellectual property rights relating to our development programs in the future, which may not be available on commercially reasonable terms, if at all.

Licensed patents and patent applications

As of February 28, 2018, our patent portfolio included 384 U.S. and foreign patents and patent applications licensed from The Children's Hospital of Philadelphia, or CHOP, the University of Iowa Research Foundation, or UIRF, The University of Pennsylvania, or Penn, Genethon, Inc., or Genethon, and the U.S. National Institutes of Health, or NIH. Our patent portfolio also includes patent applications that we have filed on our own technologies, including technologies related to our hemophilia A program and our manufacturing technologies. The patents and patent applications in our patent portfolio cover technology used in our own development programs, as well as technology used in our collaboration with Pfizer. We have granted Pfizer an exclusive worldwide license for the development and commercialization of product candidates for the treatment of hemophilia B under the patents and other rights listed below that relate to our SPK-FIX program.

Manufacturing platform

We exclusively in-license three patent application families from CHOP relating to scalable manufacturing for producing high-purity gene therapy vectors. The first family relates to manufacture of our own product candidates as well as the product candidates and development programs that are the subject of our collaboration with Pfizer, and patents have been granted in the United States, Australia and Mexico. These patents will expire in 2021, excluding any potential patent term extension or adjustment. Corresponding patent applications are pending in the United States, Brazil, Canada, China, Europe, Israel, India and Japan. We expect that patents issuing from these applications would expire in 2031, excluding any potential patent term extension or adjustment. The second and third application families relate to scalable manufacturing and purification of lentiviral vectors. The second application family is pending in the United States, Australia, Canada, Europe, Hong Kong and Japan. We expect that patents issuing from these applications, if any, would expire in 2032, excluding any potential patent term extension or adjustment. The third application family is pending in the United States, Australia, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, Russia, South Africa and South Korea. We expect that patents issuing from these applications, if any, would expire in 2034, excluding any potential patent term extension or adjustment.

We also have filed patent applications relating to manufacturing technologies that we have developed, including:

- A Patent Cooperation Treaty, or PCT, patent application relating to reduced AAV vector aggregation during manufacturing. We expect that any patents issuing from this application will expire in 2037, excluding any potential patent term extension or adjustment.

- A PCT patent application relating to improvements in AAV vector purification. We expect that any patents issuing from this application will expire in 2037, excluding any potential patent term extension or adjustment.

- A PCT patent application relating to a novel cell line for AAV vector production. We expect that any patents issuing from this application will expire in 2037, excluding any potential patent term extension or adjustment.

- A PCT patent application relating to cell transfection improvements for AAV vector production. We expect that any patents issuing from this application will expire in 2037, excluding any potential patent term extension or adjustment.

---

Table of Contents
We refer to these CHOP manufacturing-related patents and patent applications together with our manufacturing-related patent applications as our “manufacturing patent applications.”

**Modified AAV vectors and gene delivery**

We are developing additional technology in a number of different areas to improve or expand upon our current product candidates. This technology is exclusively licensed from CHOP and generally relates to modifying gene therapy vectors, adding a companion therapy or diagnostic or developing other therapeutic genes. The licensed patent rights underlying this technology include:

- Six U.S. patent applications that relate to alternate, or modified, AAV vectors for gene delivery that we believe have certain technical advantages that are broadly applicable to all of our current, and potentially to our future, clinical programs, including transducing certain target cells, modifications to AAV vectors, modifying AAV vectors to reduce antibody binding, and producing reduced amounts of contaminating AAV particles. We expect that patents issuing from these applications, if any, would expire from 2028 up until 2034, excluding any potential patent term extension or adjustment.

- Two pending U.S. patent applications that generally relate to inhibiting immune responses to AAV vector and measuring antibodies that bind to AAV. We expect that patents issuing from these applications, if any, would expire between 2032 and 2034, excluding any potential patent term extension or adjustment.

We believe our manufacturing patent applications and related know-how and trade secrets may provide us with additional intellectual property protection relating to our planned use of this technology.

**Retina-directed therapies**

In December 2015, we converted a co-exclusive in-license from Penn of certain rights to a U.S. patent co-owned by Penn, Cornell University and the University of Florida that relates to methods of treating patients with LCA due to RPE65 mutations to an exclusive license in the field of use related to the treatment of retinal disorders or diseases caused by a mutation or mutations in the RPE65 gene. This patent is expected to expire in 2022, excluding any potential patent term extension or adjustment. A related continuing application currently is pending with the United States Patent and Trademark Office, or USPTO. There are no issued patents or pending patent applications outside of the United States that correspond to this patent.

We also in-licensed from CHOP U.S. and PCT patent applications co-owned by CHOP and Penn relating to testing functional vision with a mobility course, which can be used as an assessment tool to assess improvements in vision following treatment of an IRD. We expect that any patents issuing from these applications would expire in 2034, excluding any potential patent term extension or adjustment.

We have exclusively in-licensed U.S. patents from Penn that relate to a certain plasmid used in the manufacture of SPK-7001. These patents will expire in 2032, excluding any potential patent term extensions or adjustments.

We believe our manufacturing patent applications and related know-how and trade secrets may provide us with additional intellectual property protection relating to LUXTURNA and SPK-CHM.

**Liver-directed gene therapies**

We exclusively in-licensed certain patents and patent applications from CHOP related to our hemophilia programs. In general, these patents and patent applications relate to AAV-mediated gene therapy, adjunct therapy to use with gene therapy treatment, modified AAV vectors and modified forms of factor VIII. These licensed patent rights include:

- A U.S. patent that we believe provides us with exclusivity in the United States for treating hemophilia B with a factor IX gene-containing AAV vector. A related patent provides coverage on an AAV vector with a mutated factor IX gene. These patents will expire in 2018, excluding any potential patent term extension or adjustment. Corresponding patents are issued in Australia, Europe and Japan.
• A U.S. patent relating to modified AAV vectors for delivery of factor IX. This patent will expire in 2034, excluding any potential patent term extension or adjustment. Corresponding patent applications are pending in Australia, Brazil, Canada, China, Colombia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, Saudi Arabia, Singapore, South Africa and South Korea. We expect that any patents issuing from these applications will expire in 2034, excluding any potential patent term extension or adjustment.

• A U.S. patent relating to an adjunct therapy to reduce inhibitory antibodies against factor IX administered via gene therapy. This patent will expire in 2020, excluding any potential patent term extension or adjustment.

• A U.S. patent application relating to certain modifications to a FIX gene that enhances secretion of factor IX. We expect that any patents issuing from this application will expire in 2021, excluding any potential patent term extension or adjustment.

• A U.S. patent application relating to modified factor IX expression cassettes. We expect that any patents issuing from this application will expire in 2036, excluding any potential patent term extension or adjustment. Corresponding patent applications are pending in Australia, Brazil, Canada, China, Colombia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, Saudi Arabia, Singapore, South Africa and South Korea. We expect any patents issuing from these applications will expire in 2036, excluding any potential patent term extension or adjustment.

• A U.S. patent relating to a factor VIII heavy chain with enhanced secretion. This patent will expire in 2023, excluding any potential patent term extension or adjustment. There are no issued patents or pending patent applications outside of the United States that correspond to this U.S. patent.

• U.S. patents relating to factor VIII variants having enhanced coagulation. These patents will expire in 2030, excluding any potential patent term extension or adjustment. A corresponding patent is issued in Australia. This patent will expire in 2030, excluding any potential patent term extension or adjustment. Corresponding patent applications are pending in Canada and Europe. We expect any patents issuing from these applications will expire in 2030, excluding any potential patent term extension or adjustment.

We also have filed patent applications relating to our SPK-FVIII program on technologies which we have developed, including:

• U.S. and PCT patent applications relating to modified factor VIII expression constructs. We expect that any patents issuing from these applications will expire in 2036, excluding any potential patent term extension or adjustment.

• A U.S. patent application relating to AAV gene therapy treatment of hemophilia A. We expect that any patents issuing from this application will expire in 2038, excluding any potential patent term extension or adjustment.

We also have exclusively in-licensed certain patent applications from Genethon relating to our Pompe program.

We believe our manufacturing patent applications and related know-how and trade secrets may provide us with additional intellectual property protection relating to our SPK-FIX program, SPK-FVIII program and SPK-GAA program.

CNS-directed gene therapies

We exclusively in-licensed a portfolio of approximately 167 U.S. and foreign patents and patent applications from UIRF that relate to treatment of a broad array of CNS and neurodegenerative diseases.

Trade secrets

In addition to patents and licenses, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of our AAV and lentiviral vector and manufacturing processes and gene therapies are based upon trade secrets and know-how. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, and obtain and maintain ownership of certain technologies, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how including by implementing measures intended to maintain the physical security of our premises and the physical and electronic security of our information technology systems.
Collaboration and license agreements

Pfizer

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates in our gene therapy program for the treatment of hemophilia B. Under the agreement, we have granted Pfizer an exclusive worldwide license under specified patent rights and know-how relating to any factor IX gene therapy that we develop, manufacture or commercialize prior to December 31, 2024, to develop, manufacture and commercialize such licensed factor IX gene therapy products for the diagnosis, prevention, treatment and cure of hemophilia B.

Under the terms of the agreement, we are primarily responsible for conducting research and development activities through completion of Phase 1/2 clinical trials of hemophilia B product candidates. Pfizer and we will share development costs incurred under an agreed product development plan for each product candidate, with our share of development costs under the agreement limited to $10.6 million. Following the completion of Phase 1/2 clinical trials, Pfizer will primarily be responsible for development, manufacture, regulatory approval and commercialization, including all costs associated therewith.

During the period through completion of Phase 1/2 clinical trials, which we refer to as the collaboration period, the hemophilia B program will be governed by a joint steering committee, or JSC, consisting of representatives of Pfizer and us. The JSC will, among other responsibilities, provide operational and strategic oversight to the activities to be performed under the product development plan, will monitor and assess the progress of collaboration activities and will serve as a forum for the parties to communicate regarding collaboration issues and resolve disputes. During the collaboration period, if the JSC is unable to reach agreement, we generally have final decision-making authority regarding the conduct of the agreed product development plan and, following the collaboration period, Pfizer generally has final decision-making authority regarding the further development and commercialization of licensed compounds and licensed products.

Under the terms of the agreement, we received a $20.0 million upfront payment. In each of December 2015 and December 2016, we earned a $15.0 million milestone payment and also are eligible to receive up to an additional $230.0 million in aggregate milestone payments under the agreement, $110.0 million of which relates to potential development, regulatory and commercial milestones for the first product candidate to achieve each milestone and $120.0 million of which relates to potential regulatory milestones for additional product candidates. In addition, we are entitled to receive royalties, calculated as a low-teen percentage of net sales of licensed products. The royalties may be subject to certain reductions, including for a specified portion of royalty payments that Pfizer may become required to pay under any third-party license agreements, subject to a minimum royalty. Under the agreement, we remain solely responsible for the payment of license payments payable by us under specified license agreements.

In June 2016, Pfizer and we amended the agreement to allow for the technology transfer of certain of our manufacturing processes related to SPK-9001 to be transferred to Pfizer for use in the field of hemophilia B.

In November 2017, Pfizer and we amended the agreement to provide for the enrollment of up to five additional participants in the current Phase 1/2 clinical trial each of which will receive SPK-9001 manufactured using an enhanced process to test its comparability to SPK-9001 received by the first 10 participants enrolled in the ongoing trial. Under the terms of this amendment, we received a $10.0 million upfront payment and are eligible to receive up to an additional $15.0 million in potential milestone payments.

The agreement will expire on a country-by-country basis upon the latest of: (i) the expiration of the last-to-expire valid claim, as defined in the agreement, in the licensed patent rights covering a licensed product, (ii) the expiration of the last-to-expire regulatory exclusivity granted with respect to a licensed product or (iii) 15 years after the first commercial sale of the last licensed product to be launched, in each case in the applicable country. The last to expire patent right licensed to Pfizer, if it issues as a patent, is currently expected to expire in 2034, excluding any applicable patent term extension or adjustment, although we could obtain rights to additional patents, including through the issuance of pending patent applications, with later expiration dates, which would be subject to Pfizer’s license under the agreement. After expiration, but not termination, of the agreement as to a country, Pfizer’s licenses will become fully paid-up, royalty-free, perpetual and irrevocable as to licensed products in the applicable country.

Pfizer may terminate the agreement, on a licensed product-by-licensed product and a country-by-country basis, or in its entirety, for any or no reason (i) upon 90 days’ written notice prior to the commencement of commercialization of a licensed product or (ii) upon 180 days’ written notice after the commencement of commercialization of a licensed product. Either party may, subject to a cure period, terminate the agreement in the event of the other party’s uncured material breach. Either party also may terminate the agreement upon the occurrence of specified bankruptcy events. If the agreement is terminated, rights to licensed products that were being developed, manufactured or commercialized at that time generally revert to us.

If the agreement is terminated by Pfizer after the initiation of a pivotal clinical trial, and we continue development utilizing intellectual property rights or data developed by Pfizer through its activities under the agreement, we will be required to pay...
Pfizer a royalty, calculated as a single-digit percentage of net sales of licensed products, with the percentage determined based on the stage of development or commercialization of the product candidate at the time of Pfizer’s termination.

In February 2018, we entered into a supply agreement with Pfizer for production of one batch of *SPK-9001* drug substance.

**Novartis**

In January 2018, we entered into a Licensing and Commercialization Agreement, or the Novartis License Agreement, with Novartis to develop and commercialize voretigene neparvovec outside the United States. We also entered into a Supply Agreement with Novartis, or the Novartis Supply Agreement, to manufacture and supply all of the requirements of Novartis for voretigene neparvovec. Under the terms of the Novartis License Agreement, we granted Novartis an exclusive right and license, under our intellectual property reasonably necessary or useful for the development or commercialization of LUXTURNA™, for the treatment, prevention, cure or control of *RPE65*-mediated IRD in humans outside the United States.

Novartis paid us a non-refundable, non-creditable, one-time payment of $105.0 million and we may receive an additional $25.0 million if investigational voretigene neparvovec is approved by the European Medicines Agency, or EMA, as well as an aggregate $40.0 million based upon the achievement of certain aggregate net sales in certain markets. We also are entitled to receive royalty payments at a flat mid-twenties percentage of net sales on a royalty-region by royalty-region basis, subject to reduction and extension in certain circumstances. We will retain regulatory responsibility for obtaining approval for LUXTURNA by EMA and Novartis will have regulatory responsibility for obtaining approval for LUXTURNA for countries outside of the United States and the European Union.

The Novartis License Agreement continues until the last to complete royalty term, which is on a royalty-region by royalty-region basis for 12 years from the first commercial sale in such region of LUXTURNA, but may be extended in a certain country until regulatory exclusivity expires in that country or on a region-by-region basis until aggregate net sales fall below a certain threshold. Either party may terminate the Novartis License Agreement upon the other party’s uncured material breach of the Novartis License Agreement, insolvency, or bankruptcy. Novartis may terminate the Novartis License Agreement at any time upon one year’s prior written notice to us. Novartis also may terminate the Novartis License Agreement: (i) in the event that there is an uncured material breach of the Novartis Supply Agreement by us, resulting in Novartis taking over the manufacture of LUXTURNA or (ii) in the event we undergo a change of control.

Under the Novartis Supply Agreement, we have agreed to provide all of the commercial supply of LUXTURNA required by Novartis, subject to certain conditions. The Novartis Supply Agreement continues until the expiration or early termination of the Novartis License Agreement. Either party also may terminate the Novartis Supply Agreement upon the other party’s uncured material breach of the Novartis Supply Agreement, insolvency or bankruptcy.

In-license agreements

We have rights to use and exploit multiple issued and pending patents under licenses from other entities. We consider the commercial terms of these licenses, which provide for modest milestone and royalty payments, and their provisions regarding diligence, insurance, indemnification and other similar matters, to be reasonable and customary for our industry.

**The Children’s Hospital of Philadelphia**

In October 2013, we entered into a technology assignment agreement with CHOP. Under this agreement, CHOP assigned to us CHOP’s rights to the preclinical and clinical programs and intellectual property that we are currently advancing, as well as know-how, standard operating procedures, trade secrets and proprietary processes related to our manufacturing platform. Furthermore, under this agreement, we obtained commercial rights to the drug master file, batch records and related data associated with the manufacture of AAV and lentiviral vectors using our manufacturing platform.

We also entered into a license agreement with CHOP under which CHOP granted us an exclusive worldwide license in the field of gene therapy, with the right to sublicense, under a broad portfolio of gene therapy and viral vector patent rights and gene therapy know-how related to vector manufacturing technology, the treatment of hemophilia and other gene therapy indications. CHOP also granted us a non-exclusive worldwide license in the field of gene therapy, with the right to sublicense, to other know-how owned or controlled by CHOP, existing as of the effective date of the license agreement and not explicitly covered by the exclusive licenses, that is necessary or useful for making, using, selling or importing any products we may develop that are covered by our exclusive license. Under both license grants, we have the right to research, develop, manufacture and commercialize products covered by the licensed patent rights or the licensed know-how in the field of gene therapy. Under the terms of the license agreement, we are obligated to use commercially reasonable best efforts to develop and commercialize licensed products. We are obligated under the license agreement to make milestone payments upon the treatment of the first subject treated in a U.S. Phase 3, or a foreign equivalent, clinical trial and upon the first commercial sale for the first licensed product in each of four indications. These milestone payments range from $125,000 to $5.0 million, and would, in the aggregate, reach a maximum of $7.1 million if all milestones are achieved. In addition, we are obligated to pay CHOP a low-
single-digit royalty on a country-by-country basis on net sales of licensed products covered by a valid licensed patent claim. Following the expiration of our royalty obligations as to a licensed product in a country, we will retain a perpetual, full and unrestricted right to make, use and commercialize the licensed product in such country under the licensed intellectual property rights. CHOP controls the prosecution and maintenance of the licensed patent rights. We have agreed to reimburse CHOP for fees and expenses incurred in connection with the prosecution and maintenance of the licensed patent rights, including those fees and expenses incurred prior to the effective date of the license agreement. Unless sooner terminated, the term of the license agreement continues until the expiration of the last to expire of the licensed patent rights, the latest of which is currently expected to expire in 2034. If we oppose or contest the grant or validity of any licensed patent right, or any claims thereof, CHOP may terminate the license granted to us with respect to such patent right. CHOP may terminate this license upon uncured material breaches by us of the terms of the license or if such action is legally necessary to comply with applicable federal laws or regulations relating to government march-in rights and we may terminate the license at any time upon giving 90 days’ prior written notice to CHOP.

We also have entered into a master research services agreement with CHOP under which CHOP supplies us with viral vectors. Under this master research services agreement, we expect to maintain a sufficient supply of clinical-grade gene therapy vectors produced in CHOP’s cGMP clinical facility to meet both our clinical needs and, at our option, our commercial batches to support the commercial launch of LUXTURNA. The term of the agreement extends until October 14, 2028 as to services relating to the supply of RPE65 vectors and until June 30, 2018 as to other services, and continues beyond such expiration dates as to work orders executed by the parties prior to the applicable expiration date until the completion of such work orders. We amended this agreement in March 2016 to extend the expiration date for services other than the supply of LUXTURNA vectors. We may terminate this agreement upon 30 days’ written notice for any reason, and CHOP may terminate this agreement upon 30 days’ written notice upon uncured material breaches by us of the terms of the agreement or if it reasonably determines that continuation of this agreement will have a materially adverse effect on its legal, regulatory or tax status.

We also entered into an additional licensing agreement with CHOP in November 2015. The licensing agreement supplements our existing license agreement with CHOP by granting us a worldwide exclusive license, with the right to sublicense, to use and practice a provisional patent application related to the production of gene therapies on substantially the same terms and conditions as the existing agreement.

University of Pennsylvania

In December 2015, we converted a co-exclusive license agreement to certain patent rights with Penn, Cornell University and the University of Florida relating to a method of treating and retarding the development of blindness to manufacture and commercialize products covered by the licensed patent rights in the field of research, development, manufacture and commercialization for the diagnosis, treatment, amelioration and prevention of human and animal diseases to an exclusive license in the field of use related to the treatment of retinal disorders or diseases caused by a mutation or mutations in the RPE65 gene. Penn can no longer grant an additional license to a third party with the same scope of rights that we have received under our amended license agreement with Penn, including a right to commercialize products covered by the licensed patent rights.

Under the terms of the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize licensed products, and to use such efforts to accomplish specified development and commercial launch objectives in accordance with a specified timeline as well as to expend specified resources in the development and commercialization of licensed products. If our total expenditures on development and commercialization of the licensed products in any 12-month period do not meet or exceed the applicable diligence minimum, then we must pay Penn the amount of the shortfall. Under the terms of the agreement, we are obligated to make commercial milestone payments related to the licensed products, which could, in the aggregate, reach a maximum of $3.8 million per licensed product if all milestones are achieved for such licensed product. In addition, we are obligated to pay Penn a low- to mid-single-digit royalty, on a country-by-country basis, on net sales of licensed products covered by a valid licensed patent claim. Penn controls the prosecution and maintenance of the licensed patent rights. We made an initial cash payment to Penn to cover 50% of Penn’s previously incurred patent expenses relating to the licensed patent rights, with the exception of one patent for which we agreed to reimburse Penn for all such expenses. With respect to that specific patent, we agreed to reimburse Penn for patent expenses arising during the term of the license. This license will expire upon the expiration or abandonment of all of the patents and patent applications subject to the license, the latest of which is currently expected to expire in 2022. Penn may terminate the license upon uncured material breaches by us of the terms of the license or upon the occurrence of certain events, including specified bankruptcy and insolvency events relating to us, or if we commence an action against Penn or any of the co-owners of the licensed patent rights to declare or render invalid or unenforceable the patent rights. We may terminate the license at any time upon giving 60 days’ prior written notice to Penn.

17
In December 2013, we entered into a license agreement with UIRF, which we amended in January 2016 to expand the list of patent and patent applications to which we have rights. Under the license agreement, as amended, UIRF granted us an exclusive worldwide license, with the right to sublicense, to a portfolio of approximately 96 gene therapy patents and patent applications owned by UIRF or jointly owned by UIRF and Massachusetts General Hospital related to RNA interference and gene therapy technologies, and to the results of a certain research collaboration among UIRF, Howard Hughes Medical Institute and CHOP, to manufacture and commercialize products covered by the licensed patent rights or discovered, developed, manufactured or commercialized through the use of the research collaboration results. Under the terms of the license agreement, we are obligated to use reasonable efforts to develop and commercialize licensed products. In connection with the agreement, we issued shares of our common stock and made a cash payment of approximately $157,000 to UIRF, and we are obligated to make milestone payments upon the achievement of certain regulatory milestones relating to the licensed products, which could, in the aggregate, reach a maximum of $5.5 million per licensed product if all milestones are achieved. Upon mutual agreement between UIRF and us, we could elect to pay up to 100% of such amounts with shares of our common stock. In addition, we are obligated to pay UIRF a mid-single-digit royalty, on a country-by-country basis, on net sales of licensed products covered by a licensed patent claim so long as the licensed product achieves and retains orphan designation, and if the licensed product does not receive or retain orphan product designation, we are obligated to pay UIRF a low-single digit royalty on a country-by-country basis. We are obligated to pay UIRF specified percentages of certain non-royalty payments and other consideration we may receive from any sublicense of our rights under the license agreements, with the specified percentage dependent on the timing of the sublicensing grant. UIRF controls the prosecution and maintenance of the licensed patent rights. We also made an initial cash payment to UIRF to cover all of UIRF’s previously incurred patent expenses relating to the licensed patent rights. This license will expire upon the expiration or abandonment of all of the patents and patent applications subject to the license, the latest of which, if it issues as a patent, is currently expected to expire in 2022. UIRF may terminate the license upon uncured material breaches by us of the terms of the license and upon the occurrence of certain events, including specified bankruptcy and insolvency events relating to us, or if we commence an action against UIRF to declare or render invalid or unenforceable the patent rights. We may terminate the license at any time upon giving 60 days’ prior written notice to UIRF.

Under the terms of the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize licensed products, and to use such efforts to accomplish development and commercial launch objectives as well as to expend specified resources in the development and commercialization of licensed products. If our total expenditures in any 12-month period do not meet or exceed the applicable diligence minimum, then we must pay UIRF the amount of the shortfall. Under the terms of the agreement, we issued shares of our common stock to Penn and we are obligated to make milestone payments upon the achievement of certain regulatory milestones relating to the licensed products, which could, in the aggregate, reach a maximum of $5.5 million per licensed product if all milestones are achieved for such licensed product. Upon mutual agreement between Penn and us, we could elect to pay up to 100% of such amounts with shares of our common stock. In addition, we are obligated to pay Penn a mid-single-digit royalty, on a country-by-country basis, on net sales of licensed products covered by a licensed patent claim so long as the licensed product achieves and retains orphan designation, and if the licensed product does not receive or retain orphan product designation, we are obligated to pay Penn a low-single digit royalty on a country-by-country basis. We are obligated to pay Penn specified percentages of certain non-royalty payments and other consideration we may receive from any sublicense of our rights under the license agreements, with the specified percentage dependent on the timing of the sublicensing grant. Penn controls the prosecution and maintenance of the licensed patent rights. We also made an initial cash payment to Penn to cover all of Penn’s previously incurred patent expenses relating to the licensed patent rights. This license will expire upon the expiration or abandonment of all of the patents and patent applications subject to the license, the latest of which, if it issues as a patent, is currently expected to expire in 2022. Penn may terminate the license upon uncured material breaches by us of the terms of the license and upon the occurrence of certain events, including specified bankruptcy and insolvency events relating to us, or if we commence an action against Penn to declare or render invalid or unenforceable the patent rights. We may terminate the license at any time upon giving 60 days’ prior written notice to Penn.

University of Iowa Research Foundation

In December 2014, we entered into a license agreement with Penn, under which Penn granted us an exclusive, worldwide license, with the right to sublicense, to certain patent rights owned by Penn related to certain proviral plasmids that are useful in the manufacture of certain gene therapy products for the treatment of CHM.

The license agreement and our obligation to pay royalties expire, unless earlier terminated, on a country-by-country and licensed product-by-licensed product basis, upon the expiration of the last to expire valid claim, as defined in the agreement in the licensed patent rights (including patent applications) covering the manufacture, use, sale or importation of such licensed product in such country. Following the expiration of our obligation to pay royalties on a licensed product in a country, we will retain a fully paid-up, non-royalty-bearing, perpetual license to the results of the collaboration relating to such licensed product in such country. UIRF may terminate this license or render it non-exclusive at any time if we have both (i) not put the licensed product into commercial use in any country and (ii) are not demonstrably engaged in a program directed toward achieving commercial use of the product, and if we fail to eliminate such conditions within a specified cure period following notice from UIRF. UIRF may also terminate this license upon uncured material breaches by us of the terms of the license, subject to a specified notice and cure period. The license agreement automatically terminates if we undergo certain bankruptcy or insolvency events. We may terminate the license at any time upon giving 90 days’ prior written notice to UIRF.
In December 2016, we entered into a license agreement that provides us with exclusive worldwide rights to Selecta's proprietary SVP™ platform technology for co-administration with gene therapy targets, including factor VIII for hemophilia A, as well as exclusive options for up to four additional undisclosed genetic targets.

Selecta's immune tolerance SVP, including SVP-Rapamycin, is an investigational technology intended to suppress the formation of neutralizing antibodies to an AAV capsid when used in combination with gene therapies, without altering the therapeutic profile of the gene therapy. Neutralizing antibodies form in response to an initial administration of an AAV gene therapy and prevent effective subsequent usage. The potential ability to re-dose a gene therapy may be beneficial where a patient has not achieved a sufficient therapeutic expression of the transferred gene in the initial dose.

Subject to the terms of the agreement, we made an initial $10.0 million cash payment to Selecta and purchased $5.0 million of Selecta's common stock. During 2017, we paid Selecta an additional $5.0 million in cash and purchased an additional $10.0 million of Selecta's common stock. Selecta will be eligible for up to $430.0 million in milestone payments for each target, with up to $65.0 million being based on our achievement of specified development and regulatory milestones and up to $365.0 million for specified commercial milestones. In addition, we will pay Selecta tiered mid-single to low-double-digit royalties on worldwide annual net sales of any resulting commercialized gene therapy.

Competition

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

We are aware of companies focused on developing AAV gene therapies in various indications, including Adverum Biotechnologies, Inc., Applied Genetic Technologies Corporation, or AGTC, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., AveXis, Inc., Abeona Therapeutics Inc., BioMarin Pharmaceuticals Inc., GenSight Biologics SA, Horama SAS, Lysogene SAS, MeiraGTx Limited, Nightstar Therapeutics PLC, REGENXBIO, Inc. Solid Biosciences, Inc., Ultragenyx Pharmaceuticals, Inc., uniQure N.V. and Voyager Therapeutics, Inc. as well as several companies addressing other methods for delivering or modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

For our approved product and our clinical product candidates, the main competitors include:

- **LUXTURNA**. While no approved pharmacologic agents exist for patients with RPE65 -mediated IRD, Second Sight Medical Products, Inc. has received approval from FDA and other foreign regulatory authorities for a retinal prosthesis medical device, which is being marketed to RP patients with limited or no light perception. Another retinal prosthesis medical device from Retina Implant AG has obtained a CE Certificate of Conformity from its notified body, and is similarly indicated for blinded patients. Novelion Therapeutics, Inc. (formerly QLT Inc.) completed a Phase 1b clinical trial of a vitamin A derivative to treat RP and LCA. In the gene therapy space, certain companies and several academic institutions have conducted or plan to conduct clinical trials involving RPE65-based product candidates, including MeiraGTx and Horama SAS. To date, none of these organizations has completed a trial involving injection of a subject’s second eye or has initiated a Phase 3 trial.

- **SPK-CHM**. We are aware that Nightstar Therapeutics PLC is developing an AAV-based gene therapy for the treatment of choroideremia. Nightstar Therapeutics PLC has obtained orphan product designation in the United States and the European Union for this product candidate for the treatment of choroideremia and has announced plans to initiate a Phase 3 trial in the first half of 2018.

- **SPK-FIX**. Hemophilia B patients typically are treated by a variety of plasma-derived, recombinant or long-acting products that are produced by a number of companies, including Pfizer. Many other companies are developing gene therapies to treat hemophilia B, including Shire PLC, Sangamo BioSciences, Inc., Freeline Therapeutics and uniQure N.V.

- **SPK-FVIII**. The standard of care for moderate to severe hemophilia A is intravenously administered factor VIII protein or its derivatives. The main competitors with product candidates under development or approved to treat hemophilia A include BioMarin Pharmaceutical Inc., Ultragenyx Pharmaceuticals, Inc. in collaboration with Bayer HealthCare, Shire PLC, uniQure N.V., Sangamo Biosciences, Inc., in collaboration with Pfizer, Telethon Institute for Gene Therapy in collaboration with Bioverativ Inc., Novo Nordisk A/S Roche Holding AG and Sanofi.
Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

**Regulation of gene therapies**

In the United States, FDA regulates biologic products including gene therapy products under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and regulations implementing these laws. The FDCA, PHSA and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, advertising and promotion of biologic products. Applications to FDA are required before conducting human clinical testing of biologic products. Additionally, each clinical trial protocol for a gene therapy product candidate is reviewed by FDA and, in limited instances NIH, through its Recombinant DNA Advisory Committee, or RAC. FDA approval also must be obtained before marketing of biologic products.

Within FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, or OCTGT, and FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee, or CTGTAC, a panel of medical and scientific experts and consumer representatives, to advise CBER on its reviews. CBER works closely with NIH and the RAC, which makes recommendations to NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. FDA has issued a growing body of guidance documents on chemistry, manufacturing and control, or CMC, clinical investigations and other areas of gene therapy development, all of which are intended to facilitate the industry’s development of gene therapy products.

**U.S. biologic products development process**

The process required by FDA before a biologic product candidate may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and *in vivo* studies in accordance with FDA’s current Good Laboratory Practice, or GLP, regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to FDA of an application for an Investigational New Drug exemption, or IND, which allows human clinical trials to begin unless FDA objects within 30 days;
- approval by an independent institutional review board, or IRB, reviewing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to FDA’s Good Clinical Practice, or GCP, regulations, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biologic product candidate for its intended use;
- preparation and submission to FDA of a Biologics License Application, or BLA, for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biologic product candidate is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biologic product candidate’s identity, safety, strength, quality, potency and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- payment of user fees and FDA review and approval, or licensure, of the BLA. BLA or new drug application, or NDA, application fees for products designated as orphan drugs by FDA are waived.
Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as in vivo studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, prior to the submission of an IND to FDA, a protocol and related documents must be submitted to, and the study registered with, the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA. However, many companies and other institutions, not otherwise subject to the NIH Guidelines, voluntarily follow them. NIH is responsible for convening the RAC that discusses protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA will notify FDA of the RAC’s decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA website and may be accessed by the public.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by FDA, unless FDA places the clinical trial on a clinical hold. In such a case, the IND sponsor and FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if FDA allows the IND to proceed, but the RAC decides that full public review of the protocol is warranted, FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by FDA.

**Human clinical trials under an IND**

Clinical trials involve the administration of the biologic product candidate to healthy volunteers or patients under the supervision of qualified investigators which generally are physicians not employed by, or under, the control of the trial sponsor. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with FDA’s regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent.

Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers items such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject, or his or her legal representative, and must monitor the clinical trial until completed. Clinical trials involving recombinant DNA also must be reviewed by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research that utilizes recombinant DNA at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

**Human clinical trials typically are conducted in three sequential phases that may overlap or be combined:**

- **Phase 1.** The biologic product candidate initially is introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early understanding of its effectiveness. In the case of some product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- **Phase 2.** The biologic product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- **Phase 3.** The biologic product candidate is administered to an expanded patient population at geographically dispersed clinical trial sites in adequate and well-controlled clinical trials to generate sufficient data to statistically
confirm the potency and safety of the product for approval. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to FDA.

Written IND safety reports must be promptly submitted to FDA, NIH and the investigators for: serious and unexpected adverse events; any findings from other trials, in vivo laboratory tests or in vitro testing that suggest a significant risk for human subjects; or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor’s initial receipt of the information.

FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the biologic product candidate has been associated with unexpected serious harm to patients.

Additional regulation for gene therapy clinical trials

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. FDA has issued various guidance documents regarding gene therapies, which outline additional factors that FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

NIH and FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

Compliance with cGMP requirements

Manufacturers of biologics must comply with applicable cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Manufacturers and others involved in the manufacture and distribution of such products also must register their establishments with FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to FDA upon their initial participation in the manufacturing process. Establishments may be subject to periodic, unannounced inspections by government authorities to ensure compliance with cGMP requirements and other laws. Discovery of problems may result in a government entity placing restrictions on a product, manufacturer or holder of an approved BLA, and may extend to requiring withdrawal of the product from the market. FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMP requirements and adequate to assure consistent production of the product within required specification.

Concurrent with clinical trials, companies usually complete additional preclinical studies and must also develop additional information about the physical characteristics of the biologic product candidate as well as finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents or of causing other adverse events with the use of biologic products, the PHSA emphasizes the importance of controlling manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other requirements, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biologic product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biologic product candidate does not undergo unacceptable deterioration over its shelf life.
The results of the preclinical tests and clinical trials, together with detailed information relating to the product’s CMC and proposed labeling, among other things, are submitted to FDA as part of a BLA requesting approval to market the product for one or more indications.

For gene therapies, selecting patients with applicable genetic defects is a necessary condition to effective treatment. For the therapies we are currently developing, we believe that diagnoses based on symptoms, in conjunction with existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, or CLIA, are sufficient to select appropriate patients and will be permitted by FDA. For future therapies, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to select patients or to assure the safe and effective use of therapies in appropriate patients. FDA refers to such tests as in vitro companion diagnostic devices. On July 31, 2014, FDA announced the publication of a final guidance document describing the agency’s current thinking about the development and regulation of in vitro companion diagnostic devices. The final guidance articulates a policy position that, when safe and effective use of a therapeutic product depends on a diagnostic device, FDA generally will require approval or clearance of the diagnostic device at the same time that FDA approves the therapeutic product. The final guidance allows for two exceptions to the general rule of concurrent drug/device approval, namely, when the therapeutic product is intended to treat serious and life-threatening conditions for which no alternative exists, and when a serious safety issue arises for an approved therapeutic agent, and no FDA-cleared or FDA-approved companion diagnostic test is yet available. At this point, it is unclear how FDA will apply this policy to our future gene therapy candidates, or even to our current products. Should FDA deem genetic tests used for selecting appropriate patients for our therapies to be in vitro companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval for a BLA.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biologic product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biologic product candidate for an indication for which orphan designation has been granted.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to FDA’s fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as a BLA, is $2,374,200. PDUFA also imposes an annual product fee for biologics ($114,450) and an annual establishment license fee ($585,200) on facilities used to manufacture prescription biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

FDA reviews a BLA within 60 days of submission to determine if it is substantially complete before the agency accepts it for filing. FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In that event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before FDA accepts it for filing. Once the submission is accepted for filing, FDA begins an in-depth, substantive review of the BLA.

FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and potent, or effective, for its intended use, has an acceptable purity profile and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate’s identity, safety, strength, quality, potency and purity. FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product candidate. A REMS could include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, FDA will inspect the facilities at which the product candidate is manufactured. FDA will not approve the product candidate unless it determines that the manufacturing processes and facilities comply with cGMP requirements and adequate to assure consistent production of the product candidate within required specifications. Additionally, before approving a BLA, FDA typically will inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements.
On the basis of the BLA and accompanying information, including the results of the inspection of the manufacturing facilities, FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biologic product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information for FDA to reconsider the application. If those deficiencies have been addressed to FDA’s satisfaction in a resubmission of the BLA, FDA will issue an approval letter.

If a product candidate receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited. Further, FDA may require that certain contraindications, warnings or precautions be included in the product labeling. FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, FDA may require post-marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biologic product’s safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

FDA has agreed to specified performance goals in the review of BLAs under the PDUFA. One such goal is to review 90% of standard BLAs in 10 months after FDA accepts the BLA for filing, and 90% of priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Orphan drug designation

Under the Orphan Drug Act, FDA may designate a biologic product as an “orphan drug” if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biologic product available in the United States for treatment of the disease or condition will be recovered from sales of the product). Orphan product designation must be requested before submitting a BLA. After FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by FDA. Orphan product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, meaning that FDA may not approve any other applications to market the same drug or biologic product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if the party holding the exclusivity fails to assure the availability of sufficient quantities of the drug to meet the needs of patients with the disease or condition for which the drug was designated. Competitors, however, may receive approval of different products for the same indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan medicinal product status in the European Union has similar, but not identical, benefits.

Expedited development and review programs

FDA is authorized to expedite the review of BLAs in several ways. Under the Fast Track program, the sponsor of a biologic product candidate may request FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Biologic products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with FDA, FDA may initiate review of sections of a Fast Track BLA before the application is complete, a process known as rolling review.

Any product submitted to FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- **Breakthrough therapy designation**. To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives: intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and rolling review.
• **Priority review**. A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious condition compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

• **Accelerated approval**. Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well-controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

Fast Track designation, breakthrough therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Finally, with passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy (which may include a cell therapy) that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

**Post-approval requirements**

Rigorous and extensive FDA regulation of biologic products continues after approval, particularly with respect to cGMP requirements. Manufacturers are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biologic products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. If the product is subject to official release by FDA, the manufacturer submits samples of each lot of product to FDA, together with a release protocol, showing a summary of the history of manufacture of the lot and the results of all tests performed on the lot. FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution. In addition, FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biologic products.

A sponsor also must comply with FDA’s advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product’s approved labeling (known as “off-label use”), industry-sponsored scientific and educational activities and promotional activities involving the Internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal actions and adverse publicity. These actions could include refusal to approve pending applications or supplemental applications, withdrawal of an approval, clinical hold, suspension or termination of clinical trial by an IRB, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines or other monetary penalties, refusals of government contracts, mandated corrective advertising or communications to healthcare professionals or patients, debarment, restitution, disgorgement of profits or other civil or criminal penalties.

**U.S. patent term restoration and marketing exclusivity**

Depending upon the timing, duration and specifics of FDA approval of product candidates, some of a sponsor’s U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of
1984. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. The patent term restoration period generally is one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biologic product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with FDA, reviews and approves the application for any patent term extension or restoration.

Pediatric exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States that, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to FDA’s request, the additional protection is granted. If reports of requested pediatric studies are submitted to, and accepted by, FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection that cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which FDA cannot accept or approve a biosimilar application.

Biosimilars and exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or PPACA, created an abbreviated approval pathway for biologic products shown to be similar to, or interchangeable with, an FDA-licensed reference biologic product, referred to as biosimilars. For FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. An application for a biosimilar product may not be submitted to FDA until four years following approval of the reference product, and it may not be approved until 12 years thereafter. These exclusivity provisions only apply to biosimilars—companies that rely on their own data and file a full BLA may be approved earlier than 12 years. We currently plan to rely on our own data and to file a full BLA for all of our current and future products.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increasing funding for FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes for four years the priority review voucher program for certain drugs intended to treat rare pediatric diseases; creates a new priority review voucher program for drug applications determined to be material threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved drugs; provides a new “limited population” approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

FDA approval of companion diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its
corresponding therapeutic should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product’s labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. FDA has not indicated that it would require a companion diagnostic with LUXTURNA.

**Government regulation outside of the United States**

In addition to regulations in the United States, sponsors are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of biologic products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not a sponsor obtains FDA approval for a product, a sponsor must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, much like the IND, prior to the commencement of human clinical trials. In the European Union, for example, a request for a Clinical Trial Authorization, or CTA, must be submitted to the competent regulatory authorities and the competent Ethics Committees in the European Union Member States in which the clinical trial takes place, much like FDA and the IRB, respectively. Once the CTA request is approved in accordance with the European Union and the European Union Member State’s requirements, clinical trial development may proceed.

The requirements and processes governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Failure to comply with applicable foreign regulatory requirements may result in, among other things, fines, suspension, variation or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

**European Union regulation and exclusivity**

To obtain regulatory approval of an investigational biologic product under European Union regulatory systems, applicants must submit a marketing authorization application, or MAA. The grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to EMA which provides an opinion regarding the application for marketing authorization. European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Innovative medicinal products are authorized in the European Union based on a full marketing authorization application (as opposed to an application for marketing authorization that relies on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain the results of pharmaceutical tests, preclinical tests and clinical trials conducted with the medicinal product for which marketing authorization is sought. Innovative medicinal products for which marketing authorization is granted are entitled to eight years of data exclusivity. During this period, applicants for approval of generics or biosimilars of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product to support their application. Innovative medicinal products for which marketing authorization is granted are also entitled to 10 years of market exclusivity. During these 10 years of market exclusivity, no generic or biosimilar medicinal product may be placed on the European Union market even if a generic or biosimilar marketing authorization can be submitted to the competent regulatory authorities in the European Union Member States. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company, nevertheless, could also market another
competing medicinal product for the same therapeutic indication if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Products receiving orphan designation in the European Union can receive 10 years of market exclusivity. During this 10-year period, the competent authorities of the European Union Member States and European Commission may not accept applications or grant marketing authorization for other similar medicinal product for the same orphan indication. There are, however, three exceptions to this principle. Marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- The second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- The holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- The holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

An orphan product can also obtain an additional two years of market exclusivity in the European Union for the conduct of pediatric trials. The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity.

The criteria for designating an “orphan medicinal product” in the European Union are similar, in principle, to those in the United States. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan medicinal product designation must be submitted before the application for marketing authorization. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which is set to replace the current Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive. The new Clinical Trials Regulation will become applicable no earlier than October 2018. Until the Clinical Trials Regulation will become applicable, all clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive, which will be repealed on the day of entry into application of the Clinical Trial Regulation. It will however still apply three years from that day to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opted for old system. The Clinical Trial Regulation will overhaul the current system of approvals for clinical trials in the EU. Specifically, the legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the legislation provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications.

Other healthcare laws and regulations

Healthcare professionals, physicians and third-party payers play a primary role in the recommendation and use of pharmaceutical products that are granted marketing approval. Arrangements with third-party payers, existing or potential customers and referral sources are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, and these laws and regulations may constrain the business or financial arrangements and relationships through which manufacturers market, sell and distribute the products for which they obtain marketing approval. Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, in exchange for, or to induce, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers on the other. The PPACA amends the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;
- the federal False Claims Act or FCA, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payers
that are false or fraudulent. Federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, also may implicate the FCA;

• federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

• the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians, other healthcare professionals and teaching hospitals, and ownership and investment interests held by physicians and other healthcare professionals and their immediate family members;

• HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

• HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

• state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to: items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare professionals and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare professionals or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Violation of any of the laws described above or any other governmental laws and regulations may result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly for manufacturers of branded prescription products.

Coverage and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and markets in other countries, sales of any product candidates for which regulatory approval for commercial sale is obtained will depend in part on the availability of coverage and reimbursement from third-party payers. Third-party payers include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all FDA-approved drugs for a particular indication. Moreover, a payer’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. New metrics frequently are used as the basis for reimbursement rates, such as Average Selling Price, or ASP, Average Manufacturing Price, or AMP and Actual Acquisition Cost. To obtain coverage and reimbursement for any product that might be approved for sale, it may be necessary to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost-effectiveness of the products, in addition to the costs required to obtain regulatory approvals. If third-party payers do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. Health Technology Assessment, or HTA, which is intended to take account of medical, social, economic and ethical issues when determining the suitability of a medicinal product for reimbursement is increasingly become an element of the pricing and reimbursement decisions of the competent authorities in European Union Member States.
The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the PPACA contains provisions that may reduce the profitability of drug products, including, for example, increasing the minimum rebates owed by manufacturers under the Medicaid Drug Rebate Program, extending the rebate program to individuals enrolled in Medicaid managed care plans, addressing a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected and establishing annual fees based on pharmaceutical companies’ share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

With the new Administration and Congress, there likely will be additional legislative changes, including repeal and replacement of certain provisions of the PPACA. To that end, on January 20, 2017, President Trump issued an Executive Order Minimizing the Economic Burden of the PPACA Repeal. The Executive Order declares that, pending repeal of the PPACA, it is imperative for the executive branch to ensure that the law is being efficiently implemented, take all actions consistent with law to minimize the unwarranted economic and regulatory burdens of the PPACA and prepare to provide the states more flexibility and control to create a more free and open healthcare market. The Order directs the Secretary of Health and Human Services and the heads of all other executive departments and agencies with authorities and responsibilities under the PPACA to exercise their authority and discretion to waive, defer, grant exemptions from or delay the implementation of any provision or requirement of the PPACA that would impose a fiscal burden on any state or a cost, fee, tax, penalty or regulatory burden on individuals, families, healthcare professionals, health insurers, patients, recipients of healthcare services, purchasers of health insurance or makers of medical devices, products or medications.

With respect to repeal of the Affordable Care Act and its replacement with new legislation, it is unclear when such legislation will be enacted, what it will provide and what impact it will have on the availability of healthcare and containing or lowering the costs of healthcare.

Additional regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biologic, chemical and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in third countries that impose similar obligations.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business abroad or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

Employees

As of February 22, 2018, we had 315 full-time employees, including a total of 62 employees with M.D. or Ph.D. degrees. Of our workforce, 80 employees are engaged in research and development, 91 employees are engaged in technical operations and manufacturing, 20 employees are engaged in medical affairs, 45 employees are engaged in commercial and 79 employees are engaged in corporate functions, including finance, IT, legal, human resources and general operations and management. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 28,000 square feet of office, laboratory and manufacturing space in Philadelphia, Pennsylvania, under a lease that expires in 2025, with our option for early termination in 2021. We also occupy approximately 14,000 square feet of office space in Philadelphia, Pennsylvania under a sublease that expires in November 2018. In February 2016, we entered into a lease for approximately 6,500 square feet of additional office space in Philadelphia for corporate and commercial purposes that expires in 2021.
In November 2016, we entered into a lease agreement for approximately 50,000 square feet of office space in Philadelphia, Pennsylvania, that commenced on April 1, 2017. In February 2017, we amended the lease to include approximately 25,000 additional square feet of office space that commenced on January 1, 2018. In November 2017, we amended this lease to accelerate the termination date of approximately 50,000 square feet of office space, with such termination to occur, at the latest, in December 2022.

In November 2017, we entered into a lease in Philadelphia, Pennsylvania for approximately 108,000 square feet of office and laboratory space through June 2033.

We lease approximately 5,400 square feet of office space in Waltham, Massachusetts, which expires in March 2022.

Corporate information

We were incorporated in the State of Delaware on March 13, 2013. Our principal executive offices are located at 3737 Market Street Suite 1300 Philadelphia, Pennsylvania, and our telephone number is (888) 772-7560.

Our corporate website address is www.sparktx.com. Our website is an inactive textual reference and nothing on our website is incorporated by reference in this Annual report. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. The Securities and Exchange Commission maintains an internet site that contains our public filings with the Securities and Exchange Commission and other information regarding our company, at www.sec.gov. These reports and other information concerning our company may also be accessed at the Securities and Exchange Commission’s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the Securities and Exchange Commission at 1-800-SEC-0330. The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

Legal proceedings

We are not currently a party to any material legal proceedings.
Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 5 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks related to our financial position

We have incurred net losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred net losses. Our net losses were $123.7 million and $253.5 million for the years ended December 31, 2016 and 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $505.9 million. We have financed our operations primarily through private placements of our preferred stock, our initial public offering, or IPO, which closed on February 4, 2015, and follow-on offerings which closed on December 21, 2015, June 20, 2016 and August 9, 2017. We received net proceeds from the IPO and follow-on offerings of $775.8 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have devoted substantially all our efforts to research and development, including clinical and preclinical development of our product candidates, as well as to building our team and engaging in activities to prepare for commercial launch of LUXTURNA. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

• commercially launch LUXTURNA in the United States and seek regulatory approval for LUXTURNA in the European Union, or the EU;
• seek marketing approvals for any of our product candidates that successfully complete clinical trials;
• continue to grow a marketing and distribution infrastructure to commercialize LUXTURNA in the United States, and any product candidates for which we may submit for and obtain marketing approval anywhere in the world;
• continue our clinical development of our product candidates, including our Phase 1/2 clinical trials for SPK-7001, SPK-9001 and SPK-8011;
• conduct IND-enabling studies for our preclinical programs;
• initiate additional preclinical studies and clinical trials for our product candidates;
• seek to identify additional product candidates;
• build out additional laboratory and cGMP manufacturing capacity;
• further develop our gene therapy platform;
• further expand our medical affairs activities;
• maintain, expand and protect our intellectual property portfolio; and
• acquire or in-license product candidates and technologies.

LUXTURNA is our only product that has been approved for sale and, to date, it only has been approved in the United States for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy who have viable retinal cells as determined by their treating physicians. Our ability to generate revenue will depend on the success of commercial sales of LUXTURNA. However, the successful commercialization of LUXTURNA in the United States is subject to many risks. LUXTURNA is our first commercial launch, and there is no guarantee that we will be able to do so successfully. There are numerous examples of unsuccessful launches where products fail to meet expectations of market potential, including those by pharmaceutical companies with more experience and resources than us. We do not anticipate our revenue from sales of LUXTURNA alone will be sufficient for us to become profitable.

To become and remain profitable, we must develop and commercialize additional product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that
are significant enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause our stockholders to lose all or part of their investment.

**We have never generated revenue from product sales and may never be profitable.**

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully develop and commercialize products.

While we expect to begin generating revenue from the sale of LUXTURNA in 2018, we do not expect to achieve profitability unless and until we complete the development of, and obtain the regulatory approvals necessary to commercialize, additional product candidates. Our ability to generate revenues from product sales and achieve profitability depends heavily on our, or our collaborators’, success in:

- executing the commercial launch of LUXTURNA;
- maintaining regulatory and marketing approval for LUXTURNA in the United States;
- obtaining regulatory and marketing approval for LUXTURNA in the EU;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- completing research and preclinical and clinical development of our product candidates and identifying new gene therapy product candidates;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by expanding our existing sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for, and maintaining, adequate coverage and reimbursement by government and third-party payers on a timely basis for LUXTURNA and any product candidates for which we obtain marketing approval;
- maintaining and enhancing a sustainable, scalable, reproducible and transferable manufacturing process;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development of our product candidates and the market demand for LUXTURNA and any product candidates for which we obtain marketing approval;
- identifying patients eligible for treatment with LUXTURNA for RPE65-mediated IRD;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party interference or infringement claims; and
- attracting, hiring and retaining qualified personnel.

We anticipate incurring significant costs associated with commercializing LUXTURNA in the United States and any other products for which we receive marketing approval. Even if we are able to generate revenues from sales of LUXTURNA and any other approved products, we may not become profitable and may need to obtain additional funding to continue operations.

**Our limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.**

We were founded in March 2013. Our operations to date have been limited to organizing and staff ing our company, business planning, raising capital, acquiring technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our most advanced product candidates, engaging in activities to prepare for the commercial launch
of LUXTURNA and establishing collaborations. Although we have commenced the initial phases of the commercialization of LUXTURNA, we have no history of commercializing pharmaceutical products, are still in the process of launching LUXTURNA and, to date, have not generated revenue from the sale of LUXTURNA. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history. We are in the early stages of the process of transitioning from a company with a research focus to a company that is also capable of supporting commercial activities. We may not be successful in such a transition.

We may need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our product development and commercialization efforts or other operations.

We expect our expenses to increase as we continue the research and development of, and seek marketing approval for, our product candidates. In addition, we expect to incur significant expenses related to product sales, medical affairs, diagnostics, marketing, manufacturing and distribution to support LUXTURNA and any other products for which we obtain marketing approval. Accordingly, we may need to obtain substantial additional funding for our continuing operations. If we are unable to raise capital on attractive terms, or at all, we could be forced to delay, reduce or eliminate certain of our research and development programs and/or commercialization efforts.

Our operations have consumed significant amounts of cash since inception. As of December 31, 2017, our cash and cash equivalents and marketable securities, including our equity investment in Selecta, were $540.2 million. Our research and development expenses increased from $86.4 million for the year ended December 31, 2016 to $135.2 million for the year ended December 31, 2017. We expect to incur significant operating expenses for the foreseeable future. We estimate that our cash and cash equivalents and marketable securities as of December 31, 2017, together with amounts received from Novartis in January 2018 and anticipated net revenues from the sales of LUXTURNA, will enable us to fund our operating expenses and capital expenditure requirements into 2021. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently anticipate.

Our future capital requirements will depend on many factors, including:

• the timing and our execution of our commercial launch of LUXTURNA (voretigene neparvovec) in the United States;
• the cost and our ability to maintain the commercial infrastructure and manufacturing capabilities required, including product sales, medical affairs, diagnostics, marketing, manufacturing and distribution, to support LUXTURNA in the United States, and any other products for which we receive marketing approval;
• qualifying for, and maintaining adequate coverage and reimbursement by, government and third-party payers on a timely basis for LUXTURNA and any other products for which we obtain marketing approval;
• the costs of preparing and submitting marketing approvals for any of our product candidates that successfully complete clinical trials;
• the costs and timing of manufacturing sufficient supplies of LUXTURNA to meet customer demand;
• the scope, progress, results and costs of drug discovery, recruitment, laboratory testing, preclinical development and clinical trials for our product candidates;
• the costs associated with the build out of additional laboratory and cGMP manufacturing capacity;
• the costs, timing and outcome of regulatory review of our product candidates;
• revenue, if any, received from commercial sales of LUXTURNA and any other products for which we may obtain marketing approval, including amounts reimbursed by government and third-party payers;
• the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
• our current collaboration agreements remaining in effect and our achievement of milestones and/or royalty payments under those agreements;
• our ability to establish and maintain additional collaborations on favorable terms, if at all; and
• the extent to which we acquire or in-license product candidates and technologies.
Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales for any products other than LUXTURNA. In addition, LUXTURNA or any other products for which we obtain marketing approval may not achieve commercial success. Any product revenues from product candidates, and any commercial milestones or royalty payments under our collaboration agreements will be derived from, or based on, sales of products that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. To the extent that additional capital is raised through the sale of equity or equity-linked securities, the issuance of those securities could result in substantial dilution for our current stockholders and the terms may include liquidation or other preferences that adversely affect the rights of our current stockholders. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline and existing stockholders may not agree with our financing plans or the terms of such financings. Adequate additional financing may not be available to us on acceptable terms, or at all.

**Risks related to LUXTURNA**

The commercial success of LUXTURNA depends on the extent to which patients, physicians and payers accept and adopt LUXTURNA as a treatment for inherited retinal disease, or IRD, caused by biallelic mutations in the RPE65 gene.

The commercial success of LUXTURNA depends on the extent to which patients, physicians and payers accept and adopt LUXTURNA as a treatment for inherited retinal disease, or IRD, caused by biallelic mutations in the RPE65 gene, and we do not know whether our or others’ estimates in this regard will be accurate. While we have conducted pre-commercialization activities, such as efforts to raise awareness around genetic testing and inherited retinal diseases, there is significant uncertainty in the degree of market acceptance of LUXTURNA. In addition, physicians may not prescribe LUXTURNA, and patients may be unwilling to use LUXTURNA, if coverage is not provided or reimbursement is inadequate. Additionally, the use of LUXTURNA in a non-trial setting may result in unexpected, more serious or a greater incidence of adverse reactions that may negatively affect the commercial prospects of LUXTURNA. Furthermore, a significant negative development in any other gene therapy program or our failure to satisfy any post-marketing regulatory commitments and requirements to which we are or may become subject may adversely impact the commercial results and potential of LUXTURNA. We intend to conduct a post-marketing observational study of patients treated with LUXTURNA to further evaluate the long-term safety of LUXTURNA. If the results of this long-term study negatively change the benefit/risk profile of LUXTURNA, the commercial results of LUXTURNA and potentially any other product for which we receive marketing approval, may be substantially diminished.

As part of our plan to market LUXTURNA in the United States through a limited number of centers that specialize in treating IRDs, we are training vitreoretinal surgeons to perform the surgical procedure necessary to administer LUXTURNA via sub-retinal injection. This procedure requires significant skill and training. In addition, if we are unable to recruit or train, and thereafter retain, sufficient vitreoretinal surgeons to perform the procedure properly, the availability of LUXTURNA could be substantially diminished, which would adversely affect our business, financial condition, results of operations and prospects. Our efforts to educate the medical community and third-party payers on the benefits of LUXTURNA and our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of LUXTURNA and our other potential products.

We have submitted, and had validated, a marketing authorization application, or MAA, to EMA for LUXTURNA, but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Even if a product candidate is approved, the European Commission, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. We have entered into license and commercialization agreement with Novartis for the development and commercialization of voretigene neparvovec outside of the United States. The commercial success of voretigene neparvovec outside of the United States depends on our ability to obtain approval of our MAA by EMA and Novartis’ success at commercializing voretigene neparvovec outside of the United States if and when approved. We have limited control over the amount and timing of resources that Novartis will dedicate to the commercialization of voretigene neparvovec, should it receive marketing approval.

If the RPE65-mediated IRD patient population is smaller than we estimate, our product revenues may be adversely affected and our business may suffer.

There are several factors that could contribute to making the actual number of patients who receive LUXTURNA less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions such as IRDs caused by mutations in the RPE65 gene, likely will diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. Lastly, certain patients’ immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.
If we are unable to obtain adequate coverage of LUXTURNA from third-party payers, the adoption of LUXTURNA by physicians and patients may be limited, which could affect our ability to successfully commercialize LUXTURNA.

While we have had discussions with third-party payers regarding our price for LUXTURNA, we still may receive substantial push back on our pricing of $425,000 per dose, or per eye. To assist third-party payers and patients in obtaining and covering LUXTURNA, we have proposed novel payment and distribution programs to assist with the cost of LUXTURNA, including direct sales to payers and outcomes-based rebate arrangements. Even with these programs, there may be substantial resistance to the cost of LUXTURNA by third-party payers and the public generally. Additionally, to the extent reimbursement for LUXTURNA is subject to outcomes-based rebate arrangements, we may be liable for rebate payments in the future. These novel payment programs may not be sufficient for third-party payers to grant coverage, and if we are unable to obtain adequate coverage of LUXTURNA, the adoption of LUXTURNA by physicians and patients may be limited. This in turn could affect our ability to successfully commercialize LUXTURNA and adversely impact our business, financial condition, results of operations and prospects.

Risks related to the development of our product candidates

Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval.

We have concentrated our research and development efforts on our gene therapy platform, and our future success depends on our successful development of viable gene therapy products. There can be no assurance that we will not experience problems or delays in developing new products and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. Currently, LUXTURNA is the only gene therapy product that has been approved for a genetic disease in the United States and only two such products have been approved in the EU. Although we intend to leverage our experience with LUXTURNA in our preclinical and clinical development of product candidates, we may be unable to reduce development timelines and costs for our other gene therapy development programs. We also may experience unanticipated problems or delays in expanding our manufacturing capacity, which may prevent us from completing our clinical trials, meeting the obligations of our collaborations or commercializing LUXTURNA and any other products for which we obtain marketing approval on a timely or profitable basis, if at all. We, a collaborator or another group may uncover a previously unknown risk associated with AAV, and this may prolong the period of observation required for obtaining regulatory approval or may necessitate additional clinical testing.

In addition, the clinical trial requirements of FDA, EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied product candidates. Only two gene therapy products for genetic diseases, uniQure N.V.’s Glybera and GlaxoSmithKline plc’s Strimvelis, have received marketing authorization from EMA and LUXTURNA is the only gene therapy product for a genetic disease to have received marketing approval from FDA. We do not yet know if or when it may be approved by EMA. Even if we are successful in developing additional product candidates, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for these product candidates in either the United States or the EU, or how long it will take to commercialize any other products for which we receive marketing approval. In addition, approvals by EMA may not be indicative of what FDA may require for approval and vice versa.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. FDA has established the Office of Tissue and Advanced Therapies within CBER to consolidate the review of gene therapy and related products, and has established the CTGTAC to advise CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH, also potentially are subject to review by the RAC; however, NIH announced in 2014 that the RAC will only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks. Although FDA decides whether individual gene therapy protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if FDA has reviewed the trial design and approved its initiation. Conversely, FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution, such as CHOP to conduct a clinical trial, that institution’s institutional biosafety committee as well as its IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, the European Commission may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to
Because we are developing product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, there is increased risk that certain regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results.

Except for LUXTURNA in the United States, there are no pharmacologic therapies approved to treat IRDs caused by the biallelic RPE65 gene mutations. In addition, there has been limited clinical trial experience for the development of pharmaceuticals to treat IRDs. Certain aspects of IRDs render efficacy endpoints historically used for vision clinical trials less applicable as clinical endpoints. As a result, the design and conduct of clinical trials for these disorders is subject to increased risk. In addition, the treatment of certain IRDs, such as CHM, may require assessment of clinical endpoints that reflect a stabilization, as opposed to an improvement, of functional vision. Assessing these endpoints may require longer periods of observation and may delay the completion of any trials we may undertake.

Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.

Results from preclinical studies or previous clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials.

We have limited safety and limited clinical efficacy data for the use of SPK-7001, SPK-9001 and SPK-8011 in humans. There can be no assurance that the results seen in preclinical studies for any of our product candidates ultimately will result in success in clinical trials. In addition, there can be no assurance that we will be able to achieve the same or similar success in our preclinical studies and clinical trials of our other product candidates.

There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy or requirements during the period of our product candidate development. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

We may find it difficult to enroll subjects in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and enrolling appropriate subjects to participate in clinical trials of our product candidates is critical to our success. The timing of the beginning and conclusion of clinical trials depends on our ability to recruit subjects to participate and complete clinical development programs. For example, hemophilia trials often take longer to enroll due to the availability of existing treatments. We have experienced slow enrollment in some of our prior hemophilia trials, and we may experience similar delays in any of our current or future clinical trials. Patients with the disease may be hesitant or unwilling to participate in our gene therapy studies for a variety of reasons: negative publicity from adverse events related to the biotechnology or gene therapy fields, competitive clinical trials for similar patient populations, clinical trials in products employing our vectors or our platform or for other reasons. These factors may delay the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of subjects, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Enrollment and trial completion is affected by factors including:

- size of the patient population and process for identifying subjects;
Table of Contents

- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of gene therapy-based approaches to treatment of diseases;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- availability of genetic testing for potential subjects;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

Our current product candidates are being developed to treat rare conditions. For any other product candidate that we successfully develop, we plan to seek initial marketing approvals in the United States and, subsequently, the EU. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible subjects to participate in the clinical trials required by FDA or EMA or other regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and clinical investigators;
- different standards for the conduct of clinical trials;
- absence in some countries of established groups with sufficient regulatory expertise for review of gene therapy protocols;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of subjects to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects. We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety or efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive, time consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching agreement or consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in opening clinical trial sites or obtaining required IRB or independent Ethics Committee approval at each clinical trial site;
- delays in recruiting suitable subjects to participate in our clinical trials;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, after an inspection of our clinical trial operations or trial sites or for any other reason;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with FDA GCP or applicable regulatory guidelines in the EU and other countries;
• delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
• delays in having subjects complete participation in a trial or return for post-treatment follow-up;
• clinical trial sites or subjects dropping out of a trial;
• selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
• occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
• occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; or
• changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales or to achieve regulatory and commercialization milestones or product royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product or product candidates, we may:
• be delayed in obtaining marketing approval for our product candidates, if at all;
• obtain approval for indications or patient populations that are not as broad as we intended or desired;
• obtain approval with labeling that includes significant product use or distribution restrictions or safety warnings, including contraindications, warnings or precautions;
• be subject to changes in the way the product is administered;
• be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
• have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified REMS or a similar risk mitigation strategy;
• be sued for alleged injuries caused to patients taking our products; or
• experience damage to our reputation.

Our product and product candidates and the process for administering our product and product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia and death seen in other trials using other vectors. While new recombinant vectors have been developed to reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which, while not necessarily adverse to the patient’s health, could substantially limit the effectiveness of the treatment. In previous clinical trials involving AAV vectors for gene therapy, some subjects experienced the development of a T-cell response, whereby after the vector is within the target cell, the cellular immune response system triggers the removal of transduced cells by activated T-cells. If our vectors demonstrate a similar effect, which we are unable to mitigate with immuno-suppressive regimens, we may decide or be required to halt or delay further clinical development of our product candidates and our commercial efforts could be materially and adversely affected.

In addition to any potential side effects caused by the product or product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our clinical trials could be suspended or terminated. For example, FDA placed our second open-label Phase 1 clinical trial, which we refer to as our 102 trial, on a
clinical hold temporarily when we voluntarily halted enrollment and reported a serious adverse event arising from a steroid injection given following administration of LUXTURNA to manage post-operative inflammation related to the standard vitrectomy procedure subjects undergo prior to administration of LUXTURNA. We subsequently adjusted the protocol regarding the use of local steroids and FDA released the clinical hold, allowing the trial to proceed.

If in the future we are unable to demonstrate that such adverse events were caused by the administration process or related procedures, FDA, the European Commission, EMA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

In addition, FDA could require us to adopt a REMS, and other non-US regulatory authorities could impose other specific obligations as a condition of approval to ensure that the benefits of our product candidates outweigh their risks, which could delay approval or commercial acceptance of our product candidates. A REMS may include, among other things, a communication plan to health care practitioners or patients, and elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Similar risk management programs could be imposed by EMA. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings or limitations of use in product labeling;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused by our products to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of LUXTURNA and any other products for which we receive marketing approval and could significantly harm our business, financial condition, results of operations and prospects.

We may be unable to obtain additional orphan drug designations or obtain and maintain orphan drug exclusivity for any product. If our competitors obtain orphan drug exclusivity for products that regulatory authorities determine constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, EMA’s Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the EU. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biologic product. Similar “orphan drug” designations exist in some, but not all, jurisdictions outside the EU and the United States.

Upon approval, LUXTURNA was granted orphan drug exclusivity by FDA for the treatment of IRD caused by biallelic mutations to the RPE65 gene. Pursuant to such orphan drug exclusivity in the United States, FDA is precluded, subject to certain exceptions discussed below, from approving another marketing application for a product that constitutes the same drug treating the same indication for a seven-year period, which exclusivity period can be extended by six months under certain circumstances as discussed below. Orphan drug designation does not guarantee orphan drug exclusivity and a designated orphan drug will be denied market approval if it is blocked by the orphan exclusivity of a previously approved orphan product.

LUXTURNA has received an orphan drug designation from the European Commission for the treatment of both LCA and RP due to RPE65 mutations. SPK-9001 has received both breakthrough therapy and orphan drug designation by FDA. SPK-8011 has received breakthrough therapy designation by FDA. SPK-7001 has been granted orphan drug designation by
FDA and the European Commission for the treatment of choroideremia. SPK-TPP1 has been granted orphan product designation by FDA for the treatment of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

If we request orphan drug designation for our other current or future product candidates, there can be no assurances that FDA or the European Commission will grant any of our product candidates such designation. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the EU. The exclusivity period in the United States can be extended by six months if the BLA sponsor submits pediatric data that fairly respond to a written request from FDA for such data. The exclusivity period in the EU can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we maintain orphan drug exclusivity for LUXTURNA or obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, FDA may subsequently approve another drug for the same condition if FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the EU, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

**Breakthrough therapy designation by FDA may not lead to a faster development, regulatory review or approval process and it does not increase the likelihood that any of our product candidates will receive marketing approval in the United States.**

We have received breakthrough therapy designation for SPK-9001 for the treatment of hemophilia B and SPK-8011 for the treatment of hemophilia A. We may, in the future, apply for breakthrough therapy designation for other product candidates in the United States. A breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives: (i) intensive guidance on an efficient drug development program; (ii) intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and (iii) a rolling review process whereby FDA may consider reviewing portions of a BLA before the sponsor submits the complete application. Product candidates designated as breakthrough therapies by FDA may be eligible for priority review if supported by clinical data.

Designation as a breakthrough therapy is within the discretion of FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, FDA may disagree. In any event, the receipt of a breakthrough therapy designation, or the redemption of a Rare Pediatric Disease Priority Review Voucher for a product candidate, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and, in any event, does not assure ultimate approval by FDA. In addition, even though SPK-9001 and SPK-8011 have been designated as a breakthrough therapy product candidate, FDA may later decide that either or both no longer meet the conditions for designation or decide that the time period for FDA review or approval will not be shortened.
Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions or conditions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested (such as EMA approving LUXTURNA for the treatment of patients diagnosed with LCA due to RPE65 mutations but not for the treatment of patients with RP due to RPE65 mutations or other RPE65 -mediated IRDs) or they may impose significant limitations in the form of narrow indications, contraindications or a REMS. These regulatory authorities may require warnings or precautions with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims or allow the promotional claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially and adversely affect our business, financial condition, results of operations and prospects.

Further, the regulatory authorities may require concurrent approval of a companion diagnostic device. For the product candidates we currently are developing, we believe that diagnoses based on symptoms, in conjunction with existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, or CLIA, are sufficient to diagnose patients and, with respect to LUXTURNA, have been permitted by FDA. For future product candidates, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to diagnose patients or to assure the safe and effective use of product candidates in trial subjects. FDA refers to such tests as in vitro companion diagnostic devices. On July 31, 2014, FDA announced the publication of a final guidance document describing the agency’s current thinking about the development and regulation of in vitro companion diagnostic devices. The final guidance articulates a policy position that, when safe and effective use of a therapeutic product depends on a diagnostic device, FDA generally will require approval or clearance of the diagnostic device at the same time that FDA approves the therapeutic product. The final guidance allows for two exceptions to the general rule of concurrent drug/device approval, namely, when the therapeutic product is intended to treat serious and life-threatening conditions for which no alternative exists, and when a serious safety issue arises for an approved therapeutic agent, and no FDA-cleared or FDA-approved companion diagnostic test is yet available. At this point, it is unclear how FDA will apply this policy to our current or future gene therapy product candidates. Should FDA deem genetic tests used for diagnosing patients for our therapies to be in vitro companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval of a BLA for our product candidates. In the EU, Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices will apply from 2022 and repeal the current applicable provisions. Regulation (EU) 2017/746 will impose additional obligations on us that may impact the development and authorization of our product candidates in the EU.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory oversight.

LUXTURNA, and any of our product candidates for which we obtain regulatory approval, will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates also may be subject to a REMS, or the specific obligations imposed as a condition for marketing authorization by equivalent authorities in a foreign jurisdiction, particularly by the European Commission, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, in the United States, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years, and each of our clinical trials includes a 15-year long-term follow-up phase. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with the Federal Food Drug and Cosmetic Act and implementing regulations and are subject to FDA oversight and post-marketing reporting obligations, in addition to other potentially applicable federal and state laws.

In the EU, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal
products. These laws require that promotional materials and advertising for medicinal products are consistent with the product’s Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by FDA and other regulatory authorities for compliance with current cGMP, requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements for LUXTURNA or for any other product following approval, a regulatory authority may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise demand or require the withdrawal or recall of the product from the market;
- refuse to permit the import or export of products; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects.

In addition, FDA’s policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially and adversely affect our business, financial condition, results of operations and prospects.

Both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. This includes control of compliance with cGMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third-party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with cGMP. Failure by us or by any of our third-party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial

43
In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that EMA and the competent authorities of the EU Member States have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a burdensome collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully market or commercialize our product and product candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government and public and private research institutions.

We are aware of companies focused on developing AAV gene therapies in various indications, including Adverum Biotechnologies, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., AveXis, Inc., Audentes Therapeutics Inc., BioMarin Pharmaceutical Inc., GenSight Biologics SA, Horama SAS, Lysogene SAS, MeiraGTx Limited, Nightstar Therapeutics PLC., REGENXBIO, Inc., Solid Biosciences, Inc., Ultradebnx Pharmaceuticals, Inc., uniQure N.V. and Voyager Therapeutics, Inc., as well as several companies addressing other methods for delivering or modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against LUXTURNA and any of our product candidates.

For LUXTURNA and our clinical product candidates, the main competitors include:

- **LUXTURNA.** While no other approved pharmacologic agents exist for patients with RPE65-mediated IRD, Second Sight Medical Products, Inc. has received approval from FDA and other foreign regulatory authorities for a retinal prosthesis medical device, which is being marketed to RP patients with limited or no light perception. Another retinal prosthesis medical device from Retina Implant AG has obtained a CE Certificate of Conformity from its notified body, and is similarly indicated for blinded patients. Novelion Therapeutics, Inc. (formally QLT Inc.) completed a Phase 1b clinical trial of a vitamin A derivative to treat RP and LCA. In the gene therapy space, certain companies and several academic institutions have conducted or plan to conduct clinical trials involving RPE65-based product candidates, including MeiraGTx and Horama SAS. To date, none of these organizations has completed a trial involving injection of a subject’s second eye or has initiated a Phase 3 trial.

- **SPK-CHM.** We are aware that Nightstar Therapeutics PLC is developing an AAV-based gene therapy for the treatment of choroideremia. Nightstar Therapeutics PLC has obtained orphan product designation in the United States and the European Union for this product candidate for the treatment of choroideremia and has announced plans to initiate a Phase 3 trial in the first half of 2018.

- **SPK-FIX.** Hemophilia B patients typically are treated by a variety of plasma-derived, recombinant or long-acting products that are produced by a number of companies, including Pfizer Inc., or Pfizer. Many other companies are developing gene therapies to treat hemophilia B, including Shire PLC, Sangamo BioSciences, Inc., Freeline Therapeutics and uniQure N.V.

- **SPK-FVIII.** The standard of care for moderate to severe hemophilia A is intravenously administered factor VIII protein or its derivatives. The main competitors with product candidates under development, or approved, to treat hemophilia A include BioMarin Pharmaceutical Inc., Ultradebnx Pharmaceuticals, Inc., in collaboration with Bayer HealthCare, Shire PLC, uniQure N.V., Sangamo Biosciences, Inc. in collaboration with Pfizer, Telethon Institute for Gene Therapy in collaboration with Bioverativ, Inc., Novo Nordisk A/S, Roche Holding AG, and Sanofi.
Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly or earlier than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product or product candidates uneconomical or obsolete, and we may not be successful in marketing our product or product candidates against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors’ products. The availability of our competitors’ products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Even if we obtain and maintain approval for product candidates from FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.

Approval of a product candidate in the United States by FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by FDA. Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. We have submitted, and had validated, an MAA to EMA for LUXTURNA and intend to submit for approval of our product candidates in the EU, but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Even if a product candidate is approved, FDA or the European Commission, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval.

Regulatory authorities in countries outside of the United States and the EU also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects will be adversely affected.

Risks related to the commercialization of LUXTURNA and our product candidates for which we obtain marketing approval

If we are unable to expand our market development capabilities or enter into agreements with third parties to market and sell any of our product candidates for which we obtain marketing approval, we may be unable to generate any product revenue.

To successfully commercialize any products that may result from our development programs, we need to continue to expand our market development capabilities, either on our own or with others. The development of our own market development effort is, and will continue to be, expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability.

We have entered into a collaboration with Pfizer for the development and commercialization of SPK-FI X product candidates for the treatment of hemophilia B pursuant to which Pfizer would commercialize such product candidates, and we would be eligible to receive specified milestone payments and royalties, for any product developed under the agreement. We have entered into a license and commercialization agreement with Novartis for the development and commercialization of investigational voretigene neparvovec outside the United States, and we are eligible to receive specified milestone payments and royalties pursuant to that agreement. We may enter into collaborations regarding other of our product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements.
We focus our research and product development on treatments for severe genetic and orphan diseases. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the EU and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive other potential products less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions, will likely diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. Lastly, certain patients’ immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for any of our product candidates that may be approved in the future, which would adversely affect our revenue and results of operations.

We expect that coverage and reimbursement of pharmaceutical drugs may be increasingly restricted both in the United States and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. In particular, increased public scrutiny has been placed on wholesale prices of drugs, and such prices continue to be subject to intense political and public debate in the United States and abroad. Government and private third-party payers have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments, have been made in the United States. Specifically, there have been several recent United States Congressional inquiries and proposed federal and state bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. At least seven states have passed legislation related to drug price transparency and many others have pending legislation. In addition, there have been proposals to impose federal rebates on Medicare Part D drugs, which would require federally-mandated rebates on either all drugs dispensed to Medicare Part D beneficiaries or on only those drugs dispensed to certain groups of lower income beneficiaries. In some international markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect coverage and reimbursement for medical treatment by third-party payers, which may render any products for which we obtain marketing approval not commercially viable or may adversely affect our anticipated future revenues and gross margins.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation or negative publicity related to the pricing of pharmaceutical drugs generally could restrict the amount that we are able to charge for our future products, which would adversely affect our anticipated revenue and results of operations.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

We expect the cost of a single administration of gene therapy products to be substantial. We expect that coverage and reimbursement by government and private payers will be essential for most patients to be able to afford these treatments. Accordingly, sales of any product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which the prices of such product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payers. Coverage and reimbursement by a third-party payer may depend upon several factors, including the third-party payer’s determination that use of a product is:
An HTA, of medicinal products, however, is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including the UK, France, Germany, Ireland, Italy and Sweden. HTA is the procedure...
according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU Member States. In addition, pursuant to Directive 2011/24/EU on the application of patients’ rights in cross-border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU Member States was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU Member States and in pricing and reimbursement decisions and may negatively affect price in at least some EU Member States.

**Ethical, legal and social issues related to genetic testing may reduce demand for LUXTURNA or any other gene therapy products for which we obtain marketing approval.**

We anticipate that prior to receiving certain gene therapies, patients would be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. Genetic tests for assessing a person’s likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate on the basis of genetic information, resulting in barriers to the acceptance of genetic tests by consumers. This could lead to governmental authorities restricting genetic testing or calling for limits on or regulating the use of genetic testing, particularly for diseases for which there is no known cure. Any of these scenarios could decrease demand for LUXTURNA or any other products for which we obtain marketing approval.

**The commercial success of any of our product candidates, if approved, will depend upon its degree of market acceptance by physicians, patients, third-party payers and others in the medical community.**

Even with the requisite approvals from FDA in the United States, EMA in the EU and other regulatory authorities internationally, the commercial success of any products for which we obtain marketing approval will depend, in part, on the acceptance of physicians, patients and health care payers of gene therapy products in general, and our product candidates in particular, as medically necessary, effective, safe, and cost-effective. Any product that we commercialize may not gain acceptance by physicians, patients, health care providers/payers and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of gene therapy products of any products for which we obtain marketing approval, will depend on several factors, including:

- the efficacy and safety of such product as demonstrated in clinical trials and subsequently in the market;
- the potential and perceived advantages of such product over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which such product is approved by FDA or the European Commission;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling of FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product’s approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- ethical, social and legal concerns about gene therapy that result in additional regulations restricting or prohibiting our products; and
- sufficient third-party payer coverage and reimbursement.
Even if a potential product displays a favorable benefit/risk profile in clinical trials, market acceptance of the product will not be fully known until after it is launched.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product and product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with no gene therapy product other than LUXTURNA approved for a genetic disease to date in the United States and only two gene therapy products for genetic diseases approved to date in the EU. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product and product candidates, if approved, prescribing treatments that involve the use of our product and product candidates, if approved, in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors’ products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for LUXTURNA and any other products for which we obtain marketing approval.

If we obtain approval to commercialize any of our product candidates outside of the United States, in particular in the EU, a variety of risks associated with international operations could materially adversely affect our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

Risks related to third parties

We have in the past entered, and in the future may enter, into collaborations with third parties to develop or commercialize product candidates. If these collaborations are not successful, our business could be adversely affected.

We have entered into licensing and collaboration agreements with third parties, including our collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates and our licensing and commercialization agreement with Novartis for the development and commercialization of voretigene neparvovec outside of the United States. We may enter into additional collaborations in the future. We have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our and our collaborators’ abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our collaborators have the ability to abandon research or development projects and terminate applicable agreements. Moreover, an unsuccessful outcome in any clinical trial for which our collaborator is responsible could be harmful to the public perception and prospects of our gene therapy platform.

Our global collaboration agreement with Pfizer, into which we entered in December 2014, as amended in June 2016 and as further amended in November 2017, relates to the development and commercialization of product candidates for the treatment
of hemophilia B. We entered into a supply agreement with Pfizer in February 2018 to supply Pfizer with one batch of SPK-9001 drug product. Under this collaboration, we maintain responsibility for clinical development through the completion of Phase 1/2 trials. Thereafter, Pfizer has responsibility for further clinical development, seeking regulatory approvals and commercialization.

Our licensing and commercialization agreement with Novartis, into which we entered in January 2018, relates to the development and commercialization of voretigene neparvovec outside of the United States. Under this agreement, we granted Novartis an exclusive right and license for the development and commercialization of voretigene neparvovec in humans outside of the United States. We retain responsibility for seeking regulatory approval for LUXTURNA by EMA, and Novartis is responsible for seeking regulatory approval for voretigene neparvovec outside of the United States and EU. If Novartis fails to devote sufficient financial and other resources to the future development and commercialization of voretigene neparvovec outside the United States, the development and commercialization of voretigene neparvovec outside of the United States could be delayed or could fail, which would result in a delay of receiving milestone payments or royalties with respect to voretigene neparvovec or in our not receiving milestone payments or royalties at all. Novartis has the right to terminate the license agreement at any time upon one year’s prior written notice to us. Novartis also may terminate the license agreement in the event there is an uncured material breach of our supply agreement by us, resulting in Novartis taking over manufacturing of voretigene neparvovec, or in the event we undergo a change of control. In addition, if Novartis takes over manufacturing of voretigene neparvovec because of our uncured material breach of the supply agreement, the royalties we receive under the license agreement will be reduced. If Novartis terminates our agreement at any time, because of an uncured material breach of the supply agreement or for any other reason, it would delay or prevent our further development and commercialization of voretigene neparvovec, may materially harm our business and could accelerate our need for additional capital.

We may enter into additional collaborations with third parties in the future. Our relationships with collaborators, including Pfizer and Novartis, and any future collaborations we enter in the future, may pose several risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- we may not achieve any milestones, or receive any milestone payments, under our collaborations, including milestones and/or payments that we expect to achieve or receive;
- our collaborators may not achieve sales targets and we may not receive significant royalty payments based on sales by our collaborators;
- the clinical trials conducted as part of these collaborations may not be successful;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators’ strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for clinical trials, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates developed in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of us in the business and financial communities could be adversely affected. Our collaborators are subject to similar risks with respect to product development, regulatory approval and commercialization and their business, results of operations and financial condition could be harmed should they experience any such risks, which could adversely affect our collaboration.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of several factors. If we license rights to product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

*We may not be successful in finding strategic collaborators for continuing development of certain of our product candidates or successfully commercializing or competing in the market for certain indications.*

We may seek to develop strategic partnerships for developing certain of our product candidates or commercializing certain of our products and product candidates, due to capital costs required to develop the product candidates or manufacturing constraints. We may not be successful in our efforts to establish such a strategic partnership or other alternative arrangements for our products or product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. In addition, we may be restricted under existing collaboration agreements from entering into future agreements with potential collaborators. For example, under our collaboration with Pfizer, we are subject to certain restrictions on our ability to directly or indirectly engage in certain activities relating to competing factor IX gene therapy products. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program, delay its potential commercialization, reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the
necessary development and commercialization activities, we may not be able to further develop our product candidates and our business, financial condition, results of operations and prospects may be materially and adversely affected.

**Risks related to manufacturing**

*Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs or otherwise adversely affect our business.*

We completed construction of our own manufacturing facility in 2014, and we may encounter difficulties in operating this facility. The manufacturing process we use to produce LUXTURNA and our product candidates is complex, novel and has been validated for commercial use only with respect to LUXTURNA in the United States. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our product and product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the product or product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, FDA, EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. We have experienced lot failures in the past and there is no assurance we will not experience such failures in the future. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced specialist scientific, quality control and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process or facilities also could restrict our ability to meet market demand for LUXTURNA, or any product candidates for which we may receive marketing approval, and to meet our supply obligations to Novartis. Under our supply agreement with Novartis, we have agreed to provide all of the commercial supply of LUXTURNA required by Novartis, subject to certain conditions. If we are unable to produce enough product to meet the required demand, or if the product we produce does not satisfy the quality standards set forth in the supply agreement, Novartis may be able to manufacture LUXTURNA, terminate our license agreement and/or pay reduced royalties on LUXTURNA. While we have manufactured sufficient supplies for the commercial launch of LUXTURNA in the United States, we may not be able to manufacture sufficient supplies to continue commercial sales on a long-term basis.

**Disruptions in our manufacturing process may delay or disrupt our commercialization efforts.**

Our GMP manufacturing facility was approved by FDA for the commercial manufacture of LUXTURNA in December 2017. A manufacturing authorization must also be obtained from the appropriate regulatory authorities of the EU Member States. As an approved facility, we will need to continue to ensure that all of our processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors, contract laboratories or suppliers. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

52
We may rely on CHOP and other third parties to conduct aspects of our product manufacturing, and these third parties may not perform satisfactorily.

While we expect to produce our commercial supply of LUXTURNA at our own facility, we may rely on CHOP for the production of certain of our clinical trial materials and, therefore, we can control only certain aspects of their activities. We currently have a manufacturing agreement with CHOP, which provides for continued production of product candidates for our current and future early stage clinical trials. Under certain circumstances, CHOP is entitled to terminate its arrangement with us. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on CHOP for certain manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. If CHOP does not successfully carry out its contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, or if there are disagreements between us and CHOP, we will not be able to complete, or may be delayed in completing, the preclinical studies required to support future IND submissions and the clinical trials required for approval of our product candidates. In such instances, we may need to enter into an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, which would cause additional delay or increased expense prior to the approval of our product candidates and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition to CHOP, we rely on additional third parties to manufacture ingredients of LUXTURNA and our product candidates and to perform quality testing, and reliance on these third parties entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future product candidates. Some of these events could be the basis for FDA action or action of equivalent competent authorities in foreign jurisdictions, including injunction, recall, seizure or total or partial suspension of product manufacture.

Failure to comply with ongoing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

The regulatory authorities may, at any time following approval of a product for sale, audit the manufacturing facilities for such product. If any such inspection or audit identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility. Any such remedial measures imposed upon us could materially harm our business, financial condition, results of operations and prospects.

If we fail to comply with applicable cGMP regulations, FDA and foreign regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be materially harmed.

Additionally, if supply from our facility is interrupted, there could be a significant disruption in commercial supply of LUXTURNA or any other product for which we obtain marketing approval, and in clinical supply for our product candidates. This also could affect our ability to meet our supply obligations under our agreement with Novartis. We currently do not have a backup manufacturer for commercial supply of LUXTURNA and have limited back-up manufacturing capacity for clinical trial supply for our product candidates. An alternative manufacturer would need to be qualified, through regulatory filings, which could result in further delay. The regulatory authorities also may require additional clinical trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on CHOP and other third parties to manufacture certain of our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our research and development activities, we stand to lose the protection that trade secrets offer if our third-party relationships are terminated or are otherwise disrupted.
of our gene therapy platform, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. A competitor’s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects.

Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules and adversely affect our ability to meet our supply obligations to Novartis.

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage.

Some of the raw materials and other components required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product or product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development and commercialization timelines and our business, financial condition, results of operations and prospects and could adversely affect our ability to meet our supply obligations to Novartis.

Interruptions in the supply of product or inventory loss may adversely affect our operating results and financial condition.

LUXTURNA and our product candidates are manufactured using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict government standards for the manufacture and storage of our products, subjects us to production risks. While product batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following product release. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Our product and product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product’s and product candidates’ remaining shelf-lives could be impaired or their efficacy and safety could be adversely affected, making them no longer suitable for use.

The occurrence, or suspected occurrence, of production and distribution difficulties can lead to lost inventories and, in some cases, product recalls, with consequential reputational damage and the risk of product liability. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product launches. Any interruption in the supply of finished products or the loss thereof could hinder our ability to timely distribute our products and satisfy customer demand. Any unforeseen failure in the storage of the product or loss in supply could delay our clinical trials and, with respect to LUXTURNA or any of our product candidates that may be approved, result in a loss of our market share and negatively affect our business, financial condition, results of operations and prospects.

Risks related to our business operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates based on our gene therapy platform. Research programs to identify new product candidates require substantial technical, financial and human resources. Although certain of our product candidates are currently in clinical or preclinical development, we may fail to identify other potential product candidates for clinical development for several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side
effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

**Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.**

We are dependent on members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. We do not have “key person” insurance on any of our employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel is, and will continue to be, critical to our success. There currently is a shortage of skilled individuals with substantial gene therapy experience, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

**If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.**

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources in connection with the commercial launch of LUXTURNA in the United States as well as to manage our operations, continue our research and development activities and, over the longer term, continue to build a commercial infrastructure to support commercialization of any other products for which we obtain marketing approval. Future growth would impose significant added responsibilities on members of management. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates and the commercial launch of LUXTURNA requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development, commercialization and growth goals.

**Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.**

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling
unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, is a sweeping measure intended to, among other things, expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program.

Several provisions of the law may affect us and increase certain of our costs. For example, the Medicaid rebate rate was increased and the volume of rebated drugs has been expanded to include beneficiaries in Medicaid managed care organizations. Among other things, the PPACA also expanded the 340b drug discount program (excluding orphan drugs), including the creation of new penalties for non-compliance, included a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, or “donut hole,” and imposed a new fee on certain manufacturers and importers of branded prescription drugs (excluding orphan drugs under certain conditions). The law also revised the definition of “average manufacturer price,” or AMP, for reporting purposes, which could increase the amount of the Medicaid drug rebates paid to states, and created a new Patient-Centered Outcomes Research Institute to oversee clinical effectiveness research.

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2015, will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the 115th U.S. Congress and under the Trump Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for LUXTURNA or any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

In the United States, the research, manufacturing, distribution, sale, and promotion of drugs and biologic products are subject to regulation by various federal, state, and local authorities in addition to FDA, including CMS, other divisions of the United States Department of Health and Human Services, or HHS, (e.g., the Office of Inspector General), the United States Department of Justice offices of the United States Attorney, the Federal Trade Commission and state and local governments. Our operations are directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations and equivalent provisions in other countries. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. Liability may be established under the federal Anti-
Kickback Statute without proving actual knowledge of the statute or specific intent to violate it. There are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution; however, those exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. We seek to comply with the exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient assistance programs. Violations of the Anti-Kickback Statute are subject to significant civil, criminal, and administrative penalties, including damages, fines, imprisonment, and exclusion from government-funded healthcare programs like Medicare and Medicaid;

- the federal civil False Claims Act, which prohibits any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds; or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. In recent years, several pharmaceutical and other healthcare companies have faced enforcement actions under the federal False Claims Act for allegedly submitting false or misleading pricing information to government health care programs and providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have faced enforcement actions for causing false claims to be submitted because of the company marketing a product for unapproved, and thus non-reimbursable, uses. Federal enforcement agencies also have showed increased interest in pharmaceutical companies’ product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The civil False Claims Act also permits an individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. False Claims Act liability is potentially significant because the statute provides for trebling of proved sustained damages and mandatory penalties of $10,781.40 to $21,562.80 per false claim. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may awarded in litigation proceedings. Companies may be required, however, to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Criminal prosecution is possible for making or presenting a false or fictitious or fraudulent claim to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false, fictitious, or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of, or payment for, healthcare benefits, items, or services;

- HIPAA and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers;

- numerous other federal and state laws and regulations that address privacy and data security, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act, or FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information, many of which differ from each other in significant ways, thus complicating compliance efforts;

- the federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, imposes annual reporting requirements on certain manufacturers of drugs, devices, or biologics for payments and other transfers of value, directly or indirectly, to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. A manufacturer’s failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year, and up to an aggregate of $1 million per year for “knowing failures.” Manufacturers must submit reports by the 90th day of each calendar year; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws, and state fair trade practices laws may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers. Several states also require pharmaceutical companies
to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities, including the provision of gifts, meals, or other items to certain health care providers. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our financial condition and divert the attention of our management from operating our business.

In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU Member States. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of EU Member States, such as the UK Bribery Act 2010. The UK Bribery Act applies to any company incorporated in or “carrying on business” in the UK, irrespective of where in the world the alleged bribery activity occurs, which could have implications for our interactions with physicians both in and outside of the UK. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

EU Member States, Switzerland and other countries have also adopted data protection laws and regulations, which impose significant compliance obligations. In the EU, the collection and use of personal health data is currently governed by the provisions of the EU Data Protection Directive. The EU Data Protection Directive and the national implementing legislation of the EU Member States impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. Data protection authorities from the different EU Member States may interpret the EU Data Protection Directive and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU.

Guidance on implementation and compliance practices are often updated or otherwise revised. For example, the EU Data Protection Directive prohibits the transfer of personal data to countries outside of the European Economic Area that are not considered by the European Commission to provide an adequate level of data protection. These countries include the United States.

The judgment by the Court of Justice of the European Union in the Schrems case (Case C-362/14 Maximillian Schrems v. Data Protection Commissioner) determined the safe harbor framework, which was relied upon by many United States entities as a basis for transfer of personal data from the EU to the United States, to be invalid. United States entities therefore, had only the possibility to rely on the alternate procedures for such data transfer provided in the EU Data Protection Directive.

On February 29, 2016, however, the European Commission announced an agreement with the United States Department of Commerce, or the DOC, to replace the invalidated safe harbor framework with a new “Privacy Shield”. On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the Court of Justice of the European Union in its Schrems judgment by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and the Federal Trade Commission, and making commitments on the part of public authorities regarding access to information. United States entities have been able to certify to the DOC their compliance with the privacy principles of the Privacy Shield since August 1, 2016 and rely on the Privacy Shield certification to transfer personal data from the EU to the United States.

In September 2016, the Irish privacy advocacy group Digital Rights Ireland brought an action for annulment of the European Commission decision on the adequacy of the Privacy Shield before the Court of Justice of the EU (Case T-670/16).
In October 2016, a further action for annulment was brought by three French digital rights advocacy group, La Quadrature du Net, French Data Network and the Fédération FDN (Case T-738/16). Both cases are currently pending before the European Court of Justice. If the Court of Justice of the EU invalidates the Privacy Shield, it will no longer be possible to rely on the Privacy Shield certification to transfer personal data from the EU to entities in the United States. Adherence to the Privacy Shield is not, however, mandatory. Entities based in the United States are permitted to rely either on their adherence to the Privacy Shield or on the other authorized means and procedures to transfer personal data provided by the EU Data Protection Directive.

In addition, the General EU Data Protection Regulation, or GDPR, intended to replace the current EU Data Protection Directive entered into force on May 24, 2016 and will apply from May 25, 2018. The GDPR will introduce new data protection requirements in the EU and substantial fines for breaches of the data protection rules. The GDPR will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

The GDPR will impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and using third-party processors in connection with the processing of the personal data.

Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the EU Member States may result in fines and other administrative penalties. The GDPR will introduce substantial fines for breaches of the data protection rules. Once it is enforceable, the GDPR may increase our responsibility and liability in relation to personal data that we process. To comply with the new data protection rules imposed by the GDPR we may be required to put in place additional mechanisms ensuring compliance. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

**If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, which could negatively affect our operating results and business.**

We may be subject to data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act and HIPAA), govern the collection, use, disclosure, and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions and create liability for us (which could include civil and/or criminal penalties), private litigation and/or adverse publicity that could negatively affect our operating results and business.

**If we participate in the Medicaid Drug Rebate program or other governmental pricing programs, failure to comply with reporting and payment obligations under these programs could result in additional reimbursement requirements, penalties, sanctions and fines which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.**

If we participate in the Medicaid Drug Rebate program or other governmental pricing programs with respect to LUXTURNA or any product candidate that we may commercialize, we will have certain price reporting obligations to the Medicaid Drug Rebate program, Medicare and/or other governmental pricing programs, such as state Medicaid supplemental rebate programs. If we participate in the Medicaid Drug Rebate program, we will be required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Such rebates are based on pricing data that would be reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data may include the AMP and, for certain drugs, best price, which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with any required price reporting and rebate payment obligations could negatively impact our financial results.

The PPACA made significant changes to the Medicaid Drug Rebate program, such as expanding rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well and changing the definition of AMP. The PPACA also increased the minimum Medicaid rebate, changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount at 100% of AMP. Finally, the PPACA requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the PPACA.
Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service’s 340b program in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. The 340b program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340b “ceiling price” for the manufacturer’s covered outpatient drugs. These 340b covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The PPACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts “orphan drugs” from the ceiling price requirements for these covered entities. The 340b ceiling price is calculated using a statutory formula based on AMP and the rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and, in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340b ceiling price calculation and discount requirement. Any additional future changes to the definition of AMP and the Medicaid rebate amount under the PPACA or otherwise could affect our 340b ceiling price calculations and negatively impact our results of operations.

The PPACA obligates the Secretary of the HHS to update the agreement that manufacturers must sign to participate in the 340b program to obligate a manufacturer to offer the 340b price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. The Health Resources and Services Administration, or HRSA, recently updated the agreement with participating manufacturers. The PPACA also obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340b program. On January 5, 2017, HRSA issued a final regulation regarding the calculation of the 340b ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. The effective date of the regulation has been delayed until July 1, 2018. Implementation of this final rule and the issuance of any other final regulations and guidance could affect our obligations under the 340b program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340b program to additional covered entities or would require participating manufacturers to agree to provide 340b discounted pricing on drugs used in an inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutory defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for LUXTURNA or our product candidates that achieve regulatory approval and the resulting Medicare payment rate, and could negatively impact our results of operations.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we would be obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we will be required to offer for LUXTURNA or our product candidates that achieve regulatory approval under the 340b program.

We will be liable for errors associated with our submission of pricing data if we participate in the Medicaid Drug Rebate Program. In addition to retroactive rebates and the potential for 340b program refunds, if we are found to have knowingly submitted any false price information to the government, we may be liable for civil monetary penalties in the amount of $181,071 per item of false information. If we are found to have made a misrepresentation in the reporting of our average sales price, the Medicare statute provides for civil monetary penalties of up to $13,066 for each misrepresentation for each day in which the misrepresentation was applied. Our failure to submit the required price data on a timely basis could result in a civil monetary penalty of $18,107 per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we would participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs for which we receive regulatory approval.

CMS and the HHS Office of Inspector General have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that our submissions will not be found by CMS or other governmental agencies to be incomplete or incorrect.

In order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, a manufacturer also must participate in the Department of Veterans
We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk as we commercialize LUXTURNA or any other products that we may develop. If we cannot successfully defend ourselves against claims that our product or product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for LUXTURNA and any other products that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal or reduced enrollment of clinical trial participants;
- the inability to successfully commercialize LUXTURNA and any other products that we may develop; and
- injury to our reputation and significant negative media attention.

Although we maintain product liability insurance coverage, this insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and/or commercialize an additional product. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

**If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.**

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers’ compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Moreover, pursuant to regulations issued by the DoD TRICARE Management Activity, or TRICARE, now the Defense Health Agency, or DHA, to implement Section 703 of the National Defense Authorization Act for Fiscal Year 2008, manufacturers are required to provide rebates on utilization of their innovator and single source products that are dispensed to TRICARE beneficiaries by TRICARE network retail pharmacies. The formula for determining the rebate is established in the regulations and is based on the difference between the annual Non-FAMP and the FCP (these price points are required to be calculated by us under the VHCA). The requirements under the FSS and TRICARE programs could reduce the revenue we may generate from any products that are commercialized in the future and could adversely affect our business and operating results.

**Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of LUXTURNA and any other products that we may develop.**

If we fail to comply with environmental, health and safety laws and regulations, which could materially adversely affect our business, financial condition, results of operations and prospects.61
Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product and product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in the EU, which is undergoing a continued severe economic crisis. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payers or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Third parties on which we rely and we may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. Our manufacturing facility, as well as CHOP's manufacturing facility, and substantially all of our current supply of product and product candidates, are located in Philadelphia, Pennsylvania, and we do not have any existing back-up facilities in place or plans for such back-up facilities. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our information technology systems, and those of our collaborators, contractors and consultants, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced a system failure, accident, cyber-attack or security breach that has resulted in a material interruption in our operations to date, if such an event were to occur, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed.

Risks related to our intellectual property

Our rights to develop and commercialize LUXTURNA and our product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product and product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or
commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. For example, pursuant to each of our intellectual property licenses with CHOP, Penn, Genethon, the NIH and UIRF, our licensors retain control of such activities. Therefore, we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future.

Furthermore, the research resulting in certain of our licensed patent rights and technology was funded by the United States government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to United States industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

If we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our products and technology may be adversely affected.

Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product and product candidates and manufacturing technology. Our licensors have sought and we intend to seek to protect our proprietary position by filing patent applications in the United States and abroad related to many of our novel technologies and product and product candidates that are important to our business.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, certain patents in the field of gene therapy that may have otherwise potentially provided patent protection for certain of our product and product candidates have expired or will soon expire. In some cases, the work of certain academic researchers in the gene therapy field has entered the public domain, which we believe precludes our ability to obtain patent protection for certain inventions relating to such work. As a result, we have not sought, and may be unable to seek, patent protection for SPK-CHM to treat choroideremia. Consequently, we will not be able to assert any such patents to prevent others from using our technology for, and developing and marketing competing products to treat, these indications. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

We are a party to intellectual property license agreements with CHOP, Penn and UIRF, each of which is important to our business, and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, development and commercialization timelines, milestone payments, royalties and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.
We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Even if the patent applications we license or may own in the future do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current manufacturing methods, product candidates or future methods or products, resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In each of our existing license agreements, and we expect in our future agreements, patent prosecution of our licensed technology is controlled solely by the licensor, and we are required to reimburse the licensor for their costs of patent prosecution. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. Further, in each of our license agreements we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products and minimum yearly diligence obligations in developing and commercializing the product. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

**We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.**

We currently have rights to the intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution’s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate and our business, financial condition, results of operations and prospects could suffer.

**Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.**

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we may own in the future. We rely on our outside counsel or our licensing partners to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our business.

**We may not be able to protect our intellectual property rights throughout the world.**

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. Although our license agreements with CHOP, Penn and UIRF grant us worldwide rights, certain of our in-licensed United States patent rights lack corresponding foreign patents or patent applications. For example, we license a United States patent from Penn that covers methods of treating patients with LCA due to RPE65 mutations. No patents or patent applications outside the United States corresponding to this patent were ever pursued. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.
Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Issued patents covering our product or product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If one of our licensing partners or we initiate legal proceedings against a third party to enforce a patent covering our product or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, inter partes review and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product or product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product or product candidates. Such a loss of patent protection could have a material adverse impact on our business.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell LUXTURNA and our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product and product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third-party patents relating to gene delivery to ocular cells and certain vector manufacturing methods that may relate to, and potentially could be asserted to encompass, our LUXTURNA, SPK-CHM, SPK-FIX, SPK-FVIII and SPK-TPP1 programs. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize LUXTURNA and our product candidates in our SPK-CHM, SPK-FIX, SPK-FVIII, SPK-GAA and SPK-TPP1 programs or any of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such United States patent in federal court, we would need to
overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such United States patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such United States patent. If we are found to infringe a third party’s valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product and product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys’ fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product and product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

**Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.**

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. To counter infringement or unauthorized use claims or to defend against claims of infringement can be expensive and time consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

**We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.**

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual’s current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

**Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.**

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes several significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a “first-to-invent” system to a “first-to-file” system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements
for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and “gene patents” have recently been decided by the Supreme Court of the United States, or Supreme Court. On March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., or Prometheus, a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as “administering” or “determining” steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to not patent-eligible subject matter. On June 13, 2013, the Supreme Court issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc., or Myriad, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

On March 4, 2014, the USPTO issued a guidance memorandum to patent examiners entitled “2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products.” On December 6, 2014, a memorandum entitled “2014 Interim Guidance on Subject Matter Eligibility” was published. On July 30, 2015, an update pertaining to patent subject matter eligibility was published by the USPTO. These guidelines instruct USPTO examiners on the ramifications of the Prometheus and Myriad rulings and apply the Myriad ruling to natural products and principles including all naturally occurring nucleic acids. Patents for certain of our product candidates contain claims related to specific DNA sequences that are naturally occurring and, therefore, could be the subject of future challenges made by third parties. In addition, the recent USPTO guidance could make it impossible for us to pursue similar patent claims in patent applications we may prosecute in the future.

There can be no assurance that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court’s decisions in Prometheus and Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Moreover, although the Supreme Court has held in Myriad that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

**If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.**

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of
relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. We will be seeking patent term extension on our LUXTURNA patent but there is a risk that the patent office will not approve the application. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

**If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.**

We have registered trademarks with the USPTO for the mark “SPARK” and the Spark logo and pending trademark applications in the United States and various foreign jurisdictions for marks related to our business. Whether allowed or registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks, results of operations and prospects.

**Intellectual property rights do not necessarily address all potential threats.**

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to LUXTURNA or our product candidates but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.
A significant number of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is performing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, as of [October 31, 2017], holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In January 2015, we filed a registration statement registering all shares of common stock that we may issue under our equity compensation plans. As of [February 22, 2018], we had outstanding options to purchase an aggregate of 4,095,489 shares of our common stock, of which options to purchase 1,691,141 shares were vested. These shares can be freely sold in the public market upon issuance, subject to volume limitations and black-out periods applicable to affiliates.

In addition, certain of our employees, executive officers, directors and affiliated stockholders have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer, director or affiliated stockholder. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers, directors and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to regularly publish reports on us, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is likely to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the commercial success of LUXTURNA;
- results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- commencement or termination of collaborations;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs and the commercial launch of LUXTURNA;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- negative publicity around gene therapy in general, LUXTURNA or our product candidates;
- variations in our financial results or those of companies that are perceived to be similar to us;
If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

**An active trading market for our common stock may not be sustained.**

Our shares of common stock began trading on the NASDAQ Global Select Market on January 30, 2015. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares, or at all.

**We have broad discretion in the use of our cash, cash equivalents and marketable securities and may not use them effectively.**

Our management has broad discretion in the application of our cash, cash equivalents and marketable securities and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development and commercialization of our product and product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

**We incur substantial costs as a result of operating as a public company, and our management is now required to devote substantial time to new compliance initiatives.**

As a public company, and particularly since December 31, 2016, when we ceased being an Emerging Growth Company, we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

**Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.**

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of

---

71
directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

*Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be stockholders’ sole source of gain.*

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be stockholders’ sole source of gain for the foreseeable future.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

We occupy approximately 28,000 square feet of office, laboratory and manufacturing space in Philadelphia, Pennsylvania, under a lease that expires in 2025, with our option for early termination in 2021. We also occupy approximately 14,000 square feet of office space in Philadelphia, Pennsylvania under a sublease that expires in November 2018 and approximately 6,500 square feet of additional office space in Philadelphia for corporate and commercial purposes that expires in 2021. In addition, we lease approximately 5,400 square feet of office space in Waltham, Massachusetts, which expires in March 2022.

In November 2016, we entered into an additional lease agreement for approximately 49,000 square feet of office space in Philadelphia, Pennsylvania, that commenced on April 1, 2017. In February 2017, we amended the lease to include approximately 25,000 additional square feet of office space that commenced on January 1, 2018. In November 2017, we amended this lease to accelerate the termination date of approximately 50,000 square feet of office space, with such termination to occur, at the latest, in December 2022.

In November 2017, we entered into a lease agreement for approximately 108,000 square feet in Philadelphia, Pennsylvania. The term of the lease will commence on the earliest of: (i) the date on which we first conduct business on the premises; (ii) substantial completion of certain leasehold improvements; and (iii) June 1, 2018, and will expire on the 187-month anniversary of the commencement date.
Item 3. Legal Proceedings

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.
PART II.

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is publicly traded on the Nasdaq Global Select Market under the symbol "ONCE". The following table shows the high and low sale prices per share of our common stock as reported on the Nasdaq Global Select Market for the periods indicated:

<table>
<thead>
<tr>
<th></th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2016</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Quarter</td>
<td>$44.71</td>
<td>$21.20</td>
</tr>
<tr>
<td>Second Quarter</td>
<td>$60.05</td>
<td>$28.65</td>
</tr>
<tr>
<td>Third Quarter</td>
<td>$65.99</td>
<td>$50.52</td>
</tr>
<tr>
<td>Fourth Quarter</td>
<td>$64.43</td>
<td>$35.07</td>
</tr>
<tr>
<td><strong>2017</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First Quarter</td>
<td>$65.79</td>
<td>$50.39</td>
</tr>
<tr>
<td>Second Quarter</td>
<td>$65.00</td>
<td>$48.26</td>
</tr>
<tr>
<td>Third Quarter</td>
<td>$91.00</td>
<td>$57.00</td>
</tr>
<tr>
<td>Fourth Quarter</td>
<td>$91.75</td>
<td>$41.06</td>
</tr>
</tbody>
</table>

On February 22, 2018, the last reported sale price for our common stock on the Nasdaq Global Select Market was $54.19 per share.

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on our common stock between January 30, 2015 (the first date that shares of our common stock were publicly traded) and December 31, 2017, with the cumulative total return of (a) the Nasdaq Biotechnology Index and (b) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 after the market close on January 30, 2015 in each of our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index. The graph assumes our closing sale price on January 30, 2015 of $50.00 per share as the initial value of our common stock and not the initial offering price to the public in our initial public offering of $23.00 per share.
The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.

**Comparison of Cumulative Returns: January 30, 2015 through December 31, 2017**

---

**Holders**

As of February 22, 2018, there were approximately 40 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

**Dividends**

We have not declared or paid any cash dividends on our common stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future.

**Information about our equity compensation plans**

Information required by Item 5 of Form 10-K regarding our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

**Recent Sales of Unregistered Securities**

We did not sell any shares of our common stock or our preferred stock, or grant any stock options or restricted stock awards, during the year ended December 31, 2017 that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in a Quarterly Report on Form 10-Q.
Purchase of equity securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Use of proceeds from registered securities

On February 4, 2015, we closed our initial public offering of 8,050,000 shares of our common stock, including 1,050,000 shares of our common stock pursuant to the exercise by the underwriters of an option to purchase additional shares, at a public offering price of $23.00 per share for an aggregate offering of approximately $185.2 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-201318), which was declared effective by the SEC on January 29, 2015, and a registration statement on Form S-1 MEF (File No. 333-201764) filed pursuant to Rule 462(b) of the Securities Act. J.P. Morgan Securities LLC and Credit Suisse Securities (USA) LLC acted as joint book-running managers for the offering and as representatives of the underwriters. Cowen and Company, LLC acted as lead manager and Sanford C. Bernstein & Co., LLC acted as co-manager. The offering commenced on January 29, 2015 and did not terminate until the sale of all of the shares offered.

We received aggregate net proceeds from the offering of $168.9 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours.

As of December 31, 2017, we have used approximately $47.9 million of the net proceeds from the offering primarily to fund research and development, for working capital and for other general corporate purposes. We have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act. As of December 31, 2017, the remaining amount of the net proceeds is included as cash and cash equivalents and marketable securities.
Item 6. Selected Financial Data

The following selected financial data should be read together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this Annual Report on Form 10-K. The selected financial data below are derived from our consolidated financial statements. We have derived the statements of operations data for the period from March 13, 2013 (inception) to December 31, 2013 and for the year ended December 31, 2014 and the balance sheet data as of December 31, 2013, 2014 and 2015 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2015, 2016 and 2017 and the balance sheet data as of December 31, 2016 and 2017 from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results to be expected in any future period.

<table>
<thead>
<tr>
<th>Statement of operations data:</th>
<th>Period from March 13, 2013 (inception) to December 31, 2013</th>
<th>Year ended December 31, 2014</th>
<th>Year ended December 31, 2015</th>
<th>Year ended December 31, 2016</th>
<th>Year ended December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenues</td>
<td>$ —</td>
<td>$ 634</td>
<td>$ 22,064</td>
<td>$ 20,183</td>
<td>$ 12,066</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>4,897</td>
<td>16,351</td>
<td>46,030</td>
<td>86,380</td>
<td>135,160</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>50,000</td>
<td>750</td>
<td>—</td>
<td>11,132</td>
<td>8,604</td>
</tr>
<tr>
<td>Impairment on in-process research and development</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>15,696</td>
</tr>
<tr>
<td>General and administrative</td>
<td>2,381</td>
<td>7,863</td>
<td>23,352</td>
<td>48,070</td>
<td>111,124</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>57,278</td>
<td>24,964</td>
<td>69,382</td>
<td>145,582</td>
<td>270,584</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(57,278)</td>
<td>(24,330)</td>
<td>(47,318)</td>
<td>(125,399)</td>
<td>(258,518)</td>
</tr>
<tr>
<td>Interest income, net</td>
<td>—</td>
<td>5</td>
<td>192</td>
<td>1,747</td>
<td>4,073</td>
</tr>
<tr>
<td>Loss before income taxes</td>
<td>(57,278)</td>
<td>(24,325)</td>
<td>(47,126)</td>
<td>(123,652)</td>
<td>(254,445)</td>
</tr>
<tr>
<td>Income tax benefit</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>963</td>
</tr>
<tr>
<td>Net loss</td>
<td>(57,278)</td>
<td>(24,325)</td>
<td>(47,126)</td>
<td>(123,652)</td>
<td>(253,482)</td>
</tr>
<tr>
<td>Preferred stock dividends</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(707)</td>
<td>(635)</td>
</tr>
<tr>
<td>Net loss applicable to common stockholders</td>
<td>$ (57,278)</td>
<td>$ (25,032)</td>
<td>$ (47,761)</td>
<td>$ (123,652)</td>
<td>$ (253,482)</td>
</tr>
<tr>
<td>Basic and diluted net loss per common unit/share (1)</td>
<td>$ (8.44)</td>
<td>$ (4.64)</td>
<td>$ (2.10)</td>
<td>$ (4.29)</td>
<td>$ (7.63)</td>
</tr>
<tr>
<td>Weighted average basic and diluted common units/shares outstanding (1)</td>
<td>6,788,396</td>
<td>5,397,599</td>
<td>22,710,105</td>
<td>28,804,133</td>
<td>33,242,072</td>
</tr>
</tbody>
</table>

(1) See Note 3(1) to our audited consolidated financial statements for an explanation of the method used to calculate basic and diluted net loss per common unit/share and weighted average basic and diluted common units/shares outstanding used to calculate the per common unit/share amounts
(2) Basic and diluted net loss per common unit and weighted average basic and diluted common units outstanding for the period from March 13, 2013 (inception) to December 31, 2013 do not give effect to the one-for-five reverse stock split that became effective on January 16, 2015 as only units of Spark Therapeutics, LLC were outstanding during 2013 and the reverse split was not applicable to the units.

77
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td>$</td>
<td>$74,567</td>
<td>$293,531</td>
<td>$58,923</td>
<td>$96,748</td>
</tr>
<tr>
<td>Marketable securities</td>
<td>$</td>
<td>$</td>
<td>$</td>
<td>$259,143</td>
<td>$443,454</td>
</tr>
<tr>
<td>Working capital</td>
<td>$3,369</td>
<td>$61,509</td>
<td>$289,492</td>
<td>$284,596</td>
<td>$479,479</td>
</tr>
<tr>
<td>Total assets</td>
<td>$4,861</td>
<td>$90,446</td>
<td>$329,773</td>
<td>$373,863</td>
<td>$616,796</td>
</tr>
<tr>
<td>Total stockholders' equity</td>
<td>$3,369</td>
<td>$55,206</td>
<td>$290,538</td>
<td>$330,277</td>
<td>$513,624</td>
</tr>
</tbody>
</table>
Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth under Item 1A “Risk Factors” and under "Forward-looking statements" of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis. See “Forward-looking statements.”

Overview

We are a leader in the field of gene therapy, seeking to transform the lives of patients suffering from debilitating genetic diseases by developing potentially one-time, life-altering treatments. The goal of gene therapy is to overcome the effects of a malfunctioning, disease-causing gene. Gene therapies have the potential to provide long-lasting effects, dramatically and positively changing the lives of patients with conditions where no, or only palliative, therapies exist. We have built a pipeline of gene therapy product candidates that are directed to the retina, the liver and the central nervous system, or CNS.

In December 2017, the U.S. Food and Drug Administration, or FDA, approved LUXTURN™ (voretigene neparvovec-rzyl) for the treatment of patients with viable retinal cells and confirmed biallelic RPE65 mutation-associated retinal dystrophy, a genetic blinding condition caused by mutations in the RPE65 gene. LUXTURN™ is the first FDA-approved gene therapy for a genetic disease, the first and only pharmacological treatment for an inherited retinal disease, or IRD, and the first adeno-associated virus, or AAV, vector gene therapy approved in the United States. LUXTURN™ will be manufactured at our manufacturing facility located in Philadelphia, which is the first licensed manufacturing facility in the United States for a gene therapy treating an inherited disease. LUXTURN™ has received orphan product designation and, upon approval, we received a rare pediatric disease priority review voucher. In January 2018, we entered into a license and commercialization agreement with Novartis Pharma AG, or Novartis, for the development and commercialization of investigational voretigene neparvovec outside the United States.

We are supporting the appropriate use of LUXTURN™ in the United States through small, targeted commercial and medical affairs groups to build and promote access to the product. LUXTURN™ will be administered by leading retinal surgeons at selected treatment centers in the United States that specialize in treating IRDs. In January 2018, we announced two novel payer programs to help ensure eligible patients in the United States have access to LUXTURN™: (i) an innovative contracting model; and (ii) an outcomes-based rebate arrangement with a short-term efficacy measure and a long-term durability measure.

Our clinical pipeline includes: (i) an ocular program consisting of SPK-7001, our product candidate targeting choroideremia, or CHM, currently in a Phase 1/2 clinical trial, and (ii) our hemophilia programs consisting of SPK-9001, our lead product candidate in the SPK-FIX program for hemophilia B, and SPK-8011, our lead product candidate in the SPK-FVIII program for hemophilia A, both currently in Phase 1/2 clinical trials. We retain global rights to all of our clinical-stage product candidates other than SPK-FIX product candidates, which we licensed to Pfizer, Inc., or Pfizer.

SPK-7001 is our lead product candidate for the treatment of CHM, an IRD caused by mutations in the REP-1 gene. We have completed enrollment of ten participants in two dose cohorts of our Phase 1/2 trial for SPK-7001 and continue to follow subjects in the trial. In July 2017, we completed enrollment of five additional subjects in the trial who are at an earlier stage of disease. To date, SPK-7001 has been well tolerated and we have not observed any product candidate-related serious adverse events, or SAEs, in this trial. We have received orphan product designation for SPK-7001 for the treatment of CHM in both the United States and the European Union.

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B. In July 2016, FDA granted breakthrough therapy designation to SPK-9001, the lead product candidate in our SPK-FIX program.

Throughout 2017, Pfizer and we provided periodic updates at medical meetings on the progress of the ongoing Phase 1/2 trial of SPK-9001. Most recently, in December 2017 at the American Society of Hematology, or ASH, Annual Meeting, we presented interim data, as of the November 29, 2017 cutoff date, that the annualized bleeding rate for the eleven trial subjects had been reduced by 97% and the annualized infusion rate had been reduced by 99%. No participants developed factor IX inhibitors and no SAEs or thromboembolic events have been reported. In February 2018, we entered into a supply agreement with Pfizer for production of one batch of SPK-9001 drug substance.

In our SPK-FVIII program for the treatment of hemophilia A, we initiated a dose-escalating Phase 1/2 clinical trial for our lead product candidate, SPK-8011, in 2017. In February 2018, FDA granted breakthrough therapy designation to SPK-8011. We retain global commercialization rights to the SPK-FVIII program.
In December 2017 at the ASH Annual Meeting, we presented interim data, as of the December 6, 2017 cutoff date, on the first four participants in the Phase 1/2 clinical trial, each of whom had been followed for at least 12 weeks and received a single administration of SPK-8011 at an initial dose of 5 x 10^11 or 1 x 10^12 vector genomes (vg)/kg body weight. The annualized bleeding rate for the four trial participants had been reduced by approximately 98%. No participants developed factor IX inhibitors and no SAEs or thromboembolic events have been reported.

We have several product candidates in various stages of preclinical development. The RPE65 and CHM genes are two of more than 220 genes that have been identified to cause IRDs. We have several preclinical programs targeting other IRDs. We are developing other liver-directed gene therapies, including SPK-GAA for Pompe disease, an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen in cells. We are developing neurodegenerative disease product candidates that are intended to address TPP1 deficiency, which is a form of Batten disease, and Huntington's disease, among others. We have received orphan product designation in the United States for SPK-TPP1 for the treatment of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

We have never been profitable and have incurred net losses since inception. We have an accumulated deficit of $505.9 million as of December 31, 2017. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative expenses associated with our operations. For the years ended December 31, 2016 and 2017, we incurred $86.4 million and $135.2 million of research and development expenses, respectively, and $48.1 million and $111.1 million of general and administrative expenses, respectively.

We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, hire additional personnel and initiate commercialization of approved products, including LUXTURNA. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate revenues from the sale of any commercial products, we may not become profitable. If we fail to become profitable, or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Through December 31, 2017, we have received aggregate net proceeds from sales of our equity securities, after deducting underwriting discounts and commissions and other offering expenses payable by us, of $858.2 million.

- On February 4, 2015, we completed our initial public offering, or IPO, of 8,050,000 shares of common stock, inclusive of 1,050,000 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering, at a price to the public of $23.00 per share. The aggregate net proceeds received by us were $168.9 million, net of underwriting discounts and commissions and offering expenses.

- On December 28, 2015, we closed a follow-on offering of 2,266,995 shares of common stock at a price to the public of $47.00 per share with net proceeds received by us of $99.4 million, net of underwriting discounts and commissions and offering expenses.

- On June 20, 2016, we closed a follow-on offering of 3,025,000 shares of common stock at a price to the public of $45.00 per share with net proceeds received by us of $135.2 million, net of underwriting discounts and commissions and offering expenses.

- On August 9, 2017, we closed a follow-on offering of 5,296,053 shares of common stock at a price to the public of $76.00 per share with net proceeds received by us of $379.9 million, net of underwriting discounts and commissions and offering expenses.

Financial operations overview

Revenue

To date, we have not generated any revenues from product sales. Our revenues have been derived from collaboration agreements.

In March 2014, we entered into a development and manufacturing agreement with Genable Technologies Ltd, or Genable, in which we were the exclusive manufacturer and provided development advice and expertise in the ongoing development of Genable’s lead therapeutic product candidate, RhoNova, to treat rhodopsin-linked autosomal dominant retinitis pigmentosa, or RP, or RHO-adRP. RHO-adRP is an IRD that is a genetic subtype of RP that results in severe vision loss and often blindness. Under the agreement, we granted Genable a license to certain AAV vector manufacturing patents. During the year ended December 31, 2015, we recognized $0.9 million of revenue from Genable. In March 2016, we acquired Genable. See Note 6 in our Notes to Consolidated Financial Statements for more information.
In April 2014, we entered into discussions with a pharmaceutical company concerning a potential manufacturing technology agreement. We received a one-time, nonrefundable payment of $1.0 million for engaging in due diligence. We concluded discussions on a potential arrangement with the pharmaceutical company in the first quarter of 2015 and, as a result, we recognized the nonrefundable payment of $1.0 million as revenue in the year ended December 31, 2015.

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of product candidates in our SPK-FIX program for the treatment of hemophilia B. Under this collaboration, we maintain responsibility for the clinical development of SPK-FIX product candidates through the completion of Phase 1/2 trials. Thereafter, Pfizer has responsibility for further clinical development, regulatory approvals and commercialization. In connection with entering into this agreement, we received a $20.0 million upfront payment. In November 2017, we amended our global collaboration agreement with Pfizer. Under the terms of this amendment, we received a $10.0 million payment upon execution and are eligible to receive an additional $15.0 million. During the years ended December 31, 2015, 2016 and 2017, we recognized $20.2 million, $20.2 million and $12.1 million of revenue, respectively, from this agreement and, as of December 31, 2017, there was $12.0 million of current deferred revenue included on our consolidated balance sheet.

Our ability to generate product revenue and become profitable depends upon our ability to successfully commercialize products.

Research and development expenses

Research and development expenses consist primarily of internal and external costs incurred for the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits, travel and other compensation expenses, including stock-based compensation;
- expenses incurred under our agreements with contract research organizations, or CROs, and clinical sites that will conduct our preclinical studies and clinical trials and the cost of clinical consultants;
- costs associated with regulatory filings;
- costs of laboratory supplies and the acquiring, developing and manufacturing of preclinical and clinical study materials; and
- costs of facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs for the portion of our facilities related to research and development.

Research and development costs are expensed as incurred. Expenses for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided by our vendors and our clinical sites.

We plan to increase our research and development expenses for the foreseeable future as we continue development of our product candidates. Our current and planned research and development activities include the following:

- proposed regulatory submissions and certain pre-launch activities for LUXTURNA through our approval date in December 2017;
- expanding our medical affairs group;
- clinical trials to evaluate the safety and efficacy of SPK-FIX product candidates, which are in development in collaboration with Pfizer;
- the Phase 1/2 clinical trials for SPK-CHM and SPK-8011;
- research and development for additional product candidates addressing other IRDs;
- research and development for our preclinical programs; and
- continued acquisition and manufacture of clinical trial materials in support of our clinical trials.

The successful development of our product candidates is highly uncertain and subject to numerous risks including, but not limited to:

- the scope, rate of progress and expense of our research and development activities;
- clinical trial results;
- the scope, terms and timing of regulatory approvals;
• the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
• the cost, timing and our ability to manufacture sufficient clinical and commercial supplies for any product candidates and products that we may develop; and
• the risks disclosed in the section entitled “Risk Factors” in this Annual Report on Form 10-K.

A change in the outcome of any of these variables could mean a significant change in the expenses and timing associated with the development of any product candidate.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses, for our employees in executive, operational, finance, legal, business development, commercial and human resource functions. Other general and administrative expenses include facility-related costs, professional fees for directors, accounting and legal services, consultants and expenses associated with obtaining and maintaining patents.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and the commercialization of our approved products. We also anticipate increases in expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance as a public company, director and officer insurance premiums and investor relations costs. With the approval of our first product, LUXTURNA, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to sales and marketing.

Income taxes

From inception through May 1, 2014, we were a limited liability company for federal and state tax purposes and, therefore, all items of income or loss through May 1, 2014 flowed through to the members of the limited liability company. Effective May 2, 2014, we converted from a limited liability company to a C corporation for federal and state income tax purposes. Accordingly, prior to the conversion to the C corporation, we did not record deferred tax assets or liabilities or have any net operating loss carryforwards. At December 31, 2016 and 2017, we concluded that a full valuation allowance is necessary for our deferred tax assets.

Critical accounting policies and significant judgments and estimates

Management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reporting amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be the most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue recognition

Our recognized revenues to date are primarily from our Pfizer agreement. We account for revenue arrangements that contain multiple deliverables in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, Revenue Recognition: Multiple-Element Arrangements, which addresses the determination of whether an arrangement involving multiple deliverables contains more than one unit of accounting. A delivered item within an arrangement is considered a separate unit of accounting only if both of the following criteria are met:

• the delivered item has value to the customer on a stand-alone basis; and
• if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in control of the vendor.

Under FASB ASC Topic 605-25, if both of the criteria above are not met, then separate accounting for the individual deliverables is not appropriate. Revenue recognition for arrangements with multiple deliverables constituting a single unit of accounting is recognized generally over the greater of the term of the arrangement or the expected period of performance, either on a straight-line basis or on a modified proportional performance method.
Non-refundable license fees are recognized as revenue when we have a contractual right to receive such payments, the contract price is fixed or determinable, the collection of the receivable is reasonably assured and we have no future performance obligations under the license agreement.

We will account for milestones related to research and development activities under collaboration agreements in accordance with FASB ASC Topic 605-28, Revenue Recognition: Milestone Method. FASB ASC Topic 605-28 allows for the recognition of consideration which is contingent on the achievement of a substantive milestone, in its entirety, in the period the milestone is achieved. A milestone is considered to be substantive if all of the following criteria are met: the milestone is commensurate with either (1) the performance required to achieve the milestone or (2) the enhancement of the value of the delivered items resulting from the performance required to achieve the milestone; the milestone relates solely to past performance; and the milestone payment is reasonable relative to all of the deliverables and payment terms within the agreement.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue on our consolidated balance sheet. Amounts expected to be recognized as revenue in the next twelve months following the balance sheet date are classified as current liabilities.

Research and development costs and expenses

Research and development costs are expensed as incurred. We recognize costs for certain development activities based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites. We determine accrual estimates based on estimates of the services received and efforts expended that take into account discussion with applicable personnel and service providers as to the progress or state of completion of trials. Our clinical trial accrued and prepaid assets are dependent, in part, upon the receipt of timely and accurate reporting from CROs and other third-party vendors. Although we do not expect our estimates to differ materially from amounts we actually incur, our understanding of the status and timing of services or relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low for any particular period. When contracts for outside research or testing require advance payment, they are recorded on the consolidated balance sheet as prepaid items and expensed when the service is provided or reaches a specific milestone outlined in the contract.

Impairment of goodwill and indefinite-lived intangible assets

As a result of the Genable acquisition, we are required to review, on an annual basis, the carrying value of goodwill and indefinite-lived intangible assets to determine whether impairment may exist. For goodwill, the two-step goodwill impairment test consists of the following steps. The first step compares a reporting unit’s fair value to its carrying amount to identify potential goodwill impairment. If the carrying amount of a reporting unit exceeds the reporting unit’s fair value, the second step of the impairment test must be completed to measure the amount of the reporting unit’s goodwill impairment loss, if any. Step two requires an assignment of the reporting unit’s fair value to the reporting unit’s assets and liabilities to determine the implied fair value of the reporting unit’s goodwill. The implied fair value of the reporting unit’s goodwill is then compared with the carrying amount of the reporting unit’s goodwill to determine the goodwill impairment loss to be recognized, if any. The impairment test for indefinite-lived intangible assets is a one-step test, which compares the fair value of the intangible asset to its carrying value. If the carrying value exceeds its fair value, an impairment loss is recognized in an amount equal to the excess. Based on accounting standards, it is required that these assets be assessed at least annually for impairment unless a triggering event occurs between annual assessments which would then require an assessment in the period in which a triggering event occurred.

Stock-based compensation

We issue stock-based awards to employees and non-employees, generally in the form of stock options. We account for our stock-based awards in accordance with FASB ASC Topic 718, Compensation-Stock Compensation, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statements of operations based on their fair values. We account for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, Equity-Based Payments to Non-Employees, which requires the fair value of the award to be remeasured at fair value as the award vests.

Our stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which generally is the vesting term. Compensation expense related to awards to non-employees with service-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which generally is the vesting term, using the accelerated attribution method. Compensation expense related to awards to non-employees with performance-based vesting conditions is recognized based on the then-current fair value at each financial
reporting date prior to the measurement date over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

Described below is the methodology we have utilized in measuring stock-based compensation expense. Following the consummation of our IPO, stock option values have been determined based on the quoted market price for our common stock.

We use the Black-Scholes option-pricing model to value our stock options. Use of this valuation methodology requires management to apply judgment and make estimates, including:

- the volatility of our common stock;
- the expected term of our stock options;
- the risk-free rate for a period that approximates the expected term of our stock options;
- the expected dividend yield; and
- the fair value of our common stock on date of grant.

As a privately held company prior to January 2015 with a limited operating history, we used comparable public companies to estimate our expected stock price volatility. We selected companies from the biopharmaceutical industry with similar characteristics to ours including technology, enterprise value, risk profile, position within the industry and with historical price information sufficient to meet the expected life of our stock-based awards. We intend to continue to consistently apply this process using comparable companies until a sufficient amount of historical information regarding the volatility of our own share price becomes available. The expected term is based on the simplified method provided by SEC guidance. We use the simplified method as prescribed by SEC Staff Accounting Bulletin, or SAB, No. 107, Stock-based Payment, to calculate the expected term of stock option grants to employees, as we do not have sufficient history to provide a reasonable basis upon which to make an estimate. The risk-free interest rate is based on the U.S. Treasury yield curve with a remaining term equal to the expected life assumed at grant. We utilize a dividend yield of zero, based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future.

We historically have granted restricted stock and stock options at exercise prices not less than the fair value of our common stock. As there was no public market for our common stock prior to January 2015, the estimated fair value of our common stock had been determined contemporaneously by our board of directors utilizing independent third-party valuations prepared in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation.

We performed contemporaneous valuations of our common stock concurrently with the achievement of significant milestones or with major financing events as of October 14, 2013, April 15, 2014, May 23, 2014, October 30, 2014 and December 1, 2014. In conducting these valuation analyses, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including external market conditions affecting the biotechnology industry sector and the prices at which we sold shares of preferred stock, the superior rights and preferences of securities senior to our common stock at the time of each grant and the likelihood of achieving a liquidity event.
Results of operations

Comparison of the years ended December 31, 2015 and 2016

<table>
<thead>
<tr>
<th>Year ended December 31,</th>
<th>2015 (in thousands)</th>
<th>2016 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenues</td>
<td>$22,064</td>
<td>$20,183</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>46,030</td>
<td>86,380</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>—</td>
<td>11,132</td>
</tr>
<tr>
<td>General and administrative</td>
<td>23,352</td>
<td>48,070</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>69,382</td>
<td>145,582</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(47,318)</td>
<td>(125,399)</td>
</tr>
<tr>
<td>Interest income</td>
<td>192</td>
<td>1,747</td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (47,126)</td>
<td>$ (123,652)</td>
</tr>
</tbody>
</table>

Revenues

In the year ended December 31, 2015, we recognized $22.1 million of revenue, of which $20.2 million was associated with our Pfizer agreement, and included a $15.0 million milestone payment. The other revenue we recognized was $1.0 million of a non-refundable payment after we concluded discussions on a potential agreement with a pharmaceutical company and $0.9 million in revenue associated with our Genable agreement. In the year ended December 31, 2016, we recognized $20.2 million in revenue, all of which was associated with our Pfizer agreement, including a $15.0 million milestone payment.

Research and development expenses

Our research and development expenses for the year ended December 31, 2015 were $46.0 million and for the year ended December 31, 2016 were $86.4 million. The $40.4 million increase was due to a $30.1 million increase in internal research and development expenses, due to increased effort and headcount in research, technical operations and manufacturing, medical affairs, diagnostics, quality assurance and quality control and an increase of $10.3 million in external research and development expenses, primarily from an increase of $5.6 million in expenses related to LUXTURNA and $6.3 million related to our other product candidates, offset by a decrease of $1.6 million associated with our SPK-CHM and SPK-FIX programs.

The following table summarizes our research and development expenses by product candidate or program for the years ended December 31, 2015 and 2016:

<table>
<thead>
<tr>
<th>Year ended December 31,</th>
<th>2015 (in thousands)</th>
<th>2016 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>External research and development expenses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUXTURNA</td>
<td>$5,096</td>
<td>$10,703</td>
</tr>
<tr>
<td>SPK-CHM</td>
<td>2,162</td>
<td>1,328</td>
</tr>
<tr>
<td>SPK-FIX</td>
<td>2,513</td>
<td>1,692</td>
</tr>
<tr>
<td>Other product candidates</td>
<td>4,286</td>
<td>10,584</td>
</tr>
<tr>
<td>Total external research and development expenses</td>
<td>14,057</td>
<td>24,307</td>
</tr>
<tr>
<td>Total internal research and development expenses</td>
<td>31,973</td>
<td>62,073</td>
</tr>
<tr>
<td>Total research and development expenses</td>
<td>$46,030</td>
<td>$86,380</td>
</tr>
</tbody>
</table>

We do not allocate personnel-related costs, including stock-based compensation, costs associated with broad technology platform improvements or other indirect costs, to specific programs, as they are deployed across multiple projects under development and, as such, are separately classified as internal research and development expenses in the table above.

Acquired in-process research and development expense

Our acquired in-process research and development expense for the year ended December 31, 2015 was zero. Our acquired in-process research and development expense for the year ended December 31, 2016 was $11.1 million. This amount
represents payments related to a license agreement and a portion of stock purchase, entered into with Selecta Biosciences, Inc., or Selecta, that provides us with exclusive worldwide rights to Selecta’s proprietary Synthetic Vaccine Particles, or SVP™, platform technology for co-administration with gene therapy targets. We recognized this amount as acquired-in-process research and development because additional research and development efforts and marketing approval are required in order to commercialize the licensed technology.

**General and administrative expenses**

Our general and administrative expenses for the year ended December 31, 2015 were $23.4 million and for the year ended December 31, 2016 were $48.1 million. General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, legal and patent costs and other professional fees. The $24.7 million increase was due to an increase of $15.2 million in salaries and related costs, including stock-based compensation, due to increased headcount, and an increase of $9.5 million in launch preparation activities for LUXTURNA, legal and patent expenses, professional fees and other operating costs.

**Comparison of the years ended December 31, 2016 and 2017**

<table>
<thead>
<tr>
<th></th>
<th>Year ended December 31,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2017</td>
</tr>
<tr>
<td></td>
<td>(in thousands)</td>
<td></td>
</tr>
<tr>
<td>Revenues</td>
<td>$ 20,183</td>
<td>$ 12,066</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>86,380</td>
<td>135,160</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>11,132</td>
<td>8,604</td>
</tr>
<tr>
<td>Impairment of acquired in-process research and development</td>
<td>—</td>
<td>15,696</td>
</tr>
<tr>
<td>General and administrative</td>
<td>48,070</td>
<td>111,124</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>145,582</td>
<td>270,584</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(125,399)</td>
<td>(258,518)</td>
</tr>
<tr>
<td>Interest income, net</td>
<td>1,747</td>
<td>4,073</td>
</tr>
<tr>
<td>Loss before income taxes</td>
<td>(123,652)</td>
<td>(254,445)</td>
</tr>
<tr>
<td>Income tax benefit</td>
<td>—</td>
<td>963</td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (123,652)</td>
<td>$ (253,482)</td>
</tr>
</tbody>
</table>

**Revenues**

In the year ended December 31, 2016, we recognized $20.2 million of revenue, all of which was associated with our Pfizer agreement, including a $15.0 million milestone payment. In the year ended December 31, 2017, we recognized $12.1 million in revenue, all of which was associated with our Pfizer agreement.

**Research and development expenses**

Our research and development expenses for the year ended December 31, 2016 were $86.4 million and for the year ended December 31, 2017 were $135.2 million. The $48.8 million increase was due to a $40.4 million increase in internal research and development expenses, due to increased effort and headcount in research, technical operations and manufacturing, diagnostics, quality assurance and quality control and an increase of $8.4 million in external research and development expenses. The increase in external research and development was primarily from an increase of $4.4 million in expenses related to our SPK-FVIII program, $1.9 million in our SPK-CHM and SPK-FIX programs, $1.5 million related to our other programs in preclinical development and a $0.6 million increase in expenses related to LUXTURNA.
The following table summarizes our research and development expenses by product candidate or program for the years ended December 31, 2016 and 2017:

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUXTURNA</td>
<td>$10,703</td>
<td>$11,258</td>
</tr>
<tr>
<td>SPK-CHM</td>
<td>$1,328</td>
<td>$2,240</td>
</tr>
<tr>
<td>SPK-FIX</td>
<td>$1,692</td>
<td>$2,731</td>
</tr>
<tr>
<td>SPK-FVIII</td>
<td>$3,268</td>
<td>$7,694</td>
</tr>
<tr>
<td>Other product candidates</td>
<td>$7,316</td>
<td>$8,784</td>
</tr>
<tr>
<td><strong>Total external research and development expenses</strong></td>
<td><strong>24,307</strong></td>
<td><strong>32,707</strong></td>
</tr>
<tr>
<td><strong>Total internal research and development expenses</strong></td>
<td><strong>62,073</strong></td>
<td><strong>102,453</strong></td>
</tr>
<tr>
<td><strong>Total research and development expenses</strong></td>
<td><strong>$86,380</strong></td>
<td><strong>$135,160</strong></td>
</tr>
</tbody>
</table>

We do not allocate personnel-related costs, including stock-based compensation, costs associated with broad technology platform improvements or other indirect costs, to specific programs, as they are deployed across multiple projects under development and, as such, are separately classified as internal research and development expenses in the table above.

**Acquired in-process research and development expense**

We recognize acquired-in-process research and development expense for licensed technologies because of the additional research and development efforts and marketing approval required for commercialization. Our acquired in-process research and development expense for the year ended December 31, 2016 was $11.1 million. Our acquired in-process research and development expense for the year ended December 31, 2017 was $8.6 million. This amount includes $6.9 million of expense related to payments made in connection with a license agreement entered into with Selecta that provides us with exclusive worldwide rights to Selecta’s proprietary SVP platform technology for co-administration with gene therapy targets.

**Impairment of acquired in-process research and development expense**

During the year ended December 31, 2017, it was determined that we would no longer pursue product candidates utilizing the technology acquired from Genable in March 2016 and, accordingly, we recorded a non-cash impairment charge of $15.7 million. Additionally, we recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the acquired in-process research and development during the year ended December 31, 2017.

**General and administrative expenses**

Our general and administrative expenses for the year ended December 31, 2016 were $48.1 million and for the year ended December 31, 2017 were $111.1 million. General and administrative expenses consisted primarily of salaries and related costs, including stock-based compensation, legal and patent costs, professional fees and other operating costs. The $63.0 million increase primarily was due to an increase of $27.8 million in salaries and related costs, including stock-based compensation, due to increased headcount, an increase of $11.9 million in launch preparation activities for LUXTURNA and $14.7 million in legal and patent expenses, professional fees and other operating costs. It also includes an increase in facility-related costs of $8.6 million, primarily driven by $6.9 million of expense related to an early termination of one of our leases that was amended in November 2017.
Liquidity and capital resources

The following table sets forth the primary sources and uses of cash and cash equivalents for each period set forth below:

<table>
<thead>
<tr>
<th>Year ended December 31,</th>
<th>2015 (in thousands)</th>
<th>2016 (in thousands)</th>
<th>2017 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net cash provided by (used in):</td>
<td>$47,478</td>
<td>$80,442</td>
<td>$154,536</td>
</tr>
<tr>
<td>Operating activities</td>
<td>$47,478</td>
<td>$80,442</td>
<td>$154,536</td>
</tr>
<tr>
<td>Investing activities</td>
<td>(4,522)</td>
<td>(285,520)</td>
<td>(207,732)</td>
</tr>
<tr>
<td>Finishing activities</td>
<td>270,964</td>
<td>131,367</td>
<td>400,274</td>
</tr>
<tr>
<td>Net cash provided by (used in):</td>
<td>$218,964</td>
<td>$ (234,607)</td>
<td>$37,825</td>
</tr>
</tbody>
</table>

Effect of exchange rate changes on cash and cash equivalents

The net cash used in operating activities was $47.5 million for the year ended December 31, 2015, and consisted of a net loss of $47.1 million adjusted for non-cash items, including depreciation and amortization expense of $1.7 million, stock-based compensation expense of $13.6 million, non-cash rent expense of $0.2 million and a net change in operating assets and liabilities of $15.8 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $6.6 million, of which $5.2 million is related to our Pfizer agreement, $1.0 million is related to the non-refundable payment received for engaging in due diligence with a potential manufacturing technology partner and $0.4 million is related to our Genable agreement, and an increase of $9.1 million in accounts payable and accrued expenses and an increase of $16.7 million in other receivables, primarily due to the $15.0 million milestone earned from Pfizer in December 2015.

The net cash used in operating activities was $80.4 million for the year ended December 31, 2016, and consisted of a net loss of $123.7 million adjusted for non-cash items, including depreciation and amortization expense of $3.6 million, acquired in-process research and development of $11.1 million, stock-based compensation expense of $24.5 million, non-cash rent income of $0.5 million and a net change in operating assets and liabilities of $4.3 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $5.2 million, all of which is related to our Pfizer agreement, and an increase of $10.0 million in accounts payable and accrued expenses mainly due to an increase in accruals related to bonus and other related salary accruals as a result of increased headcount, and an increase of $0.5 million in prepaid expenses and other assets and other receivables.

The net cash used in operating activities was $154.5 million for the year ended December 31, 2017, and consisted of a net loss of $253.5 million adjusted for non-cash items and other adjustments, including a $15.7 million impairment charge on our acquired in-process research and development associated with our Genable acquisition in March 2016 and a non-cash income tax benefit for the reversal of the deferred tax liability associated with the impairment of $1.0 million. Other adjustments include an $8.6 million charge for acquired in-process research and development, which included additional payments and equity investments related to our collaboration agreement with Selecta, depreciation and amortization expense of $4.9 million, stock-based compensation expense of $41.4 million and non-cash rent expense of $0.5 million. Net cash used in operating activities also included a net change in operating assets and liabilities of $30.1 million. The significant items in the change in operating assets and liabilities include a decrease in other receivables of $8.9 million, primarily driven by a $15.0 million payment received on our Pfizer receivable, and an increase of $3.2 million in prepaid expenses and other assets as a result of prepayments related to preclinical and clinical expenses. The significant items in the change in operating liabilities include an increase in accounts payable and accrued expenses of $13.0 million, mainly due to an increase in accruals related to bonus and other related salary accruals as a result of increased headcount. The change in operating liabilities also includes an increase in deferred rent of $1.6 million related to tenant improvement allowances, an increase in deferred revenue of $2.9 million due to an amendment to our Pfizer agreement executed in November 2017, and an increase in other liabilities of $6.8 million due to a lease termination liability related to the November 2017 amendment to one of our leases.

Net cash used in investing activities

Net cash used in investing activities for the year ended December 31, 2015 was $4.5 million, consisting of costs related to the purchase of property and equipment. Net cash used in investing activities for the year ended December 31, 2016 was $285.5 million, consisting of net purchases of marketable securities of $259.9 million and $11.1 million for the investment in the Selecta License Agreement.
entered into in December 2016. In addition, $8.5 million was used for costs related to the purchase of property and equipment and $5.9 million of cash consideration for the acquisition of Genable, net of cash acquired.

Net cash used in investing activities for the year ended December 31, 2017 was $207.7 million, consisting of net purchases of marketable securities of $189.9 million, purchases of property and equipment of $9.6 million and payments related to our license agreements of $8.2 million.

Net cash provided by financing activities

Net cash provided by financing activities for the year ended December 31, 2015 was $271.0 million, consisting of $270.4 million of proceeds from the issuance of common stock in our IPO that closed in February 2015 and our follow-on offering that closed in December 2015, net of expenses paid and $1.1 million from the exercise of stock options during the year. This was partially offset by our repurchase of stock for tax withholding obligations on restricted stock that vested during 2015.

Net cash provided by financing activities for the year ended December 31, 2016 was $131.4 million, which consisted of $127.6 million of net proceeds from our follow-on public offering in June 2016, $2.6 million in proceeds from the exercise of stock options, $1.6 million in proceeds from long-term debt and $0.3 million in proceeds from the issuance of common stock under our employee stock purchase plan, offset by expenses of $0.7 million paid in the first quarter of 2016 related to our follow-on offering in December 2015 and payments on long-term debt.

Net cash provided by financing activities for the year ended December 31, 2017 was $400.3 million, which consisted of $379.9 million of net proceeds from our follow-on public offering in August 2017, $20.7 million from the exercise of stock options and $0.6 million of proceeds from the issuance of common stock under our employee stock purchase plan, offset by $0.7 million for our repurchase of stock for tax withholding obligations on restricted stock that vested during 2017 and $0.3 million in payments of long-term debt.

Funding requirements

We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we prepare for commercialization of LUXTURNA, continue research and development, continue and initiate clinical trials and seek regulatory approvals for our product candidates.

The expected use of our cash, cash equivalents and marketable securities of $540.2 million as of December 31, 2017 represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development programs, the status of, and results from, clinical trials, the potential need to conduct additional clinical trials to obtain approval of our product candidates for all intended indications, the timing and outcome of regulatory filings and actions, commercialization of approved products, as well as any technology acquisitions or additional collaborations into which we may enter with third parties for our product candidates and any unforeseen cash needs. As a result, our management retains broad discretion over the allocation of our existing cash and cash equivalents and marketable securities.

Based on our planned use of our cash and cash equivalents and marketable securities, we estimate that such funds will be sufficient to enable us to commercialize LUXTURNA, complete our Phase 1/2 trials for SPK-7001, SPK-9001 and SPK-8011, advance certain of our other pipeline product candidates and fund our operating expenses and capital expenditure requirements into 2021. The foregoing estimate does not contemplate the receipt of any milestone payments under our collaboration with Pfizer. Moreover, we have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Contractual obligations

The following table summarizes our contractual obligations as of December 31, 2017:

<table>
<thead>
<tr>
<th>Payments due by period (in thousands)</th>
<th>Total</th>
<th>Less than 1 year</th>
<th>1-3 years</th>
<th>3-5 years</th>
<th>More than 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating leases (1)</td>
<td>$ 95,591</td>
<td>$ 5,520</td>
<td>$ 14,975</td>
<td>$ 16,199</td>
<td>$ 58,897</td>
</tr>
<tr>
<td>Long-term debt obligations</td>
<td>1,224</td>
<td>312</td>
<td>655</td>
<td>257</td>
<td>—</td>
</tr>
<tr>
<td>Total (2)</td>
<td>$ 96,815</td>
<td>$ 5,832</td>
<td>$ 15,630</td>
<td>$ 16,456</td>
<td>$ 58,897</td>
</tr>
</tbody>
</table>

(1) Operating lease obligations reflect our obligation to make payments in connection with leases for our corporate headquarters and our office in Waltham, Massachusetts.
This table does not include: (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty; (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known with certainty; and (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

Off-balance sheet arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Recent accounting pronouncements

In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, Leases. ASU 2016-02 requires that lease arrangements longer than 12 months result in an entity recognizing an asset and liability. ASU 2016-02 is effective for interim and annual periods beginning after December 15, 2018, and early adoption is permitted. We are currently evaluating the impact of the updated guidance on our consolidated financial statements.

In May 2014, the FASB issued a new standard regarding the accounting for, and disclosures of, revenue recognition, with an effective date for annual and interim periods beginning after December 15, 2017. The new standard provides a single comprehensive model for accounting for revenue from contracts with customers. The model requires that revenue recognized reflect the actual consideration to which the entity expects to be entitled in exchange for the goods or services defined in the contract, including in situations with multiple performance obligations. The allowable adoption methods are the full retrospective method, which requires the standard to be applied to each prior period presented, or the modified retrospective method which requires the cumulative effect of adoption to be recognized as an adjustment to opening retained earnings in the period of adoption. We will adopt this guidance using the modified retrospective method and the adoption will have no cumulative adjustment to our consolidated financial statements as it relates to the Pfizer collaboration agreement discussed in note 14 in the notes to consolidated financial statements.

In January 2016, the FASB issued ASU No. 2016-01, Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities. ASU 2016-01 changes accounting for equity investments, financial liabilities under the fair value option, and presentation and disclosure requirements for financial instruments. ASU 2016-01 does not apply to equity investments in consolidated subsidiaries or those accounted for under the equity method of accounting. In addition, the FASB clarified guidance related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. Equity investments with readily determinable fair values will be measured at fair value with changes in fair value recognized in net income. Companies have the option to either measure equity investments without readily determinable fair values at fair value or at cost, adjusted for changes in observable prices, minus impairment. Changes in measurement under either alternative will be recognized in net income. Companies that elect the fair value option for financial liabilities must recognize changes in fair value related to instrument-specific credit risk in other comprehensive income (OCI). Companies must assess valuation allowances for deferred tax assets related to available-for-sale debt securities in combination with their other deferred tax assets. ASU 2016-01 will be effective beginning the first quarter of 2018. We are currently evaluating the impact of the updated guidance on our consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2017, we had cash and cash equivalents and marketable securities, including our investment in Selecta, of $540.2 million, primarily invested in U.S. government agency and corporate securities, cash and money market accounts. We have policies requiring us to invest in the securities of high-quality issuers, limit our exposure to any individual issuer and ensure adequate liquidity. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 100 basis points from levels at December 31, 2017, the net fair value of our marketable securities would have resulted in a hypothetical decline of approximately $2.9 million.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-26 of this Annual Report of Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.
Item 9A. Controls and Procedures

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed in a company's reports is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed in a company's reports is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms.

Based on the evaluation of ours disclosure controls and procedures as of December 31, 2017, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. However, because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, our management used the criteria set forth in the Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2017 based on those criteria.

Our independent registered public accounting firm, which has audited the consolidated financial statements included in this Annual Report on Form 10-K, has also issued an audit report on the effectiveness of our internal control over financial reporting as of December 31, 2017. Their report appears on page F-2 of this Annual Report on Form 10-K.

Changes in internal control over financial reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

91
PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.


The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accountant Fees and Services

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.
Table of Contents

PART IV

Item 15. Exhibits, Financial Statement Schedules

The consolidated financial statements listed in the Index to the Financial Statements beginning on page F-1 are filed as part of this Annual Report on Form 10-K.

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our consolidated financial statements or notes thereto.
### Table of Contents

The following is a list of the Company's Exhibits:

<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Description of Exhibit</th>
<th>Form</th>
<th>File Number</th>
<th>Date of Filing</th>
<th>Exhibit Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>Restated Certificate of Incorporation of the Registrant</td>
<td>8-K</td>
<td>001-36819</td>
<td>2/6/2015</td>
<td>3.1</td>
</tr>
<tr>
<td>3.2</td>
<td>Amended and Restated By-Laws of the Registrant</td>
<td>8-K</td>
<td>001-36819</td>
<td>2/6/2015</td>
<td>3.2</td>
</tr>
<tr>
<td>4.1</td>
<td>Specimen Stock Certificate evidencing the shares of common stock</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>4.1</td>
</tr>
<tr>
<td>4.2</td>
<td>Investors’ Rights Agreement dated as of May 23, 2014</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>4.2</td>
</tr>
<tr>
<td>10.1+</td>
<td>2014 Stock Incentive Plan</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.1</td>
</tr>
<tr>
<td>10.2+</td>
<td>Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.2</td>
</tr>
<tr>
<td>10.3+</td>
<td>Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.3</td>
</tr>
<tr>
<td>10.4+</td>
<td>Form of Restricted Stock Agreement under 2014 Stock Incentive</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.4</td>
</tr>
<tr>
<td>10.5+</td>
<td>2015 Stock Incentive Plan</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.5</td>
</tr>
<tr>
<td>10.6+</td>
<td>Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.6</td>
</tr>
<tr>
<td>10.7+</td>
<td>Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.7</td>
</tr>
<tr>
<td>10.8+</td>
<td>2015 Employee Stock Purchase Plan</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.8</td>
</tr>
<tr>
<td>10.9†</td>
<td>License Agreement dated October 14, 2013 between the Registrant and The Children’s Hospital of Philadelphia, as amended</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.9</td>
</tr>
<tr>
<td>10.10†</td>
<td>Technology Assignment Agreement dated October 14, 2013 between the Registrant and The Children’s Hospital of Philadelphia</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.10</td>
</tr>
<tr>
<td>10.11†</td>
<td>Master Research Services Agreement dated October 14, 2013 between the Registrant and The Children’s Hospital of Philadelphia</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.11</td>
</tr>
<tr>
<td>10.13†</td>
<td>License Agreement dated October 14, 2013 between the Registrant and the University of Iowa Research Foundation, as amended</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.13</td>
</tr>
<tr>
<td>10.14†</td>
<td>Patent License Agreement dated October 14, 2013 between the Registrant and The Trustees of the University of Pennsylvania</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.14</td>
</tr>
<tr>
<td>10.15†</td>
<td>License Agreement dated December 6, 2014 between the Registrant and Pfizer Inc.</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.18</td>
</tr>
<tr>
<td>Exhibit Number</td>
<td>Description of Exhibit</td>
<td>Form</td>
<td>File Number</td>
<td>Date of Filing</td>
<td>Exhibit Number</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------------------------------------------------------------------------------</td>
<td>------</td>
<td>-------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>10.16†</td>
<td>Lease Agreement, dated as of March 31, 2014, between the Registrant and Wexford-UCSC 3737, LLC</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.19</td>
</tr>
<tr>
<td>10.17+</td>
<td>Common Share Membership Agreement between the Registrant and Katherine A. High</td>
<td>S-1</td>
<td>333-201318</td>
<td>12/30/2014</td>
<td>10.21</td>
</tr>
<tr>
<td>10.18+</td>
<td>Employment Agreement between the Registrant and Jeffrey D. Marrazzo</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.21</td>
</tr>
<tr>
<td>10.19+</td>
<td>Form of Indemnification Agreement between the Registrant and each of the executive officers and directors</td>
<td>S-1/A</td>
<td>333-201318</td>
<td>1/20/2015</td>
<td>10.26</td>
</tr>
<tr>
<td>10.20†</td>
<td>Amendment No. 2, dated March 23, 2015 to License Agreement dated October 14, 2013 between the Registrant and the University of Iowa Research Foundation, as amended</td>
<td>10-Q</td>
<td>001-36819</td>
<td>5/11/2015</td>
<td>10.1</td>
</tr>
<tr>
<td>10.21</td>
<td>Amendment No. 1 dated August 5, 2015 to the Services Agreement dated December 26, 2013 between the Registrant and the Children's Hospital of Philadelphia</td>
<td>10-Q</td>
<td>001-36819</td>
<td>11/6/2015</td>
<td>10.1</td>
</tr>
<tr>
<td>10.22†</td>
<td>Amendment No. 4 dated October 8, 2015 to the License Agreement dated October 14, 2013 between the Registrant and the Children's Hospital of Philadelphia</td>
<td>10-Q</td>
<td>001-36819</td>
<td>11/6/2015</td>
<td>10.2</td>
</tr>
<tr>
<td>10.23†</td>
<td>License Agreement dated November 23, 2015 between the Registrant and the The Children's Hospital of Philadelphia</td>
<td>8-K</td>
<td>001-36819</td>
<td>11/23/2015</td>
<td>99.1</td>
</tr>
<tr>
<td>10.24†</td>
<td>Amended and Restated Patent License Agreement dated December 31, 2015, between the Registrant and The Trustees of the University of Pennsylvania</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.31</td>
</tr>
<tr>
<td>10.25+</td>
<td>Amendment, dated January 5, 2016 to the Employment Agreement between the Registrant and Jeffrey D. Marrazzo</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.32</td>
</tr>
<tr>
<td>10.26†</td>
<td>Amendment No. 3, dated January 6, 2016 to License Agreement dated October 14, 2013 between the Registrant and the University of Iowa Research Foundation</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.33</td>
</tr>
<tr>
<td>10.27†</td>
<td>Amendment No. 1, dated March 10, 2016 to Master Research Services Agreement dated October 14, 2013 between the Registrant and The Children's Hospital of Philadelphia</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.34</td>
</tr>
<tr>
<td>10.28</td>
<td>Lease Agreement, dated as of February 1, 2016, between the Registrant and Wexford-UCSC II, LP</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.35</td>
</tr>
<tr>
<td>10.29†</td>
<td>Amendment dated March 10, 2016, to the License Agreement dated November 23, 2015 between the Registrant and The Children's Hospital of Philadelphia</td>
<td>10-K</td>
<td>001-36819</td>
<td>3/14/2016</td>
<td>10.36</td>
</tr>
<tr>
<td>10.30†</td>
<td>Amendment No. 1, dated June 9, 2016, to the License Agreement dated December 6, 2014 between the Registrant and Pfizer</td>
<td>10-Q</td>
<td>001-36819</td>
<td>8/10/2016</td>
<td>10.1</td>
</tr>
</tbody>
</table>

95
<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Description of Exhibit</th>
<th>Form</th>
<th>File Number</th>
<th>Date of Filing</th>
<th>Exhibit Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.31+</td>
<td>Form of Employment Agreement for Executive Officer</td>
<td>10-Q</td>
<td>001-36819</td>
<td>8/10/2016</td>
<td>10.2</td>
</tr>
<tr>
<td>10.32†</td>
<td>License and Option Agreement, dated December 2, 2016 between the Registrant and Selecta Biosciences, Inc.</td>
<td>10-K</td>
<td>001-36819</td>
<td>2/28/2017</td>
<td>10.32</td>
</tr>
<tr>
<td>10.33†</td>
<td>Letter Agreement, dated June 6, 2017, amending the License and Option Agreement dated December 2, 2016 between the Registrant and Selecta Biosciences, Inc.</td>
<td>10-Q</td>
<td>001-36819</td>
<td>8/2/2017</td>
<td>10.1</td>
</tr>
<tr>
<td>10.34</td>
<td>Lease Agreement, dated as of November 20, 2017, between the Registrant and Brandywine 3025 Market, LP</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>10.35††</td>
<td>Amendment No. 2, dated November 6, 2017, to the License Agreement dated December 6, 2014 between the Registrant and Pfizer</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>10.36††</td>
<td>Supply Agreement, dated January 24, 2018, between the Registrant and Novartis Pharma AG</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>10.37††</td>
<td>License and Commercialization Agreement dated January 24, 2018 between the Registrant and Novartis Pharma AG</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>21.1</td>
<td>Subsidiaries of the Registrant</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>23.1</td>
<td>Consent of KPMG LLP</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>31.1</td>
<td>Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>31.2</td>
<td>Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>32.1</td>
<td>Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>32.2</td>
<td>Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
† Confidential treatment has been granted as to certain portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

†† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

97
None.
<table>
<thead>
<tr>
<th>Audited consolidated financial statements</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report of Independent Registered Public Accounting Firm</td>
<td>F-2</td>
</tr>
<tr>
<td>Consolidated Balance Sheets as of December 31, 2016 and December 31, 2017</td>
<td>F-4</td>
</tr>
<tr>
<td>Consolidated Statements of Operations and Comprehensive Income (Loss) for the Years Ended December 31, 2015, 2016 and 2017</td>
<td>F-5</td>
</tr>
<tr>
<td>Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2015, 2016 and 2017</td>
<td>F-5</td>
</tr>
<tr>
<td>Consolidated Statements of Cash Flows for the Years Ended December 31, 2015, 2016 and 2017</td>
<td>F-7</td>
</tr>
<tr>
<td>Notes to Consolidated Financial Statements</td>
<td>F-9</td>
</tr>
</tbody>
</table>
Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Spark Therapeutics, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Spark Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2016 and 2017, the related consolidated statements of operations and comprehensive income (loss), stockholders’ equity, and cash flows for each of the years in the three-year period ended December 31, 2017, and the related notes (collectively, the consolidated financial statements). We also have audited the Company’s internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2016 and 2017, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company’s management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management’s report on internal control over financial reporting. Our responsibility is to express an opinion on the Company’s consolidated financial statements and an opinion on the Company’s internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company’s assets that could have a material effect on the financial statements.
Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ KPMG LLP

We have served as the Company's auditor since 2014.

Philadelphia, Pennsylvania
February 27, 2018
<table>
<thead>
<tr>
<th><strong>Assets</strong></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td>$58,923,097</td>
<td>$96,748,444</td>
</tr>
<tr>
<td>Marketable securities</td>
<td>237,242,655</td>
<td>423,418,752</td>
</tr>
<tr>
<td>Other receivables</td>
<td>16,780,917</td>
<td>7,905,653</td>
</tr>
<tr>
<td>Prepaid expenses</td>
<td>1,647,008</td>
<td>5,092,877</td>
</tr>
<tr>
<td><strong>Total current assets</strong></td>
<td>314,593,677</td>
<td>533,165,726</td>
</tr>
<tr>
<td>Marketable securities</td>
<td>21,900,129</td>
<td>20,035,553</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>19,794,306</td>
<td>61,712,793</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>15,490,000</td>
<td>—</td>
</tr>
<tr>
<td>Goodwill</td>
<td>1,160,104</td>
<td>1,254,005</td>
</tr>
<tr>
<td>Other assets</td>
<td>924,579</td>
<td>628,235</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$373,862,795</td>
<td>$616,796,312</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Liabilities and Stockholders’ Equity</strong></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounts payable</td>
<td>$9,928,737</td>
<td>$14,182,804</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>13,826,920</td>
<td>24,697,225</td>
</tr>
<tr>
<td>Current portion of long-term debt</td>
<td>302,013</td>
<td>311,976</td>
</tr>
<tr>
<td>Current portion of deferred rent</td>
<td>771,196</td>
<td>968,534</td>
</tr>
<tr>
<td>Current portion of deferred revenue</td>
<td>5,168,674</td>
<td>11,968,915</td>
</tr>
<tr>
<td>Current other liabilities</td>
<td>—</td>
<td>1,557,062</td>
</tr>
<tr>
<td><strong>Total current liabilities</strong></td>
<td>29,997,540</td>
<td>53,686,516</td>
</tr>
<tr>
<td>Long-term debt</td>
<td>1,224,003</td>
<td>912,027</td>
</tr>
<tr>
<td>Long-term deferred rent</td>
<td>7,498,419</td>
<td>8,317,952</td>
</tr>
<tr>
<td>Long-term deferred revenue</td>
<td>3,865,885</td>
<td>—</td>
</tr>
<tr>
<td>Deferred tax liability</td>
<td>1,000,235</td>
<td>—</td>
</tr>
<tr>
<td>Other liabilities</td>
<td>—</td>
<td>40,255,605</td>
</tr>
<tr>
<td><strong>Total liabilities</strong></td>
<td>43,586,082</td>
<td>103,172,100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Stockholders’ equity:</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred stock, $0.001 par value. Authorized, 5,000,000 shares; no shares issued or outstanding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common stock, $0.001 par value. Authorized, 150,000,000 shares; 30,837,430 shares issued and 30,864,224 shares outstanding as of December 31, 2016; 37,131,626 shares issued and 37,111,404 shares outstanding as of December 31, 2017</td>
<td>30,874</td>
<td>37,132</td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td>583,973,682</td>
<td>1,026,589,507</td>
</tr>
<tr>
<td>Accumulated other comprehensive loss</td>
<td>(794,296)</td>
<td>(5,913,595)</td>
</tr>
<tr>
<td>Treasury stock, at cost, 9,206 shares as of December 31, 2016 and 20,222 shares as of December 31, 2017</td>
<td>(552,636)</td>
<td>(1,225,949)</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(252,380,911)</td>
<td>(505,862,883)</td>
</tr>
<tr>
<td><strong>Total stockholders’ equity</strong></td>
<td>330,276,713</td>
<td>513,624,212</td>
</tr>
<tr>
<td><strong>Total liabilities and stockholders’ equity</strong></td>
<td>$373,862,795</td>
<td>$616,796,312</td>
</tr>
</tbody>
</table>

See accompanying notes to consolidated financial statements.
Spark Therapeutics, Inc.
Consolidated statements of operations and comprehensive income (loss)

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenues</strong></td>
<td>$22,063,674</td>
<td>$20,182,835</td>
<td>$12,065,644</td>
</tr>
<tr>
<td><strong>Operating expenses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>46,029,314</td>
<td>86,379,405</td>
<td>135,160,047</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>—</td>
<td>11,132,146</td>
<td>8,604,258</td>
</tr>
<tr>
<td>Impairment of in-process research and development</td>
<td>—</td>
<td>—</td>
<td>15,696,017</td>
</tr>
<tr>
<td>General and administrative</td>
<td>23,352,171</td>
<td>48,070,317</td>
<td>111,123,247</td>
</tr>
<tr>
<td><strong>Total operating expenses</strong></td>
<td>$69,381,485</td>
<td>$145,581,868</td>
<td>$270,583,569</td>
</tr>
<tr>
<td><strong>Loss from operations</strong></td>
<td>(47,317,811)</td>
<td>(125,399,033)</td>
<td>(258,171,925)</td>
</tr>
<tr>
<td><strong>Interest income, net</strong></td>
<td>192,033</td>
<td>1,746,506</td>
<td>4,072,912</td>
</tr>
<tr>
<td><strong>Loss before income taxes</strong></td>
<td>(47,125,778)</td>
<td>(123,652,527)</td>
<td>(254,445,013)</td>
</tr>
<tr>
<td><strong>Income tax benefit</strong></td>
<td>—</td>
<td>—</td>
<td>963,041</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>(47,125,778)</td>
<td>(123,652,527)</td>
<td>(253,481,972)</td>
</tr>
<tr>
<td><strong>Preferred stock dividends</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net loss applicable to common stockholders</strong></td>
<td>$47,125,778</td>
<td>$123,652,527</td>
<td>$253,481,972</td>
</tr>
<tr>
<td><strong>Basic and diluted net loss per common share</strong></td>
<td>$2.10</td>
<td>$4.29</td>
<td>$7.63</td>
</tr>
<tr>
<td><strong>Weighted average basic and diluted common shares outstanding</strong></td>
<td>22,710,105</td>
<td>28,804,133</td>
<td>33,242,072</td>
</tr>
<tr>
<td><strong>Other comprehensive income (loss):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrealized loss on available-for-sale securities</td>
<td>—</td>
<td>(801,717)</td>
<td>(5,162,259)</td>
</tr>
<tr>
<td>Foreign exchange translation adjustment</td>
<td>—</td>
<td>7,421</td>
<td>42,960</td>
</tr>
<tr>
<td><strong>Total comprehensive loss</strong></td>
<td>$47,125,778</td>
<td>$124,446,823</td>
<td>$258,601,271</td>
</tr>
</tbody>
</table>

See accompanying notes to consolidated financial statements.

Spark Therapeutics, Inc.
Statement of stockholders’ equity
For the year ended December 31, 2015

<table>
<thead>
<tr>
<th>Series A convertible preferred stock</th>
<th>Series B convertible preferred stock</th>
<th>Common stock in treasury</th>
<th>Common stock</th>
<th>Additional paid-in capital</th>
<th>Accumulated deficit</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
</tr>
<tr>
<td>5,000,000</td>
<td>$10,000,000</td>
<td>45,186,334</td>
<td>$72,437,203</td>
<td>—</td>
<td>—</td>
<td>6,290,317</td>
</tr>
<tr>
<td>Conversion of Series A preferred stock and dividends to common stock upon initial public offering</td>
<td>5,000,000</td>
<td>(10,000,000)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Conversion of Series B preferred stock and dividends to common stock upon initial public offering</td>
<td>—</td>
<td>—</td>
<td>45,186,334</td>
<td>(72,437,203)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of common stock, net of issuance costs</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of common stock for services</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of restricted stock</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
### Purchase of common stock in treasury

<p>| | | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9,206</td>
<td>(552,636)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(552,636)</td>
</tr>
</tbody>
</table>

### Exercise of stock options

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>221,825</th>
<th>222</th>
<th>1,115,821</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1,116,043</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Stock-based compensation expense

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>13,378,594</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Net loss

<p>| | | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(47,125,778)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(47,125,778)</td>
</tr>
</tbody>
</table>

### Balance. December 31, 2015

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>27,082,493</th>
<th>27,083</th>
<th>$419,791,732</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>($128,728,384)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$290,537,795</td>
</tr>
</tbody>
</table>

See accompanying notes to consolidated financial statements.
Spark Therapeutics, Inc.
Consolidated statement of stockholders' equity
For the years ended December 31, 2016 and 2017

<table>
<thead>
<tr>
<th></th>
<th>Common stock in treasury</th>
<th>Common stock</th>
<th>Additional paid-in capital</th>
<th>Accumulated other comprehensive loss</th>
<th>Accumulated deficit</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
<td></td>
<td></td>
<td>$128,728,384</td>
</tr>
<tr>
<td>Balance, December 31, 2015</td>
<td>9,206</td>
<td>$ (552,636)</td>
<td>27,082,493</td>
<td>$27,083</td>
<td>$419,791,732</td>
<td>$290,537,795</td>
</tr>
<tr>
<td>Issuance of common stock, net of issuance costs</td>
<td>—</td>
<td>—</td>
<td>3,025,000</td>
<td>3,025</td>
<td>127,563,039</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of restricted stock, not vested</td>
<td>—</td>
<td>—</td>
<td>40,000</td>
<td>40</td>
<td>(40)</td>
<td>—</td>
</tr>
<tr>
<td>Restricted stock canceled</td>
<td>—</td>
<td>—</td>
<td>(2,213)</td>
<td>(2)</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Purchase of common stock under ESPP</td>
<td>—</td>
<td>—</td>
<td>8,012</td>
<td>8</td>
<td>339,861</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of stock for acquisition</td>
<td>—</td>
<td>—</td>
<td>265,000</td>
<td>265</td>
<td>9,150,185</td>
<td>—</td>
</tr>
<tr>
<td>Exercise of stock options</td>
<td>—</td>
<td>—</td>
<td>455,138</td>
<td>455</td>
<td>2,591,467</td>
<td>—</td>
</tr>
<tr>
<td>Unrealized loss on investments</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(801,717)</td>
<td>—</td>
</tr>
<tr>
<td>Unrealized gain on foreign currency translation</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>7,421</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>24,537,436</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(252,380,911)</td>
</tr>
<tr>
<td>Balance, December 31, 2016</td>
<td>9,206</td>
<td>$ (552,636)</td>
<td>30,873,430</td>
<td>$30,874</td>
<td>$583,973,682</td>
<td>$330,276,713</td>
</tr>
<tr>
<td>Issuance of common stock, net of issuance costs</td>
<td>—</td>
<td>—</td>
<td>5,296,053</td>
<td>5,296</td>
<td>379,864,789</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of restricted stock</td>
<td>—</td>
<td>—</td>
<td>1,193</td>
<td>1</td>
<td>(1)</td>
<td>—</td>
</tr>
<tr>
<td>Restricted stock canceled</td>
<td>—</td>
<td>—</td>
<td>(4,107)</td>
<td>(4)</td>
<td>4</td>
<td>—</td>
</tr>
<tr>
<td>Purchase of common stock in treasury</td>
<td>11,016</td>
<td>(673,313)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(673,313)</td>
</tr>
<tr>
<td>Purchase of common stock under ESPP</td>
<td>—</td>
<td>11,804</td>
<td>12</td>
<td>645,903</td>
<td>—</td>
<td>645,915</td>
</tr>
<tr>
<td>Exercise of stock options</td>
<td>—</td>
<td>—</td>
<td>953,253</td>
<td>953</td>
<td>20,732,487</td>
<td>—</td>
</tr>
<tr>
<td>Unrealized loss on investments</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(5,162,259)</td>
<td>—</td>
</tr>
<tr>
<td>Unrealized gain on foreign currency translation</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>42,960</td>
<td>—</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>41,372,643</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(253,481,972)</td>
</tr>
<tr>
<td>Balance, December 31, 2017</td>
<td>20,222</td>
<td>$(1,225,949)</td>
<td>37,131,626</td>
<td>$37,132</td>
<td>$1,026,589,507</td>
<td>$513,624,212</td>
</tr>
</tbody>
</table>

See accompanying notes to consolidated financial statements.
Spark Therapeutics, Inc.
Consolidated statements of cash flows
For the Year ended December 31,

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cash flows from operating activities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(47,125,778)</td>
<td>$(123,652,527)</td>
<td>$(253,481,972)</td>
</tr>
<tr>
<td><strong>Adjustments to reconcile net loss to net cash used in operating activities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noncash rent expense</td>
<td>181,979</td>
<td>(530,853)</td>
<td>(531,133)</td>
</tr>
<tr>
<td>Depreciation and amortization expense</td>
<td>1,732,983</td>
<td>3,634,349</td>
<td>4,860,428</td>
</tr>
<tr>
<td>Loss on disposal of property and equipment</td>
<td>—</td>
<td>101,490</td>
<td>32,176</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>—</td>
<td>11,132,146</td>
<td>8,604,258</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>13,572,503</td>
<td>24,537,436</td>
<td>41,372,643</td>
</tr>
<tr>
<td>Impairment of acquired in-process research and development</td>
<td>—</td>
<td>—</td>
<td>15,696,017</td>
</tr>
<tr>
<td>Non-cash income tax benefit</td>
<td>—</td>
<td>—</td>
<td>(1,013,539)</td>
</tr>
<tr>
<td>Non-cash interest income</td>
<td>—</td>
<td>—</td>
<td>(126,782)</td>
</tr>
<tr>
<td><strong>Changes in operating assets and liabilities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>(1,627,602)</td>
<td>(264,230)</td>
<td>(3,157,214)</td>
</tr>
<tr>
<td>Other receivables</td>
<td>(16,700,175)</td>
<td>(234,803)</td>
<td>8,856,911</td>
</tr>
<tr>
<td>Accounts payable and accrued expenses</td>
<td>9,052,260</td>
<td>10,018,084</td>
<td>12,981,007</td>
</tr>
<tr>
<td>Deferred rent</td>
<td>—</td>
<td>—</td>
<td>1,610,115</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>(6,564,397)</td>
<td>(5,182,835)</td>
<td>2,934,356</td>
</tr>
<tr>
<td>Other liabilities</td>
<td>—</td>
<td>—</td>
<td>6,826,833</td>
</tr>
<tr>
<td><strong>Net cash used in operating activities</strong></td>
<td>(47,478,227)</td>
<td>(80,441,743)</td>
<td>(154,535,896)</td>
</tr>
<tr>
<td><strong>Cash flows from investing activities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchase of acquired in-process research and development</td>
<td>—</td>
<td>(11,132,146)</td>
<td>(8,217,474)</td>
</tr>
<tr>
<td>Payment for acquisition, net of cash acquired</td>
<td>—</td>
<td>(5,911,243)</td>
<td>—</td>
</tr>
<tr>
<td>Purchase of marketable securities</td>
<td>—</td>
<td>(279,944,501)</td>
<td>(441,485,816)</td>
</tr>
<tr>
<td>Proceeds from maturities of marketable securities</td>
<td>—</td>
<td>20,000,000</td>
<td>251,625,252</td>
</tr>
<tr>
<td>Purchases of property and equipment</td>
<td>(4,521,769)</td>
<td>(8,532,397)</td>
<td>(9,653,710)</td>
</tr>
<tr>
<td><strong>Net cash used in investing activities</strong></td>
<td>(4,521,769)</td>
<td>(285,520,287)</td>
<td>(207,731,748)</td>
</tr>
<tr>
<td><strong>Cash flows from financing activities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proceeds from exercise of options</td>
<td>1,116,043</td>
<td>2,591,922</td>
<td>20,733,440</td>
</tr>
<tr>
<td>Purchase of treasury stock</td>
<td>(552,636)</td>
<td>—</td>
<td>(673,313)</td>
</tr>
<tr>
<td>Proceeds from public offerings of common stock, net</td>
<td>270,400,216</td>
<td>126,908,733</td>
<td>379,870,085</td>
</tr>
<tr>
<td>Proceeds from issuance of common stock under ESPP</td>
<td>—</td>
<td>339,869</td>
<td>645,915</td>
</tr>
<tr>
<td>Proceeds from long-term debt</td>
<td>—</td>
<td>1,550,610</td>
<td>—</td>
</tr>
<tr>
<td>Payments on long-term debt</td>
<td>—</td>
<td>(24,594)</td>
<td>(302,013)</td>
</tr>
<tr>
<td><strong>Net cash provided by financing activities</strong></td>
<td>270,963,623</td>
<td>131,366,540</td>
<td>400,274,114</td>
</tr>
<tr>
<td>Effect of exchange rate changes on cash and cash equivalents</td>
<td>—</td>
<td>(12,003)</td>
<td>(181,123)</td>
</tr>
<tr>
<td>Net increase (decrease) in cash and cash equivalents</td>
<td>218,963,627</td>
<td>(234,607,493)</td>
<td>37,825,347</td>
</tr>
<tr>
<td><strong>Cash and cash equivalents, beginning of year</strong></td>
<td>74,566,963</td>
<td>293,530,590</td>
<td>58,923,097</td>
</tr>
<tr>
<td><strong>Cash and cash equivalents, end of year</strong></td>
<td>$ 293,530,590</td>
<td>$ 58,923,097</td>
<td>$ 96,748,444</td>
</tr>
</tbody>
</table>

See accompanying notes to the consolidated financial statements.
### Consolidated statements of cash flows

#### For the Year ended December 31,

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deferred financing costs included in accounts payable and accrued expenses</strong></td>
<td>$657,331</td>
<td>$—</td>
<td>$—</td>
</tr>
<tr>
<td><strong>Property and equipment purchases included in accounts payable and accrued expenses</strong></td>
<td>$2,683,487</td>
<td>$681,790</td>
<td>$2,788,665</td>
</tr>
<tr>
<td><strong>One Drexel Plaza lease cost included in other liabilities</strong></td>
<td>$—</td>
<td>$—</td>
<td>$34,985,836</td>
</tr>
</tbody>
</table>

*See accompanying notes to the consolidated financial statements.*
Spark Therapeutics, Inc.
Notes to consolidated financial statements

(1) Background

Spark Therapeutics, Inc. was formed on March 13, 2013 in the state of Delaware as AAVenue Therapeutics, LLC and amended its Certificate of Formation in October 2013 to change its name to Spark Therapeutics LLC. In May 2014, the Company converted from a limited liability company (LLC) to a C corporation, Spark Therapeutics, Inc. (the Company). The Company is a gene therapy company, seeking to transform the lives of patients suffering from debilitating genetic diseases by developing one-time, life-altering treatments. The Company operates in one segment and has its principal offices in Philadelphia, Pennsylvania.

In December 2017, the U.S. Food and Drug Administration, or FDA, approved LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy and viable retinal cells.

(a) Public Offerings

On February 4, 2015, the Company completed its initial public offering, or IPO, having sold 8,050,000 shares of common stock at an IPO price of $23.00 per share, for aggregate gross proceeds of $185.2 million. The Company received net proceeds from the IPO of $168.9 million, after deducting underwriting discounts and commissions and other offering costs. As part of the IPO, all of the outstanding shares of preferred stock, including shares of preferred stock issued as accrued dividends, were converted into an aggregate of 10,200,050 shares of common stock.

On December 28, 2015, the Company completed its follow-on public offering, having sold 2,266,995 shares of common stock at a public offering price of $47.00 per share, for aggregate gross proceeds of $106.5 million. The Company received net proceeds from the public offering of $99.4 million, after deducting underwriting discounts and commissions and other offering costs.

On June 20, 2016, the Company completed a follow-on public offering, having sold 3,025,000 shares of common stock at an offering price of $45.00 per share, for aggregate gross proceeds of $136.1 million. The Company received net proceeds from the public offering of $127.6 million, after deducting underwriting discounts and commissions and other offering costs.

On August 9, 2017, the Company completed a follow-on public offering, having sold 5,296,053 shares of common stock at an offering price of $76.00 per share, for aggregate gross proceeds of $402.5 million. The Company received net proceeds from the public offering of $379.9 million, after deducting underwriting discounts and commissions and other offering costs.

(2) Development-stage risks

The Company has incurred losses and negative cash flows from operations since inception and had an accumulated deficit of $505.9 million at December 31, 2017. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of LUXTURNA and its other product candidates in development. Additional financing may be needed by the Company to fund its operations and to commercially develop its other product candidates.

The Company’s future operations are highly dependent on a combination of factors, including: (i) the success of its research and development; (ii) regulatory approval and market acceptance of LUXTURNA and the Company’s proposed future products; (iii) the timely and successful completion of additional financing; and (iv) the development of competitive therapies by other biotechnology and pharmaceutical companies.

(3) Summary of significant accounting policies

(a) Use of estimates

The preparation of consolidated financial statements in conformity with U.S. generally accepted accounting principles (GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from such estimates.

(b) Principles of consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries: Spark Therapeutics, Inc., Spark Therapeutics Ireland Limited, Spark Therapeutics UK Limited, Spark Therapeutics Argentina Limited, Spark Therapeutics Switzerland Limited, Spark Therapeutics Germany Limited and Spark Therapeutics France Limited. All intercompany balances and transactions have been eliminated in consolidation.

(c) Fair value of financial instruments

Management believes that the carrying amounts of the Company’s financial instruments, including cash equivalents, other receivables and accounts payable and accrued expenses, approximate fair value due to the short-term nature of those instruments. Management believes the carrying value of debt approximates fair value as the interest rates are reflective of the rate the Company could obtain on debt with similar terms and conditions.

(d) Cash and cash equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents as of December 31, 2016 and 2017 consisted primarily of money market funds.

(e) Marketable securities

The Company classifies its marketable security investments as available-for-sale securities and the securities are stated at fair value. At December 31, 2017, the balance in the Company’s accumulated other comprehensive loss included activity related to the Company’s available-for-sale marketable securities. There were no material realized gains or losses recognized on the maturity of available-for-sale securities during the year ended December 31, 2017 and, as a result, the Company did not reclassify any amount out of accumulated other comprehensive loss for the same period. In addition, as part of the license and stock purchase...
agreements entered into with Selecta Biosciences, Inc. (Selecta) (note 14), the Company purchased restricted common shares of Selecta. The investment is classified as available-for-sale and is stated at fair value.

(f) Property and equipment
Property and equipment consists of computer and laboratory equipment, software, office equipment, furniture and leasehold improvements and is recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, retirement or sale, the related cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Property and equipment are depreciated on a straight-line basis over their estimated useful lives. The Company uses a life of three years for computer equipment and software, five years for laboratory and office equipment and seven years for furniture. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

The Company reviews long-lived assets, such as property and equipment, for impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to estimated undiscounted future cash flows that the assets are expected to generate. If the carrying amount of an asset exceeds its estimated future cash flows, then an impairment charge is recognized for the amount by which the carrying value of the asset exceeds the fair value of the asset. No impairment charges have been recorded since inception.

(g) Acquired in-process research and development and goodwill
The acquired in-process research and development (IPR&D) asset was an indefinite-lived intangible asset and was assessed for impairment annually or more frequently if impairment indicators existed. During the year ended December 31, 2017, the Company determined that it would no longer pursue product candidates utilizing the technology acquired from Genable Technologies, Ltd. (Genable) in March 2016 and, accordingly, recorded an impairment charge of $15.7 million within its consolidated statement of operations. Additionally, the Company recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the IPR&D during the year ended December 31, 2017.

Goodwill represents the excess of purchase price over the fair value of net assets acquired by the Company. Goodwill is not amortized, but assessed for impairment on an annual basis or more frequently if impairment indicators exist. The Company operates as one reporting unit.

The Company has the option to perform a qualitative assessment of goodwill prior to completing the two-step method described below to determine whether or not it is more likely than not that the fair value of its reporting units is less than its carrying amount, including goodwill and other intangible assets. If the Company concludes that this is the case, it must perform the two-step process.

The first step compares a reporting unit’s fair value to its carrying amount to identify potential goodwill impairment. If the carrying amount of a reporting unit exceeds the reporting unit’s fair value, the second step of the impairment test must be
completed to measure the amount of the reporting unit’s goodwill impairment loss, if any. Step two requires an assignment of the reporting unit’s fair value to the reporting unit’s assets and liabilities to determine the implied fair value of the reporting unit’s goodwill. The implied fair value of the reporting unit’s goodwill is then compared with the carrying amount of the reporting unit’s goodwill to determine the goodwill impairment loss to be recognized, if any.

The Company performs its annual goodwill impairment test as of October 1st. The Company performed a qualitative assessment in 2017 and determined that there was no impairment to goodwill for the year ended December 31, 2017.

Research and development and in-process research and development
Research and development costs are expensed as incurred. Research and development expenses consist of internal and external expenses. Internal expenses include employee compensation and overhead. External expenses include development, clinical trials, statistical analysis and report writing and regulatory compliance costs incurred with clinical research organizations and other third-party vendors. At the end of the reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the service provided, the Company may record net prepaid or accrued expense relating to these costs. When the Company is reimbursed by a collaboration partner for work performed, the costs incurred are recorded as research and development expenses and the related reimbursement is recorded as a reduction to research and development expenses.

Upfront and milestone payments made to third parties who perform research and development services on the Company’s behalf are expensed as services are rendered. Costs incurred in obtaining technology licenses are charged to research and development expense as acquired in-process research and development if the technology licensed has not reached technological feasibility and has no alternative future use.

Income taxes
The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of its assets and liabilities and the expected benefits of net operating loss carryforwards. The impact of changes in tax rates and laws on deferred taxes, if any, is applied during the years in which temporary differences are expected to be settled and net operating losses used and is reflected in the consolidated financial statements in the period of enactment. The measurement of deferred tax assets is reduced, if necessary, if, based on weight of the evidence, it is more likely than not that some, or all, of the deferred tax assets will not be realized. At December 31, 2016 and 2017, the Company has concluded that a full valuation allowance is necessary for its deferred tax assets.

Revenue recognition
The Company has generated revenue solely through license and collaborative agreements. The Company recognizes revenue in accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Subtopic 605-25, Revenue Recognition: Multiple-Element Arrangements, which addresses the determination of whether an arrangement involving multiple deliverables contains more than one unit of accounting. A delivered item within an arrangement is considered a separate unit of accounting only if both of the following criteria are met:

- the delivered item has value to the customer on a stand-alone basis; and
- if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in control of the vendor.

Under FASB ASC Subtopic 605-25, if both of the criteria above are not met, then separate accounting for the individual deliverables is not appropriate. Revenue recognition for arrangements with multiple deliverables constituting a single unit of accounting is recognized generally over the greater of the term of the arrangement or the expected period of performance, either on a straight-line basis or on a modified proportional performance method.

Milestones related to research and development activities are accounted for in accordance with FASB ASC Subtopic 605-28, Revenue Recognition: Milestone Method. FASB ASC Subtopic 605-28 allows for the recognition of consideration, which is contingent on the achievement of a substantive milestone in its entirety, in the period the milestone is achieved. A milestone is considered to be substantive if all of the following criteria are met:

- the milestone is commensurate with either: (1) the performance required to achieve the milestone or (2) the enhancement of the value of the delivered items resulting from the performance required to achieve the milestone;

F-10
Notes to consolidated financial statements

- the milestone relates solely to past performance; and
- the milestone payment is reasonable relative to all of the deliverables and payment terms within the agreement.

Nonrefundable license fees are recognized as revenue upon delivery provided there are no undelivered elements in the arrangement. For licenses with no standalone value, revenues are recognized on a straight-line basis over the related performance period.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue on the Company’s consolidated balance sheet. Amounts expected to be recognized as revenue in the next 12 months following the balance sheet date are classified as current liabilities.

To date, the Company has not generated any revenues from the commercial sale of products.

(k) Stock-based compensation and fair value of stock

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, Compensation—Stock Compensation. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock units and modifications to existing stock options, to be recognized in the consolidated statement of operations based on their fair values. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted.

The Company’s stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to non-employees with service-based vesting conditions is recognized based on the then-current fair value at each financial reporting date prior to the measurement date over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period to the extent achievement of the performance condition is probable.

The Company estimates the fair value of its option awards to employees and directors using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the calculation of the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of substantial Company-specific historical and implied volatility data of its common stock, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry and with historical share price information sufficient to meet the expected term of the stock-based awards. The Company computes historical volatility data using the daily closing prices for the selected companies’ shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Consistent with the guidance in FASB ASC Topic 505-50, Equity-Based Payments to Non-Employees, the fair value of each non-employee stock option and restricted stock award is estimated at the date of grant using the Black-Scholes option pricing model with assumptions generally consistent with those used for employee stock options, with the exception of expected term, which is over the contractual life.
(l) Net loss per common share

Basic and diluted net loss per common share is determined by dividing net loss by the weighted average number of common shares outstanding during the period. For all periods presented, unvested restricted shares and common stock options have been excluded from the calculation because their effect would be anti-dilutive. Therefore, the weighted average shares outstanding used to calculate both basic and diluted loss per share are the same.

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of December 31, 2015, 2016 and 2017 as they would be anti-dilutive:

<table>
<thead>
<tr>
<th></th>
<th>December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015</td>
</tr>
<tr>
<td>Unvested restricted common shares</td>
<td>373,655</td>
</tr>
<tr>
<td>Options issued and outstanding</td>
<td>3,071,372</td>
</tr>
</tbody>
</table>

Amounts in the table above reflect the common stock equivalents of the noted instruments.

(m) Deferred rent

Rent expense, including rent holidays and scheduled rent increases, is recorded on a straight-line basis over the term of the lease commencing on the date the Company takes possession of the leased property. Tenant improvement allowances from the lessor are included in the accompanying consolidated balance sheet as deferred rent and amortized as a reduction of rent expense over the term of the lease from the possession date. Deferred rent as of December 31, 2016 and 2017 represents the net excess of rent expense over the actual cash paid for rent and the tenant improvement allowances received.

(n) Other comprehensive loss

The Company follows the provisions of FASB ASC Topic 220, Comprehensive Income, which establishes standards for the reporting and display of comprehensive income and its components. Comprehensive income is defined to include all changes in equity during a period except those resulting from investments by owners and distributions to owners. The Company recorded gains and losses related to changes in available-for-sale securities and foreign currency translation.

The accumulated balances related to each component of other comprehensive loss are summarized as follows:

<table>
<thead>
<tr>
<th></th>
<th>Net unrealized losses on available for sale securities</th>
<th>Foreign currency translation adjustments</th>
<th>Accumulated other comprehensive loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance as of December 31, 2016</td>
<td>$ (801,717)</td>
<td>$ 7,421</td>
<td>$(794,296)</td>
</tr>
<tr>
<td>Current period other comprehensive income (loss)</td>
<td>$ (5,162,259)</td>
<td>$ 42,960</td>
<td>$(5,119,299)</td>
</tr>
<tr>
<td>Balance as of December 31, 2017</td>
<td>$ (5,963,976)</td>
<td>$ 50,381</td>
<td>$(5,913,595)</td>
</tr>
</tbody>
</table>

(o) Recent accounting pronouncements

In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, Leases. ASU 2016-02 requires that lease arrangements longer than 12 months result in an entity recognizing an asset and liability. ASU 2016-02 is effective for interim and annual periods beginning after December 15, 2018, and early adoption is permitted. The Company is currently evaluating the impact of the updated guidance on the Company's consolidated financial statements.

In May 2014, the FASB issued a new standard regarding the accounting for, and disclosures of, revenue recognition, with an effective date for annual and interim periods beginning after December 15, 2017. The new standard provides a single comprehensive model for accounting for revenue from contracts with customers. The model requires that revenue recognized reflect the actual consideration to which the entity expects to be entitled in exchange for the goods or services defined in the contract, including in situations with multiple performance obligations. The allowable adoption methods are the full retrospective method, which requires the standard to be applied to each prior period presented, or the modified retrospective method which requires the cumulative effect of adoption to be recognized as an adjustment to opening retained earnings in the
period of adoption. The Company will adopt this guidance using the modified retrospective method and the adoption will have no cumulative adjustment to its consolidated financial statements as it relates to the Pfizer Inc. (Pfizer) collaboration agreement discussed in note 14.

In January 2016, the FASB issued ASU No. 2016-01, Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities. ASU 2016-01 changes accounting for equity investments, financial liabilities under the fair value option, and presentation and disclosure requirements for financial instruments. ASU 2016-01 does not apply to equity investments in consolidated subsidiaries or those accounted for under the equity method of accounting. In addition, the FASB clarified guidance related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. Equity investments with readily determinable fair values will be measured at fair value with changes in fair value recognized in net income. Companies have the option to either measure equity investments without readily determinable fair values at fair value or at cost, adjusted for changes in observable prices, minus impairment. Changes in measurement under either alternative will be recognized in net income. Companies that elect the fair value option for financial liabilities must recognize changes in fair value related to instrument-specific credit risk in other comprehensive income (OCI). Companies must assess valuation allowances for deferred tax assets related to available-for-sale debt securities in combination with their other deferred tax assets. ASU 2016-01 will be effective beginning the first quarter of 2018. The Company currently is evaluating the impact of the updated guidance on the Company's consolidated financial statements.

(4) Marketable securities

The following table summarizes the available-for-sale securities held at December 31, 2016 and 2017:

<table>
<thead>
<tr>
<th>Description</th>
<th>Amortized cost</th>
<th>Unrealized gains</th>
<th>Unrealized losses</th>
<th>Fair value</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 31, 2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. government agency</td>
<td>$133,690,267</td>
<td>$10,907</td>
<td>$(85,714)</td>
<td>$133,615,460</td>
</tr>
<tr>
<td>Corporate securities</td>
<td>$126,253,903</td>
<td>$</td>
<td>$(726,579)</td>
<td>$125,527,324</td>
</tr>
<tr>
<td>December 31, 2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. government agency</td>
<td>$222,179,753</td>
<td>$</td>
<td>$(640,341)</td>
<td>$221,539,412</td>
</tr>
<tr>
<td>Corporate securities</td>
<td>$227,237,638</td>
<td>$</td>
<td>$(5,322,745)</td>
<td>$221,914,893</td>
</tr>
</tbody>
</table>

No available-for-sale securities held as of December 31, 2017 had remaining maturities greater than two years.

(5) Fair value of financial instruments

The Company follows FASB accounting guidance on fair value measurements for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements to maximize the use of “observable inputs.” The three-level hierarchy of inputs to measure fair value are as follows:

- Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities
- Level 2: Significant other observable inputs other than Level 1 prices such as quoted prices in markets that are not active, or inputs that are observable, either directly or indirectly, for substantially the full term of the asset or liability
- Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity)
Fair value measurements at reporting date using

<table>
<thead>
<tr>
<th>Quoted prices in active markets for identical assets (Level 1)</th>
<th>Significant other observable inputs (Level 2)</th>
<th>Significant unobservable inputs (Level 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>As of December 31, 2016:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Money market funds (included in cash and cash equivalents)</td>
<td>$ 53,452,424</td>
<td>—</td>
</tr>
<tr>
<td>Corporate securities (included in cash and cash equivalents)</td>
<td>$ 5,029,838</td>
<td>—</td>
</tr>
<tr>
<td>Marketable securities - U.S. government agencies</td>
<td>$ 133,615,460</td>
<td>—</td>
</tr>
<tr>
<td>Marketable securities - corporate securities</td>
<td>$ 122,144,692</td>
<td>$ 3,382,632</td>
</tr>
<tr>
<td>As of December 31, 2017:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Money market funds (included in cash and cash equivalents)</td>
<td>$ 90,347,897</td>
<td>—</td>
</tr>
<tr>
<td>Corporate securities (included in cash and cash equivalents)</td>
<td>$ 5,548,478</td>
<td>—</td>
</tr>
<tr>
<td>Marketable securities - U.S. government agencies</td>
<td>$ 221,539,412</td>
<td>—</td>
</tr>
<tr>
<td>Marketable securities - corporate securities</td>
<td>$ 220,020,150</td>
<td>$ 1,894,743</td>
</tr>
</tbody>
</table>

(6) Business acquisition of Genable and impairment of acquired in-process research and development

On March 7, 2016, the Company acquired Genable, an Ireland-based private gene therapy company with which the Company had collaborated since 2014 in the development of Genable's therapeutic program targeting a genetic inherited retinal disease (IRD). With the acquisition, the Company acquired RhoNova™, a potential gene therapy targeting rhodopsin-linked autosomal dominant retinitis pigmentosa (RHO-adRP), an IRD that routinely leads to visual impairment and in the most severe cases to blindness. The consideration paid by the Company to Genable shareholders consisted of $6.1 million in cash and 265,000 shares of the Company's common stock with a fair value of $9.2 million, for total consideration of $15.3 million. In connection with the acquisition, a receivable due from Genable also was settled on the date of acquisition for $0.5 million. The Company incurred acquisition-related costs of approximately $0.3 million, which are included in general and administrative expenses in the consolidated statement of operations for the year ended December 31, 2016.

The Company accounted for the acquisition as a business combination under the acquisition method of accounting. The Company allocated the purchase price for the purchase of Genable based upon the estimated fair value of net assets acquired and liabilities assumed at the date of acquisition.
Recognition and measurement of assets acquired and liabilities assumed

The following table summarizes the fair values of the tangible and intangible assets acquired and liabilities assumed at the acquisition date:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash acquired</td>
<td>$196,307</td>
<td></td>
</tr>
<tr>
<td>Other current assets</td>
<td>102,506</td>
<td></td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>15,490,000</td>
<td></td>
</tr>
<tr>
<td>Goodwill</td>
<td>1,160,104</td>
<td></td>
</tr>
<tr>
<td>Total assets assumed</td>
<td>16,948,917</td>
<td></td>
</tr>
<tr>
<td>Other non-current liabilities</td>
<td>254,753</td>
<td></td>
</tr>
<tr>
<td>Deferred tax liability</td>
<td>1,000,235</td>
<td></td>
</tr>
<tr>
<td>Total liabilities assumed</td>
<td>1,254,988</td>
<td></td>
</tr>
<tr>
<td>Total allocation of purchase price</td>
<td>$15,693,929</td>
<td></td>
</tr>
</tbody>
</table>

Acquired in-process research and development and related impairment

The Company’s allocation of purchase price to acquired IPR&D was $15.5 million. The estimated fair value of the IPR&D was determined using the “income approach,” which is a valuation technique that provides an estimate of the fair value of an asset based on market participant expectations of the cash flows an asset would generate over its remaining useful life. Some of the more significant assumptions inherent in the development of those asset valuations include the estimated net cash flows for each year for the asset or product (including net revenues, cost of sales, research and development costs, selling and marketing costs and working capital/asset contributory asset charges), the appropriate discount rate to select in order to measure the risk inherent in each future cash flow stream, the assessment of the asset’s life cycle, the potential regulatory and commercial success risks, competitive trends impacting the asset cash flow stream as well as other factors.

During the year ended December 31, 2017, the Company determined that it would no longer pursue product candidates utilizing the technology acquired from Genable in March 2016 and, accordingly, recorded an impairment charge of $15.7 million within its consolidated statement of operations. Additionally, the Company recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the IPR&D during the year ended December 31, 2017.

(7) Property and equipment, net

Property and equipment consist of the following:

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory equipment</td>
<td>$5,833,616</td>
<td>$6,380,580</td>
</tr>
<tr>
<td>Computer and software</td>
<td>530,663</td>
<td>1,325,403</td>
</tr>
<tr>
<td>Furniture and fixtures</td>
<td>470,151</td>
<td>1,770,475</td>
</tr>
<tr>
<td>Office equipment</td>
<td>537,756</td>
<td>725,982</td>
</tr>
<tr>
<td>Leasehold improvements</td>
<td>16,981,989</td>
<td>23,653,219</td>
</tr>
<tr>
<td>Construction in progress</td>
<td>967,945</td>
<td>38,179,619</td>
</tr>
<tr>
<td>Property and equipment, gross</td>
<td>25,322,120</td>
<td>72,035,278</td>
</tr>
<tr>
<td>Less accumulated depreciation and amortization</td>
<td>(5,527,814)</td>
<td>(10,322,485)</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>$19,794,306</td>
<td>$61,712,793</td>
</tr>
</tbody>
</table>

At December 31, 2017, the costs related to the One Drexel Plaza lease (Note 12(a)) approximated $35.0 million within construction in progress. Depreciation and amortization expense was $1.7 million, $3.6 million and $4.9 million for the years ended December 31, 2015, 2016 and 2017, respectively.
(8) Accrued expenses

Accrued expenses consist of the following:

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compensation and benefits</td>
<td>$9,613,275</td>
<td>$15,011,597</td>
</tr>
<tr>
<td>Consulting and professional fees</td>
<td>995,614</td>
<td>4,846,360</td>
</tr>
<tr>
<td>Research and development</td>
<td>2,717,777</td>
<td>2,809,043</td>
</tr>
<tr>
<td>Other</td>
<td>500,254</td>
<td>2,030,225</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$13,826,920</td>
<td>$24,697,225</td>
</tr>
</tbody>
</table>

(9) Debt

In August 2016, the Company executed an agreement with the Commonwealth of Pennsylvania to fund machinery and equipment and other assets purchased (MELF Loan) in the amount of $1.6 million. Borrowings under the MELF Loan are secured by equipment, as defined in the loan agreement. Under the terms of the MELF Loan, the Company has a five-year period of monthly payments of approximately $29,000 of principal and interest at an annual interest rate of 3.25%. For the years ended December 31, 2016 and 2017, the Company recorded interest expense of approximately $15,000 and $48,000, respectively, related to the MELF Loan.

(10) Stockholders’ equity

The Company’s certificate of incorporation and bylaws contain the rights, preferences and privileges of the Company’s stockholders and their respective shares. The Company has authorized 150,000,000 shares of common stock and 5,000,000 shares of preferred stock.

In 2013 and 2014, the Company issued restricted stock to various employees, directors and consultants of the Company. The vesting terms of the restricted stock issued varied, but primarily, shares vested 25% on the first anniversary of the vesting commencement date and then quarterly over three years, with accelerated vesting in the event of a change in control, as defined. Any unvested shares are forfeited in the event that the individual ceases to provide services to the Company. Additionally, in 2014, 200,000 restricted shares of common stock were issued to The Trustees of the University of Pennsylvania (Penn) in connection with a license agreement, of which 100,000 shares have vested. The remaining shares are subject to certain milestone-based vesting conditions. No milestone vesting conditions were achieved in 2016 or 2017.

For the year ended December 31, 2015, the Company recorded compensation expense of $0.1 million and $1.8 million in general and administrative expense and research and development expense, respectively, related to restricted shares. For the year ended December 31, 2016, the Company recorded compensation expense of $0.1 million and $1.3 million in general and administrative expense and research and development expense, respectively, related to restricted shares. For the year ended December 31, 2017, the Company recorded compensation expense of approximately $34,000 and $4.4 million in general and administrative expense and research and development expense, respectively, related to restricted shares.

At December 31, 2017, there was an immaterial amount of unrecognized compensation expense related to the restricted shares which is expected to be recognized over a weighted-average period of less than a year.
(11) Stock incentive plans

In January 2015, the Company established the 2015 Stock Incentive Plan (the 2015 Plan), which became effective immediately prior to the closing of the IPO. The 2015 Plan replaced the 2014 Stock Incentive Plan (the 2014 Plan) and the 209,500 shares available for future grants under the 2014 Plan were rolled into the 2015 Plan. The 2015 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards to employees, officers, directors, consultants and advisors. Under the 2015 Plan, the number of shares of common stock reserved for issuance is the sum of: (1) 1,830,000 plus; (2) the number of shares (up to 2,543,299 shares) equal to the sum of the number of shares of common stock then available for issuance under the 2014 Plan and the number of shares of common stock subject to outstanding awards under the 2014 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2016 and continuing until, and including, the fiscal year ending December 31, 2025, equal to the lowest of 1,724,000 shares of common stock, 4% of the number of shares of common stock outstanding on the first day of such fiscal year and an amount determined by the board of directors. In January 2017, the number of shares of common stock authorized for issuance under the 2015 Plan automatically increased, pursuant to the terms of the 2015 Plan, by 1,234,641 shares. As of December 31, 2017, 727,229 shares were available for future grants under the 2015 Plan.

In January 2015, the Company established the 2015 employee stock purchase plan (the 2015 ESPP), which became effective immediately prior to the closing of the IPO. The 2015 ESPP initially provided participating employees with the opportunity to purchase an aggregate of 220,000 shares of common stock. The number of shares of common stock reserved for issuance under the 2015 ESPP automatically will increase on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2016 and continuing until, and including, the fiscal year ending December 31, 2026, in an amount equal to the lowest of: (1) 440,000 shares of common stock; (2) 1% of the total number of shares of common stock outstanding on the first day of the applicable fiscal year; and (3) an amount determined by the board of directors. For the year ended December 31, 2017, 11,804 shares were issued under the 2015 ESPP. In January 2017, the number of shares of common stock authorized for issuance under the 2015 ESPP automatically increased, pursuant to the terms of the 2015 ESPP, by 308,660 shares. The 2015 ESPP provides participating employees with the opportunity to purchase an aggregate of 779,672 shares of common stock.

Stock-based compensation expense

Stock-based compensation expense by award type was as follows:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock options</td>
<td>$9,874,709</td>
<td>$22,376,794</td>
<td>$28,001,032</td>
</tr>
<tr>
<td>Restricted stock</td>
<td>1,680,145</td>
<td>632,298</td>
<td>8,452,262</td>
</tr>
<tr>
<td>Employee stock purchase plan</td>
<td>—</td>
<td>177,767</td>
<td>437,599</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$11,554,854</td>
<td>$23,186,859</td>
<td>$36,890,893</td>
</tr>
</tbody>
</table>

F-17
Of the $36.9 million of stock-based compensation expense incurred during the year ended December 31, 2017, $15.1 million is classified as research and development expense and $21.8 million is classified as general and administrative expense in the consolidated statement of operations and comprehensive income (loss). Of the $23.2 million of stock-based compensation expense incurred during the year ended December 31, 2016, $9.6 million is classified as research and development expense and $13.6 million is classified as general and administrative expense in the consolidated statement of operations and comprehensive income (loss). Of the $11.6 million of stock-based compensation expense incurred during the year ended December 31, 2015, $5.0 million is classified as research and development expense and $6.6 million is classified as general and administrative expense in the consolidated statement of operations and comprehensive income (loss).

Stock options
The following table summarizes stock option activity:

<table>
<thead>
<tr>
<th></th>
<th>Number of shares</th>
<th>Weighted-average exercise price</th>
<th>Aggregate intrinsic value(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outstanding at December 31, 2015</td>
<td>3,071,372</td>
<td>$22.99</td>
<td></td>
</tr>
<tr>
<td>Granted</td>
<td>1,722,950</td>
<td>$43.16</td>
<td></td>
</tr>
<tr>
<td>Exercised</td>
<td>(455,138)</td>
<td>$5.69</td>
<td></td>
</tr>
<tr>
<td>Forfeited</td>
<td>(157,191)</td>
<td>$21.17</td>
<td></td>
</tr>
<tr>
<td>Outstanding at December 31, 2016</td>
<td>4,181,993</td>
<td>$33.25</td>
<td></td>
</tr>
<tr>
<td>Granted</td>
<td>701,300</td>
<td>$56.78</td>
<td></td>
</tr>
<tr>
<td>Exercised</td>
<td>(953,253)</td>
<td>$21.75</td>
<td></td>
</tr>
<tr>
<td>Forfeited</td>
<td>(407,166)</td>
<td>$41.30</td>
<td></td>
</tr>
<tr>
<td>Outstanding at December 31, 2017</td>
<td>3,522,874</td>
<td>$40.11</td>
<td>$34,379,774</td>
</tr>
<tr>
<td>Vested at December 31, 2017</td>
<td>1,483,330</td>
<td>$32.46</td>
<td>$34,379,774</td>
</tr>
<tr>
<td>Vested at December 31, 2017 and expected to vest</td>
<td>3,170,491</td>
<td>$40.11</td>
<td>$48,691,490</td>
</tr>
</tbody>
</table>

(a) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock that were in the money at December 31, 2017.

The weighted average remaining contractual term of options outstanding as of December 31, 2017 is 7.9 years. The weighted average remaining contractual term of options exercisable as of December 31, 2017 is 7.3 years.

At December 31, 2017, there was $55.5 million of unrecognized compensation expense related to stock options, which is expected to be recognized over a weighted average period of 2.4 years.

The intrinsic value of options exercised during the years ended December 31, 2016 and 2017 was $21.1 million and $45.9 million, respectively.

The weighted average grant date fair value of the options granted in 2015, 2016 and 2017 was $40.51, $28.56 and $39.27 per share, respectively, using the Black-Scholes option-pricing model with the following weighted-average assumptions:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected volatility</td>
<td>76.8%</td>
<td>75.2%</td>
<td>78.1%</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>1.67%</td>
<td>1.71%</td>
<td>2.06%</td>
</tr>
<tr>
<td>Expected term (in years)</td>
<td>6.10</td>
<td>5.95</td>
<td>6.10</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
**Restricted Stock**

The following table summarizes restricted common stock activity:

<table>
<thead>
<tr>
<th>Description</th>
<th>Number of shares</th>
<th>Weighted-average grant date fair value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonvested shares at December 31, 2015</td>
<td>25,100</td>
<td>$60.03</td>
</tr>
<tr>
<td>Shares granted</td>
<td>59,500</td>
<td>$44.35</td>
</tr>
<tr>
<td>Shares canceled</td>
<td>(1,000)</td>
<td>$60.03</td>
</tr>
<tr>
<td>Shares vested</td>
<td>(6,667)</td>
<td>$37.06</td>
</tr>
<tr>
<td>Nonvested shares at December 31, 2016</td>
<td>76,933</td>
<td>$49.90</td>
</tr>
<tr>
<td>Shares granted</td>
<td>713,400</td>
<td>$63.34</td>
</tr>
<tr>
<td>Shares canceled</td>
<td>(55,457)</td>
<td>$48.93</td>
</tr>
<tr>
<td>Shares vested</td>
<td>(37,209)</td>
<td>$55.77</td>
</tr>
<tr>
<td>Nonvested shares at December 31, 2017</td>
<td>697,667</td>
<td>$63.40</td>
</tr>
</tbody>
</table>

At December 31, 2017, there was $36.9 million of unrecognized compensation expense related to the restricted common stock, which is expected to be recognized over a weighted average period of 3.3 years.

**ESPP stock activity:**

For the year ended December 31, 2016, 8,012 shares were issued under the 2015 ESPP. For the year ended December 31, 2017, 11,804 shares were issued under the 2015 ESPP.

At December 31, 2017, there was $0.2 million in unrecognized compensation expense related to the 2015 ESPP.

(12) Commitments and contingencies

(a) Leases

In March 2014, the Company entered into an operating lease for laboratory and office space at its corporate headquarters in Philadelphia, Pennsylvania, through October 2025. Under this lease, the Company received $8.0 million of tenant improvement allowances during 2014. In November 2015, the Company entered into a sublease agreement for approximately 14,000 square feet of additional office space at its corporate headquarters. The sublease will terminate on November 30, 2018. In February 2016, the Company leased 6,500 square feet of additional office space in Philadelphia under a lease that expires in June 2021. In addition, the Company leases approximately 5,400 square feet of office space in Waltham, Massachusetts under a lease that expires in March 2022.

In November 2016, the Company entered into a lease agreement for approximately 49,000 square feet of office space in Philadelphia that will terminate on March 31, 2027. Under this lease, the Company received $1.6 million of tenant improvement allowances during 2017. In January 2017, the Company amended its lease for office space in Philadelphia to lease an additional 24,800 square feet that commenced on January 1, 2018, and terminate on December 31, 2028. In November 2017, the Company amended this lease to accelerate the termination date of approximately 50,000 square feet of office space, with such termination to occur, at the latest, in December 2022. The Company recorded an expense of $6.9 million associated with the change in termination date in 2017. As of December 31, 2017, $5.3 million is recorded as long-term other liabilities and $1.5 million is recorded as current other liabilities on the accompanying consolidated balance sheet related to the termination expense.

The following table reconciles the termination cost discussed above:

<table>
<thead>
<tr>
<th>Description</th>
<th>Balance as of November 10, 2017</th>
<th>Recognized during the quarter</th>
<th>Balance as of December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contract termination liability</td>
<td>$6,880,161</td>
<td>$53,328</td>
<td>$6,826,833</td>
</tr>
</tbody>
</table>

F-19
In November 2017, the Company entered into a lease for the new research facility at One Drexel Plaza in Philadelphia, Pennsylvania for approximately 108,000 square feet through June 2033.

Based on the terms of the lease agreement for One Drexel Plaza, the Company has construction period risks during the construction period and the Company is deemed the owner of the building (for accounting purposes only) during the construction period. Accordingly, the Company recorded an asset of $35.0 million at December 31, 2017, representing the Company’s leased portion of the building, and recorded a corresponding liability. Upon completion of leasehold improvement construction, the Company may not meet the sale-leaseback criteria for de-recognition of the building asset and liability. Therefore, the lease may be accounted for as a financing obligation. The asset will be depreciated over the expected duration of the lease of 15.5 years, and rental payments will be treated as principal and interest payments on the lease financing obligation liability. The underlying accounting for this transaction has no impact on cash flows associated with the underlying lease or construction in process.

At December 31, 2017, the lease financing obligation balance was $35.0 million and was recorded as a long-term liability within other liabilities on the consolidated balance sheets. The remaining future minimum payments under the lease financing obligation as of December 31, 2017 are included in the table below.

Rent expense under these leases was $1.9 million and $10.5 million for the years ended December 31, 2016 and 2017, respectively.

Future minimum lease payments under these leases are as follows:

<table>
<thead>
<tr>
<th>Year Ending December 31,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>$5,520,167</td>
</tr>
<tr>
<td>2019</td>
<td>$7,156,064</td>
</tr>
<tr>
<td>2020</td>
<td>$7,819,394</td>
</tr>
<tr>
<td>2021</td>
<td>$8,071,918</td>
</tr>
<tr>
<td>2022</td>
<td>$8,126,544</td>
</tr>
<tr>
<td>2023 and thereafter</td>
<td>$58,897,069</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$95,591,156</strong></td>
</tr>
</tbody>
</table>

(b) License agreements

See note 13 for a discussion of the Children's Hospital of Philadelphia (CHOP) license agreement.

In October 2013, the Company entered into a patent license agreement with Penn, as amended, for certain intellectual property licenses to be provided by Penn to the Company in the fields of research, development, manufacture and commercialization. The license agreement requires the Company to reimburse Penn for the patent costs related to the underlying licensed rights. The Company is obligated to make payments to Penn upon the occurrence of first commercial sale for certain licensed products in both the United States and Europe. The Company must pay a low-single-digit royalty based on net sales of licensed products by territory, which royalties will be reduced if the Company is required to license patents or intellectual property from third parties.

In December 2014, the Company entered into a license agreement with Penn for certain intellectual property licenses. The Company issued to Penn 200,000 shares of restricted common stock (note 10), which are subject to performance-based vesting conditions, in connection with the agreement and is obligated to make milestone payments upon the achievement of certain regulatory milestones up to $5.5 million in the aggregate. Additionally, the Company is obligated to pay Penn single-digit-royalties based on its net sales of licensed products by territory.

In October 2013, the Company entered into a license agreement with the University of Iowa Research Foundation (UIRF) for certain intellectual property licenses. The license agreement requires the Company to reimburse UIRF for the patent costs related to the underlying licensed rights. The Company is obligated to make payments to UIRF upon the occurrence of various development and commercialization milestones. The Company must pay a low-single-digit royalty to UIRF based on net sales of licensed products by territory.
(13) Related-party transactions

As of December 31, 2016, CHOP was considered a significant equity holder. In October 2013, the Company entered into technology and license agreements with CHOP for certain commercialization licenses to be provided to the Company in order to develop services, methods and marketable products for commercialization. The license agreement requires the Company to reimburse CHOP for the patent costs related to the underlying licensed rights incurred after the effective date. For the years ended December 31, 2015, 2016 and 2017, the Company recorded $0.7 million, $0.9 million and $0.8 million, respectively, of general and administrative expense related to the reimbursement of such patent costs in the accompanying consolidated statements of operations and comprehensive income (loss).

In 2013, the Company entered into a number of services agreements with CHOP. The Master Research Services Agreement provides for certain research, development and manufacturing services to be provided to the Company by CHOP. A separate Services Agreement provides for clinical, technical and administrative services to be provided by CHOP to the Company. For the years ended December 31, 2015, 2016 and 2017, the Company recorded $5.2 million, $7.4 million and $6.1 million, respectively, as research and development expense.

As of December 31, 2016, $1.1 million and $0.9 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP. As of December 31, 2017, $0.3 million and $1.4 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP.

(14) Collaboration and license agreements

(a) Pfizer

In December 2014, the Company entered into a global collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B. Under the agreement, the Company granted Pfizer an exclusive worldwide license to any Factor IX gene therapy that it develops, manufactures or commercializes prior to December 31, 2024. The Company will be primarily responsible for conducting all research and development activities through completion of Phase 1/2 clinical trials of hemophilia B product candidates. Pfizer and the Company will share development costs incurred under an agreed product development plan for each product candidate with the Company’s share of development costs under the agreement limited to $10.6 million. Following the completion of Phase 1/2 clinical trials, Pfizer will be primarily responsible for development, manufacture, regulatory approval and commercialization, including all costs associated therewith. In connection with this agreement, the Company received a $20.0 million upfront payment for the license in December 2014. As there is no stand-alone value for the license, the Company is recognizing revenue (through the estimated completion date of Phase 1/2 clinical trials). In December of both 2015 and 2016, the Company earned a $15.0 million milestone payment. The $15.0 million payment earned in 2016 is included in other receivables on the accompanying consolidated balance sheet as of December 31, 2016. In November 2017, the Company amended its global collaboration agreement with Pfizer. Under the terms of this amendment, the Company received a $10.0 million upfront payment and is eligible to receive an additional $15.0 million in payments upon completion of certain transition activities. The $25.0 million of consideration is being recognized as revenue over the remaining estimated performance period associated with the global collaboration agreement. During the years ended December 31, 2015, 2016 and 2017, the Company recognized $20.2 million, $20.2 million and $12.1 million of revenue, respectively. As of December 31, 2017, there is $12.0 million of current deferred revenue on the consolidated balance sheet. During the years ended December 31, 2015, 2016 and 2017, the Company recorded $1.3 million, $2.4 million and $2.9 million, respectively, as a reduction to research and development expenses for the reimbursement of costs from Pfizer.

The Company is eligible to receive up to an additional $230.0 million in aggregate milestone payments, $110.0 million of which relate to potential development, regulatory and commercial milestones for the first product candidate to achieve each milestone and $120.0 million of which relate to potential regulatory milestones for additional product candidates. In addition, the Company is entitled to receive royalties calculated as a low-teem percentage of net sales of licensed products. The royalties may be subject to certain reductions, including for a specified portion of royalty payments that Pfizer may become required to pay under any third-party license agreements, subject to a minimum royalty. Under the agreement, the Company remains solely responsible for the payment of license payments payable by the Company under specified license agreements.

The agreement will expire on a country-by-country basis upon the latest of: (i) the expiration of the last-to-expire valid claim, as defined in the agreement, in licensed patent rights covering a licensed product; (ii) the expiration of the last-to-expire regulatory exclusivity granted with respect to a licensed product; or (iii) 15 years after the first commercial sale of the last licensed product to be launched, in each case, in the applicable country. Pfizer may terminate the agreement on a licensed product-by-licensed product and country-by-country basis, or in its entirety, for any or no reason subject to notice requirements.

F-21
In February 2018, the Company entered into a supply agreement with Pfizer to begin production in 2018 for one batch of drug substance expected to be used for Phase 3 development. The Company will receive $7.0 million upfront and will receive up to $7.0 million upon delivery.

**b) Selecta**

In December 2016, the Company entered into a License and Option Agreement (the License Agreement) with Selecta that provides the Company with exclusive worldwide rights to Selecta’s proprietary Synthetic Vaccine Particles (SVP™) platform technology for co-administration with gene therapy targets. Under the terms of the License Agreement, Selecta has granted the Company certain exclusive, worldwide, royalty-bearing licenses to Selecta’s intellectual property and know-how relating to its SVP technology to research, develop and commercialize gene therapies for factor VIII, an essential blood clotting protein relevant to the treatment of hemophilia A, which is the initial target under the license. In addition, for a specified period of time, the Company may exercise options to research, develop and commercialize gene therapies utilizing the SVP technology for up to four additional targets, subject to the Company’s payment of the applicable option exercise fee, in a range of $1.4 million to $2.0 million depending on the incidence of the applicable indication, to Selecta in each case.

Pursuant to a letter agreement (Letter Agreement), entered into between the Company and Selecta on June 6, 2017, Selecta agreed to reimburse the Company for all costs and expenses related to research and development for any licensed products for a specified amount of time, up to an agreed upon cap. Additionally, the Company has agreed to reimburse Selecta in respect of full-time equivalents and out-of-pocket costs incurred in performing certain tasks or assistance specifically requested by the Company. Selecta retains the responsibility to manufacture the Company’s preclinical, clinical and commercial requirements for the SVP technology, subject to the terms of the License Agreement.

In connection with the execution of the License Agreement, the Company paid Selecta an upfront payment of $10.0 million in December 2016. Additional payments in the aggregate of $5.0 million were paid in June 2017 and October 2017 pursuant to the terms of the License Agreement and the Letter Agreement. On a target-by-target basis, the Company will be responsible to pay up to an aggregate of $430.0 million in milestone payments for each target, with up to $65.0 million being based on the Company’s achievement of specified development and regulatory milestones and up to $365.0 million for commercial milestones, as well as tiered royalties on global net sales at percentages ranging from mid-single to low-double digits. For a period of three years, the Company has the right to fund up to 50% of any development or regulatory milestone payable to Selecta by issuing to Selecta shares of the Company’s common stock having a fair market value equal to the percentage of such development or regulatory milestone, as applicable. The License Agreement will continue on a country-by-country and product-by-product basis until the expiration of the Company's royalty payment obligations with respect to such product in such country unless earlier terminated by the parties. The License Agreement may be terminated by the Company for convenience upon 90 days’ notice and the Company will not be required to make any payments. Either party may terminate the License Agreement on a target-by-target basis for material breach with respect to such target.

In connection with the License Agreement, the Company entered into a Stock Purchase Agreement (SPA) with Selecta pursuant to which the Company purchased 197,238 unregistered shares of Selecta’s common stock for $5.0 million in December 2016. An additional 324,362 unregistered shares of Selecta's common stock were purchased for $5.0 million in June 2017, and 205,254 unregistered shares of Selecta’s common stock were purchased for $5.0 million in October 2017. The fair value of these shares is classified as available-for-sale securities at December 31, 2017.

In December 2016, the Company accounted for payments under the License Agreement and SPA as a basket transaction and allocated the $15.0 million in cash payments to the shares of Selecta’s common stock and the License Agreement in the amounts of $3.5 million and $11.5 million, respectively. The Company calculated the $3.5 million allocated to the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $11.5 million to the License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.

In June 2017, the Company accounted for the payments under the License Agreement, Letter Agreement and SPA as a basket transaction and allocated the $7.5 million in cash payments to the shares of Selecta’s common stock and the License Agreement in the amounts of $4.4 million and $3.1 million, respectively. The Company calculated the $4.4 million allocated to the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $3.1 million to the License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.

In October 2017, the Company accounted for the payments under the License Agreement, Letter Agreement and SPA as a basket transaction and allocated the $7.5 million in cash payments to the shares of Selecta’s common stock and the License Agreement in the amounts of $4.1 million and $3.4 million, respectively. The Company calculated the $4.1 million allocated to the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $3.4 million to the License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.
(15) Income taxes

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the Tax Act). The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the U.S. federal corporate tax rate from 35 percent to 21 percent; eliminating the corporate alternative minimum tax (AMT) and changing how existing AMT credits can be realized; creating a new limitation on deductible interest expense; changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017; limitations on the deductibility of certain executive compensation; and changes to the calculation of the orphan drug credit.

In December 2017, the SEC issued Staff Accounting Bulletin No. 118 (SAB 118), which addresses situations where the accounting is incomplete for the income tax effects of the Tax Act. SAB 118 directs taxpayers to consider the impact of the Tax Act as “provisional” when the Company does not have the necessary information available, prepared or analyzed (including computations) to finalize the accounting for the change in tax law. Companies are provided a measurement period of up to one year to obtain, prepare, and analyze information necessary to finalize the accounting for provisional amounts or amounts that cannot be estimated as of December 31, 2017.

With regards to the Tax Act impact on the tax provision as it relates to the Company for the year ended December 31, 2017, the Company has recognized the provisional impact of tax reform related to the revaluation of deferred tax assets and liabilities from 35% to 21% of $44.9 million of tax expense, which is offset by a reduction in the valuation allowance.

As a result of changes made by the Tax Act, starting with executive compensation paid in 2018, Section 162(m) of the Internal Revenue Code will limit the Company from deducting compensation, including performance-based compensation, in excess of $1 million paid to certain executives. The only exception to this rule is for compensation that is paid pursuant to a binding contract in effect on November 2, 2017 that would have otherwise been deductible under the prior Section 162(m) rules. The Company has not yet completed an analysis of the binding contract requirement on the various compensation plans to determine the impact of the law change that may affect its deferred tax asset for stock compensation.

With regards to the one-time transition tax, the Company did not record any tax liability as it believes that the accumulated earnings and profits of foreign subsidiaries will be in a deficit position. Because of the complexity of the new international tax provisions included in the Tax Act that are not applicable to the Company until 2018, and the Company's recent international expansion, the Company is continuing to evaluate these provisions of the Tax Act and the application of ASC 740, Income Taxes.

The Company will continue to refine its calculations as additional analysis is completed related to the Tax Act. Additional information that may affect its provisional amounts would include further clarification and guidance on how the IRS will implement tax reform, including guidance with respect to the above, further clarification and guidance on how state taxing authorities will implement tax reform and the related effect on its state income tax returns, completion of its 2017 tax return filings, and the potential for additional guidance from the SEC or the FASB related to tax reform. The accounting is expected to be completed when the Company's 2017 U.S. corporate income tax return is filed in 2018.

Loss before income taxes attributable to domestic and international operations, consists of the following:

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015</td>
</tr>
<tr>
<td>Domestic</td>
<td>(47,125,778)</td>
</tr>
<tr>
<td>Foreign</td>
<td>(842,898)</td>
</tr>
<tr>
<td>Loss before income taxes</td>
<td>$ (47,125,778)</td>
</tr>
</tbody>
</table>

F-23
Income tax expense (benefit) consists of the following:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current tax:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domestic</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Foreign</td>
<td>—</td>
<td>—</td>
<td>110,305</td>
</tr>
<tr>
<td><strong>Deferred tax:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domestic</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Foreign</td>
<td>—</td>
<td>—</td>
<td>(1,073,346)</td>
</tr>
<tr>
<td><strong>Total income tax benefit</strong></td>
<td>$</td>
<td>$</td>
<td>$(963,041)</td>
</tr>
</tbody>
</table>

A reconciliation of income tax benefit computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Federal income tax benefit at statutory rate</strong></td>
<td>34.0%</td>
<td>34.0%</td>
<td>34.0%</td>
</tr>
<tr>
<td>State and local tax, net of federal benefit</td>
<td>8.0%</td>
<td>10.4%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Permanent differences</td>
<td>(2.7)</td>
<td>3.1%</td>
<td>(0.3)%</td>
</tr>
<tr>
<td>Tax credits</td>
<td>13.1%</td>
<td>9.1%</td>
<td>9.2%</td>
</tr>
<tr>
<td><strong>Tax Cuts and Jobs Act impact</strong></td>
<td>—%</td>
<td>—%</td>
<td>(17.6)%</td>
</tr>
<tr>
<td>Foreign rate differential</td>
<td>—%</td>
<td>(0.1)%</td>
<td>(1.3)%</td>
</tr>
<tr>
<td>Change in valuation allowance</td>
<td>(52.4)%</td>
<td>(56.5)%</td>
<td>(33.9)%</td>
</tr>
<tr>
<td>Effective income tax rate</td>
<td>—%</td>
<td>—%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes and for net operating loss and tax credit carryforwards. The significant components of the Company’s deferred tax assets are comprised of the following:

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deferred tax assets (liabilities):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net operating loss carryforwards</td>
<td>$55,710,846</td>
<td>$114,152,143</td>
</tr>
<tr>
<td>Tax credit carryforwards</td>
<td>$28,327,477</td>
<td>$51,585,618</td>
</tr>
<tr>
<td>Stock-based compensation</td>
<td>$10,342,547</td>
<td>$14,643,667</td>
</tr>
<tr>
<td>Deferred rent</td>
<td>$3,356,430</td>
<td>$4,697,221</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>$4,057,998</td>
<td>$956,071</td>
</tr>
<tr>
<td>Accruals and other</td>
<td>$9,262,530</td>
<td>$8,997,857</td>
</tr>
<tr>
<td><strong>Total deferred tax assets</strong></td>
<td>111,057,828</td>
<td>195,032,577</td>
</tr>
<tr>
<td><strong>Less valuation allowance</strong></td>
<td>(107,616,937)</td>
<td>(193,795,798)</td>
</tr>
<tr>
<td><strong>Net deferred tax assets</strong></td>
<td>$3,440,891</td>
<td>$1,236,779</td>
</tr>
<tr>
<td><strong>Intangible assets</strong></td>
<td>$1,936,250</td>
<td>—</td>
</tr>
<tr>
<td><strong>Fixed assets</strong></td>
<td>(2,504,876)</td>
<td>(1,236,779)</td>
</tr>
<tr>
<td><strong>Total deferred tax liabilities</strong></td>
<td>$4,441,126</td>
<td>$1,236,779</td>
</tr>
<tr>
<td><strong>Net deferred tax liability</strong></td>
<td>$(1,000,235)</td>
<td>$—</td>
</tr>
</tbody>
</table>
As of December 31, 2017, the Company had U.S. federal net operating loss carryforwards of $331.0 million, which may be available to offset future income tax liabilities and will expire beginning in 2034. As of December 31, 2017, the Company also had U.S. state net operating loss carryforwards of $342.8 million, which may be available to offset future income tax liabilities and will expire beginning in 2034.

The Company has recorded a full valuation allowance against its net deferred tax assets as of December 31, 2017 and 2016, respectively, because the Company has determined that it is more likely than not that these assets will not be fully realized due to historic net operating losses incurred. The Company experienced a net change in valuation allowance of $73.8 million and $86.2 million in the years ended December 31, 2016 and 2017, respectively.

As of December 31, 2017, the Company had federal research and development and orphan drug tax credit carryforwards of $46.9 million and $4.6 million, respectively, available to reduce future tax liabilities, which expire beginning in 2034.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed financing since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal, state, and foreign jurisdictions, where applicable. The company’s tax years are still open under status from 2014 to present. All open years may be examined to the extent that tax credit or net operating loss carryforward are used in future periods. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2017, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company’s consolidated statements of operations.

(16) Subsequent events

In January 2018, the Company entered into a license and commercialization agreement with Novartis Pharma AG (Novartis) for the development and commercialization of investigational voretigene neparvovec outside the United States. Novartis paid the Company a non-refundable, non-creditable, one-time cash payment of $105.0 million. The Company is eligible to receive an additional $25.0 million cash payment if investigational voretigene neparvovec is approved by the European Medicines Agency, as well as an aggregate $40.0 million in cash based upon the achievement of certain aggregate net sales levels in certain markets outside the United States. In addition, the Company is entitled to royalty payments at a flat mid-twenties percentage of net sales on a royalty-region by royalty-region basis, subject to reduction and extension in certain circumstances. The Company will manufacture and supply all of the requirements of Novartis for voretigene neparvovec.
(17) Selected quarterly financial data (unaudited)

The following table contains quarterly financial information for 2016 and 2017. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

### 2016 (1)

<table>
<thead>
<tr>
<th></th>
<th>First quarter</th>
<th>Second quarter</th>
<th>Third quarter</th>
<th>Fourth quarter</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenues</td>
<td>$1,288,628</td>
<td>$1,288,629</td>
<td>$1,302,789</td>
<td>$16,302,789</td>
<td>$20,182,835</td>
</tr>
<tr>
<td>Research and development</td>
<td>18,251,900</td>
<td>19,621,536</td>
<td>22,384,109</td>
<td>26,121,860</td>
<td>86,379,405</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>11,132,146</td>
<td>11,132,146</td>
</tr>
<tr>
<td>General and administrative</td>
<td>8,873,861</td>
<td>10,676,752</td>
<td>12,049,954</td>
<td>16,469,750</td>
<td>48,070,317</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>27,125,761</td>
<td>30,298,288</td>
<td>34,434,063</td>
<td>53,723,756</td>
<td>145,581,868</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(25,837,133)</td>
<td>(29,009,659)</td>
<td>(33,131,274)</td>
<td>(37,420,967)</td>
<td>(125,399,033)</td>
</tr>
<tr>
<td>Basic and diluted net loss per common share</td>
<td>$ (0.95)</td>
<td>$ (1.04)</td>
<td>$ (1.07)</td>
<td>$ (1.21)</td>
<td>$ (4.29)</td>
</tr>
</tbody>
</table>

### 2017 (1)

<table>
<thead>
<tr>
<th></th>
<th>First quarter</th>
<th>Second quarter</th>
<th>Third quarter</th>
<th>Fourth quarter</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenues</td>
<td>$1,274,467</td>
<td>$1,483,233</td>
<td>$1,899,575</td>
<td>$7,408,369</td>
<td>$12,065,644</td>
</tr>
<tr>
<td>Research and development</td>
<td>32,348,249</td>
<td>32,989,267</td>
<td>39,341,386</td>
<td>30,481,145</td>
<td>135,160,047</td>
</tr>
<tr>
<td>Acquired in-process research and development</td>
<td>386,784</td>
<td>3,070,358</td>
<td>1,750,000</td>
<td>3,397,116</td>
<td>8,604,258</td>
</tr>
<tr>
<td>Impairment of acquired in-process research and development</td>
<td>—</td>
<td>15,696,017</td>
<td>—</td>
<td>—</td>
<td>15,696,017</td>
</tr>
<tr>
<td>General and administrative</td>
<td>21,413,818</td>
<td>26,728,606</td>
<td>26,640,443</td>
<td>36,340,380</td>
<td>111,123,247</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>54,128,851</td>
<td>78,484,248</td>
<td>67,731,829</td>
<td>70,218,641</td>
<td>270,583,569</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(52,874,384)</td>
<td>(77,001,015)</td>
<td>(65,832,254)</td>
<td>(62,810,272)</td>
<td>(258,517,925)</td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (52,289,332)</td>
<td>$ (74,359,781)</td>
<td>$ (65,011,911)</td>
<td>$ (61,820,948)</td>
<td>(253,481,972)</td>
</tr>
<tr>
<td>Basic and diluted net loss per common share</td>
<td>$ (1.70)</td>
<td>$ (2.40)</td>
<td>$ (1.90)</td>
<td>$ (1.68)</td>
<td>$ (7.63)</td>
</tr>
</tbody>
</table>

(1) The sum of the quarterly per share amounts may not equal per share amounts reported for the year due to rounding.

F-26
Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: February 27, 2018

SPARK THERAPEUTICS, INC.

By: /s/ Jeffrey D. Marrazzo

Jeffrey D. Marrazzo
Chief Executive Officer
(Principal Executive Officer)

By: /s/ Stephen W. Webster

Stephen W. Webster
Chief Financial Officer
(Principal Financial Officer)

Pursuant to the requirements of the Securities and Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

<table>
<thead>
<tr>
<th>Signature</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>/s/ Jeffrey D. Marrazzo</td>
<td>Director and Chief Executive Officer</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Jeffrey D. Marrazzo</td>
<td>(Principal Executive Officer)</td>
<td></td>
</tr>
<tr>
<td>/s/ Stephen W. Webster</td>
<td>Chief Financial Officer</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Stephen W. Webster</td>
<td>(Principal Financial and Accounting Officer)</td>
<td></td>
</tr>
<tr>
<td>/s/ Katherine A. High, M.D.</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Katherine A. High, M.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Steven M. Altschuler, M.D.</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Steven M. Altschuler, M.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Lars Ekman, M.D., Ph.D.</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Lars Ekman, M.D., Ph.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Anand Mehra, M.D.</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Anand Mehra, M.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Vincent Milano</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Vincent Milano</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Robert Perez</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Robert Perez</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Elliott Sigal, M.D., Ph.D.</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Elliott Sigal, M.D., Ph.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Lota Zoth, CPA</td>
<td>Director</td>
<td>February 27, 2018</td>
</tr>
<tr>
<td>Lota Zoth, CPA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
LEASE

THIS LEASE (“Lease”) is entered into as of November 20, 2017, between BRANDYWINE 3025 MARKET, LP, a Pennsylvania limited partnership (“Landlord”), and SPARK THERAPEUTICS, INC., a Delaware corporation (“Tenant”).

In consideration of the mutual covenants stated below, and intending to be legally bound, the parties covenant and agree as follows:

1. KEY DEFINED TERMS.

   (a) “Abatement Period” means the period that begins on the Commencement Date and ends on the day immediately prior to the 7-month anniversary of the Commencement Date. During the Abatement Period, no Fixed Rent is due or payable, but Tenant shall pay to Landlord: (i) Tenant’s Share (as defined in Section 5(a)) of Operating Expenses (as defined in Section 5(a)); (ii) utilities as set forth in Section 6; (iii) use and occupancy taxes; and (iv) all other amounts due Landlord with the exception of Fixed Rent.

   (b) “Additional Rent” means all costs and expenses other than Fixed Rent that Tenant is obligated to pay Landlord pursuant to this Lease.

   (c) “Broker” means Jones Lang LaSalle.

   (d) “Building” means the building located at 3001-3025 Market Street, Philadelphia, Pennsylvania 19104, containing approximately 282,709 rentable square feet. Landlord represents and warrants that the Building and the Premises have been measured in accordance with the Building Owners and Managers Association International Standard Method for Measuring Floor Area in Office Buildings, ANSI/BOMA Z65.1-2010.

   (e) “Business Hours” means the hours of 8:30 a.m. to 5:30 p.m. on weekdays, and 8:00 a.m. to 1:00 p.m. on Saturdays, excluding Building holidays.

   (f) “Commencement Date” means the date that is the earliest of: (i) the date on which Tenant first conducts any business in all or any portion of the Lower Level Space or Suite 200; (ii) Substantial Completion (as defined in Exhibit C) of the Leasehold Improvements (as defined in Exhibit C) in the Lower Level Space and Suite 200; or (iii) the Outside Commencement Date. The “Outside Commencement Date” means June 1, 2018; provided however, the Outside Commencement Date shall be pushed back on a day-for-day basis for each day, if any, that Substantial Completion is delayed due to Force Majeure Events (as defined in Section 25(g)) or Landlord Delay (as defined in Exhibit C).

   (g) “Common Areas” means, to the extent applicable, the lobby, parking facilities, passenger elevators, rooftop terrace, fitness or health center, plaza and sidewalk areas, multi-tenanted floor restrooms, and other similar areas of general access at the Project or designated for the benefit of Building tenants, and the areas on multi-tenant floors in the Building devoted to corridors, elevator lobbies, and other similar facilities serving the Premises.

   (h) “Delivery Date” means the date that Landlord and Tenant execute this Lease.

   (i) “Expiration Date” means the last day of the Term, or such earlier date of termination of this Lease pursuant to the terms hereof.

   (j) “Fixed Rent” means fixed rent in the amounts set forth below:

Office Lease
### With respect to Suite 200 only:

<table>
<thead>
<tr>
<th>TIME PERIOD</th>
<th>FIXED RENT PER R.S.F. OF SUITE 200</th>
<th>ANNUALIZED FIXED RENT</th>
<th>MONTHLY INSTALLMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commencement Date – end of Abatement Period</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
</tr>
<tr>
<td>Fixed Rent Start Date – end of Rent Period 1</td>
<td>$35.00</td>
<td>$1,842,925.00</td>
<td>$153,577.08</td>
</tr>
<tr>
<td>Rent Period 2</td>
<td>$35.88</td>
<td>$1,889,261.40</td>
<td>$157,438.45</td>
</tr>
<tr>
<td>Rent Period 3</td>
<td>$36.78</td>
<td>$1,936,650.90</td>
<td>$161,387.58</td>
</tr>
<tr>
<td>Rent Period 4</td>
<td>$37.70</td>
<td>$1,985,093.50</td>
<td>$165,424.46</td>
</tr>
<tr>
<td>Rent Period 5</td>
<td>$38.64</td>
<td>$2,034,589.20</td>
<td>$169,549.10</td>
</tr>
<tr>
<td>Rent Period 6</td>
<td>$39.61</td>
<td>$2,085,664.55</td>
<td>$173,805.38</td>
</tr>
<tr>
<td>Rent Period 7</td>
<td>$40.60</td>
<td>$2,137,793.00</td>
<td>$178,149.42</td>
</tr>
<tr>
<td>Rent Period 8</td>
<td>$41.62</td>
<td>$2,191,501.10</td>
<td>$182,625.09</td>
</tr>
<tr>
<td>Rent Period 9</td>
<td>$42.66</td>
<td>$2,246,262.30</td>
<td>$187,188.53</td>
</tr>
<tr>
<td>Rent Period 10</td>
<td>$43.73</td>
<td>$2,302,603.15</td>
<td>$191,883.60</td>
</tr>
<tr>
<td>Rent Period 11</td>
<td>$44.82</td>
<td>$2,359,997.10</td>
<td>$196,666.43</td>
</tr>
<tr>
<td>Rent Period 12</td>
<td>$45.94</td>
<td>$2,418,970.70</td>
<td>$201,580.89</td>
</tr>
<tr>
<td>Rent Period 13</td>
<td>$47.09</td>
<td>$2,479,523.95</td>
<td>$206,627.00</td>
</tr>
<tr>
<td>Rent Period 14</td>
<td>$48.27</td>
<td>$2,541,654.55</td>
<td>$211,804.74</td>
</tr>
<tr>
<td>Rent Period 15 – End of Initial Term</td>
<td>$49.48</td>
<td>$2,605,369.40</td>
<td>$217,114.12</td>
</tr>
</tbody>
</table>

### With respect to the Lower Level Space only:

<table>
<thead>
<tr>
<th>TIME PERIOD</th>
<th>FIXED RENT PER R.S.F. OF LOWER LEVEL SPACE</th>
<th>ANNUALIZED FIXED RENT</th>
<th>MONTHLY INSTALLMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commencement Date – end of Abatement Period</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
</tr>
<tr>
<td>Fixed Rent Start Date – end of Rent Period 1</td>
<td>$17.50</td>
<td>$120,032.50</td>
<td>$10,002.71</td>
</tr>
<tr>
<td>Rent Period 2</td>
<td>$17.94</td>
<td>$123,050.46</td>
<td>$10,254.21</td>
</tr>
<tr>
<td>Rent Period 3</td>
<td>$18.39</td>
<td>$126,137.01</td>
<td>$10,511.42</td>
</tr>
<tr>
<td>Rent Period 4</td>
<td>$18.85</td>
<td>$129,292.15</td>
<td>$10,774.35</td>
</tr>
<tr>
<td>Rent Period 5</td>
<td>$19.32</td>
<td>$132,515.88</td>
<td>$11,042.99</td>
</tr>
<tr>
<td>Rent Period 6</td>
<td>$19.80</td>
<td>$135,808.20</td>
<td>$11,317.55</td>
</tr>
<tr>
<td>Rent Period 7</td>
<td>$20.30</td>
<td>$139,237.70</td>
<td>$11,603.14</td>
</tr>
<tr>
<td>Rent Period 8</td>
<td>$20.81</td>
<td>$142,735.79</td>
<td>$11,894.65</td>
</tr>
<tr>
<td>Rent Period 9</td>
<td>$21.33</td>
<td>$146,304.47</td>
<td>$12,191.87</td>
</tr>
<tr>
<td>Rent Period 10</td>
<td>$21.86</td>
<td>$149,937.74</td>
<td>$12,494.81</td>
</tr>
<tr>
<td>Rent Period 11</td>
<td>$22.41</td>
<td>$153,710.19</td>
<td>$12,809.18</td>
</tr>
<tr>
<td>Rent Period 12</td>
<td>$22.97</td>
<td>$157,551.23</td>
<td>$13,129.27</td>
</tr>
<tr>
<td>Rent Period 13</td>
<td>$23.54</td>
<td>$161,460.86</td>
<td>$13,455.07</td>
</tr>
<tr>
<td>Rent Period 14</td>
<td>$24.13</td>
<td>$165,507.67</td>
<td>$13,792.31</td>
</tr>
<tr>
<td>Rent Period 15 – End of Initial Term</td>
<td>$24.73</td>
<td>$169,623.07</td>
<td>$14,135.26</td>
</tr>
</tbody>
</table>
With respect to Suite 300 only:

<table>
<thead>
<tr>
<th>TIME PERIOD</th>
<th>FIXED RENT PER R.S.F. OF SUITE 300</th>
<th>ANNUALIZED FIXED RENT</th>
<th>MONTHLY INSTALLMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suite 300 Abatement Period (if any)</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
</tr>
<tr>
<td>Suite 300 Rent Commencement Date – end of Rent Period 2</td>
<td>$35.88</td>
<td>$1,727,801.40</td>
<td>$147,959.08</td>
</tr>
<tr>
<td>Rent Period 3</td>
<td>$36.78</td>
<td>$1,771,140.90</td>
<td>$151,286.96</td>
</tr>
<tr>
<td>Rent Period 4</td>
<td>$37.70</td>
<td>$1,815,443.50</td>
<td>$155,059.10</td>
</tr>
<tr>
<td>Rent Period 5</td>
<td>$38.64</td>
<td>$1,860,709.20</td>
<td>$158,951.63</td>
</tr>
<tr>
<td>Rent Period 6</td>
<td>$39.61</td>
<td>$1,907,419.55</td>
<td>$162,924.42</td>
</tr>
<tr>
<td>Rent Period 7</td>
<td>$40.60</td>
<td>$1,955,093.00</td>
<td>$167,017.59</td>
</tr>
<tr>
<td>Rent Period 8</td>
<td>$41.62</td>
<td>$2,004,211.10</td>
<td>$171,191.03</td>
</tr>
<tr>
<td>Rent Period 9</td>
<td>$42.66</td>
<td>$2,054,292.30</td>
<td>$175,484.85</td>
</tr>
<tr>
<td>Rent Period 10</td>
<td>$43.73</td>
<td>$2,105,818.15</td>
<td>$179,858.93</td>
</tr>
<tr>
<td>Rent Period 11</td>
<td>$44.82</td>
<td>$2,158,307.10</td>
<td>$184,353.39</td>
</tr>
<tr>
<td>Rent Period 12</td>
<td>$45.94</td>
<td>$2,212,240.70</td>
<td>$188,968.25</td>
</tr>
<tr>
<td>Rent Period 13</td>
<td>$47.09</td>
<td>$2,267,618.95</td>
<td>$193,703.49</td>
</tr>
<tr>
<td>Rent Period 14</td>
<td>$48.27</td>
<td>$2,324,441.85</td>
<td>$198,559.12</td>
</tr>
<tr>
<td>Rent Period 15 – End of Initial Term</td>
<td>$49.48</td>
<td>$2,382,709.40</td>
<td>$203,359.12</td>
</tr>
</tbody>
</table>

(k) “Fixed Rent Start Date” means the day immediately following the end of the Abatement Period.

(l) “Initial Term” means the period commencing on the Commencement Date, and ending at 11:59 p.m. on: (i) if the Commencement Date is the first day of a calendar month, the day immediately prior to the 187-month anniversary of the Commencement Date; or (ii) if the Commencement Date is not the first day of a calendar month, the last day of the calendar month containing the 187-month anniversary of the Commencement Date.

(m) “Laws” means federal, state, county, and local governmental and municipal laws, statutes, ordinances, rules, regulations, codes, decrees, orders, and other such requirements, and decisions by courts in cases where such decisions are considered binding precedents in the state or commonwealth in which the Premises are located ("State"), and decisions of federal courts applying the laws of the State, including without limitation Title III of the Americans with Disabilities Act of 1990, 42 U.S.C. §12181 et seq. and its regulations.

(n) “Lower Level Space” means the following suites in the Building, which are deemed to contain 6,859 rentable square feet in the aggregate and are shown on Exhibit A attached hereto: (i) Suite 016, which is deemed to contain 1,684 rentable square feet; and (ii) Suite 026, which is deemed to contain 5,175 rentable square feet.

(o) “Premises” means, collectively, the Lower Level Space and Suite 200, and, from and after Suite 300 Commencement Date (as defined in Section 2(b) below), Suite 300.

(p) “Project” means the Building, together with the parcel of land upon which the Building is located, and all Common Areas.

(q) “Rent” means Fixed Rent and Additional Rent. Landlord may apply payments received from Tenant to any obligations of Tenant then due and owing without regard to any contrary Tenant instructions or requests.
Additional Rent shall be paid by Tenant in the same manner as Fixed Rent, without setoff, deduction, or counterclaim, except as otherwise expressly set forth in this Lease.

(r) “Rent Period” means, with respect to the first Rent Period, the period that begins on the Commencement Date and ends on the last day of the calendar month preceding the month in which the first anniversary of the Commencement Date occurs; thereafter each succeeding Rent Period shall commence on the day following the end of the preceding Rent Period, and shall extend for 12 consecutive months, except for Rent Period 15 which ends on the last day of the Initial Term.

(s) “Suite 200” means Suite 200 in the Building, as shown on Exhibit A attached hereto, which is deemed to contain 52,655 rentable square feet.

(t) “Suite 300” means Suite 300 in the Building, as shown on Exhibit A attached hereto, which is deemed to contain 48,155 rentable square feet.

(u) “Tenant’s NAICS Code” means Tenant’s 6-digit North American Industry Classification number under the North American Industry Classification System as promulgated by the Executive Office of the President, Office of Management and Budget, which is 541711.

(v) “Term” means the Initial Term together with any extension of the term of this Lease either pursuant to the express terms of this Lease or as otherwise agreed to by the parties in writing.

2. PREMISES.

(a) Landlord leases to Tenant, and Tenant leases from Landlord, the Premises for the Term subject to the terms and conditions of this Lease. Tenant accepts the Premises in their “AS IS”, “WHERE IS”, “WITH ALL FAULTS” condition except that Landlord shall: (i) provide Tenant with the Improvement Allowance (as defined in and pursuant to Exhibit C); (ii) provide Tenant with the Restroom Improvement Allowance (as defined in and pursuant to Exhibit C); (iii) perform any and all such additional repairs, maintenance, or replacements, if any, necessary to cause the Building and the Building’s structural, roof, electrical, mechanical, plumbing, and fire and life safety systems to be in good and proper working order and in full compliance with all applicable Laws as of the Delivery Date or, so long as Tenant’s legal occupancy of the Premises for the Permitted Use is not delayed, then in a timely manner (“Landlord’s Warranty Work”); and (iv) reimburse Tenant upon thirty (30) days’ invoice (together with reasonable supporting documentation and lien waivers) for costs incurred by Tenant in correcting and/or addressing material unexpected deficiencies related to Landlord’s Warranty Work in the Building and Premises discovered by Tenant in the planning and performance of the Leasehold Improvements (as defined in and pursuant to Exhibit C) and in all cases for additional costs incurred by Tenant with respect to demolition, remediation, and disposal of Hazardous Materials located within the Building or Premises during completion of the Leasehold Improvements and any initial leasehold improvements to the garden level or the fourth floor pursuant to Section 26 and 27, including, but not limited to, asbestos containing materials such as floor tile and mastic. Notwithstanding the foregoing, with respect to the removal of asbestos containing materials by Tenant during completion of the Leasehold Improvements and any initial leasehold improvements to the garden level or the fourth floor pursuant to Sections 26 or 27, Landlord and Tenant shall split equally all costs incurred by Tenant relating to the demolition, remediation and disposal of asbestos containing materials located within the Building or Premises during completion of the Leasehold Improvements or any initial leasehold improvements to the garden level or the fourth floor pursuant to Sections 26 or 27, provided if the total costs exceed $600,000 per floor (such that Tenant’s share of such costs would exceed $300,000 per floor), in addition to Landlord’s obligation to reimburse Tenant for the first $300,000 of such costs per floor (as Landlord’s 50% share of such costs), Landlord shall also pay 100% of any costs in excess of $600,000 per floor. On the Delivery Date, Landlord shall deliver possession of the Premises to Tenant for Tenant’s completion of the Leasehold Improvements. Landlord shall cooperate and coordinate the performance and scheduling of Landlord’s Warranty Work such that Landlord does not unreasonably interfere with, or delay, Tenant’s performance of the Leasehold Improvements.

(b) The Term for Suite 300 commences on the date (“Suite 300 Commencement Date”) that is the earliest of: (i) the date on which Tenant first conducts any business in all or any portion of Suite 300; (ii) Substantial
Completion of the Leasehold Improvements in Suite 300; or (ii) the Suite 300 Rent Commencement Date, and ends on the Expiration Date. The “Suite 300 Rent Commencement Date” means June 1, 2020; provided, however, the Suite 300 Rent Commencement Date shall be pushed back on a day-for-day basis for: (i) each day (if any) that Substantial Completion of the Leasehold Improvements in Suite 300 is delayed due to a Force Majeure Event or Landlord Delay (as defined in Exhibit C); and (ii) each day (if any) that the Suite 300 Delivery Date is delayed beyond May 1, 2019. The “Suite 300 Delivery Date” means the date that Landlord delivers possession of Suite 300 to Tenant in the condition Landlord is required to deliver the Lower Level Premises and Suite 200 to Tenant. The terms of Section 2(a) of this Lease shall apply with respect to the delivery of Suite 300 to Tenant. “Third Floor Space Abatement Period” means the period, if the Suite 300 Commencement Date occurs prior to the Suite 300 Rent Commencement Date, commencing on the Suite 300 Commencement Date and ending on the day prior to the Suite 300 Rent Commencement Date. During the Suite 300 Abatement Period (if any), no Fixed Rent is due or payable with respect to Suite 300, but Tenant shall pay to Landlord: (i) Tenant’s Share of Operating Expenses with respect to Suite 300; (ii) utilities as set forth in Section 6; and (ii) use and occupancy taxes with respect to Suite 300.

3. TERM; RENTABLE AREA. The Term shall commence on the Commencement Date. The terms and provisions of this Lease are binding on the parties upon Tenant’s and Landlord’s execution of this Lease notwithstanding a later Commencement Date for the Term. The rentable area of the Premises and the Building shall be deemed to be as stated in Section 1. By the Confirmation of Lease Term substantially in the form of Exhibit B attached hereto (“COLT”), Landlord shall notify Tenant of the Commencement Date, rentable square footage of the Premises and all other matters stated therein. The COLT shall be conclusive and binding on Tenant as to all matters set forth therein unless, within 15 days following delivery of the COLT to Tenant, Tenant contests any of the matters contained therein by notifying Landlord in writing of Tenant’s objections.

4. FIXED RENT; LATE FEE.

(a) Tenant covenants and agrees, except as otherwise expressly set forth in this Lease, to pay to Landlord during the Term, without notice, demand, setoff, deduction, or counterclaim, Fixed Rent in the amounts set forth in Section 1. The Monthly Installment of Fixed Rent, the monthly amount of Estimated Operating Expenses as set forth in Section 5, and any estimated amount of utilities as set forth in Section 6, shall be payable to Landlord in advance on or before the first day of each month of the Term. If the Fixed Rent Start Date is not the first day of a calendar month, then the Fixed Rent due for the partial month commencing on the Fixed Rent Start Date shall be prorated based on the number of days in such month. All Rent payments shall be made by electronic transfer as follows (or as otherwise directed in writing by Landlord to Tenant from time to time): (i) ACH debit of funds, provided Tenant shall first complete Landlord’s then-current forms authorizing Landlord to automatically debit Tenant’s bank account; or (ii) ACH credit of immediately available funds to an account designated by Landlord. “ACH” means Automated Clearing House network or similar system designated by Landlord. All Rent payments shall include the Building number and the Lease number, which numbers will be provided to Tenant in the COLT.

(b) Contemporaneously with Tenant’s execution and delivery of this Lease, Tenant shall pay to Landlord the monthly Fixed Rent for the first full calendar month after the Abatement Period.

(c) If Landlord does not receive the full payment from Tenant of any Rent when due under this Lease (without regard to any notice and/or cure period to which Tenant might be entitled), Tenant shall also pay to Landlord as Additional Rent a late fee in the amount of 5% of such overdue amount. Notwithstanding the foregoing, upon Tenant’s written request, Landlord shall waive the above-referenced late fee 1 time during any 12 consecutive months of the Term provided Tenant makes the required payment within 3 business days after receipt of notice of such late payment. With respect to any Rent payment (whether it be by check, ACH/wire, or other method) that is returned unpaid for any reason, Landlord shall have the right to assess a fee to Tenant as Additional Rent, which fee is currently $40.00 per returned payment.

5. OPERATING EXPENSES.

(a) Certain Definitions.
(i) “Janitorial Expenses” means all costs associated with trash and garbage removal, recycling, cleaning, and sanitizing the Building, including the Premises and the items of work set forth in Exhibit D attached hereto.

(ii) “Operating Expenses” means collectively Project Expenses, Janitorial Expenses, and Taxes.

(iii) “Project Expenses” means all costs and expenses paid, incurred, or accrued by Landlord in connection with the maintenance, operation, repair, and replacement of the Project including, without limitation: a management fee not to exceed 5% of gross rents from the Project; all costs associated with the removal of snow and ice from the Project; property management office rent; security measures; transportation program costs; capital expenditures, repairs, and replacements, if such capital expenditures, repairs and replacements are (x) required to comply with any applicable Laws that first came into effect after the Commencement Date, or are amended, become effective, or are interpreted differently after the Commencement Date or (y) intended to reduce other Project Expenses, and only if and to the extent of any actual savings resulting therefrom; and such capital expenditures, repairs and replacements shall constitute Project Expenses, only to the extent of the amortized costs of such capital item over the useful life of the improvement as reasonably determined by Landlord or, if greater, the actual savings created by such capital item for each year of the Term; concierge costs; all insurance premiums and deductibles paid or payable by Landlord with respect to the Project; and the cost of providing those services required to be furnished by Landlord under this Lease. Notwithstanding the foregoing, “Project Expenses” shall not include any of the following: (A) repairs or other work occasioned by fire, windstorm, or other insured casualty or by the exercise of the right of eminent domain to the extent Landlord actually receives insurance proceeds or condemnation awards therefor; (B) leasing commissions, accountants’, consultants’, auditors or attorneys’ fees, costs and disbursements and other expenses incurred in connection with negotiations or disputes with other tenants or prospective tenants or other occupants, or associated with the enforcement of any other leases or the defense of Landlord’s title or interest in the real property or any part thereof; (C) costs incurred by Landlord in connection with the original construction of the Building and related facilities; (D) costs (including permit, licenses and inspection fees) incurred in renovating or otherwise improving or decorating, painting, or redecorating leased space for other tenants or other occupants or vacant space; (E) interest on debt or amortization payments on any mortgage or deeds of trust or any other borrowings and any ground rent; (F) any compensation paid to clerks, attendants or other persons in commercial concessions operated by Landlord; (G) any fines or fees for Landlord’s failure to comply with Laws; (H) legal, accounting, and other expenses related to Landlord’s financing, refinancing, mortgaging, or selling the Building or the Project; (I) any increase in an insurance premium caused by the non-general office use, occupancy or act of another tenant; (J) costs for sculpture, decorations, painting or other objects of art in excess of amounts typically spent for such items in office buildings of comparable quality in the competitive area of the Building; (K) cost of any political, charitable, or civic contribution or donation; (L) reserves for repairs, maintenance, and replacements; (M) Taxes; (N) cost of utilities directly metered or submetered to Building tenants and paid separately by such tenants; (O) fines, interest, penalties, or liens arising by reason of Landlord’s failure to pay any Project Expenses when due, except that Project Expenses shall include interest or similar charges if the collecting authority permits such Project Expenses to be paid in installments with interest thereon, such payments are not considered overdue by such authority and Landlord pays the Project Expenses in such installments; (P) costs and expenses associated with hazardous waste or hazardous substances not generated or brought to the Project by Tenant or its agents including but not limited to the cleanup of such hazardous waste or hazardous substances and the costs of any litigation (including, but not limited to reasonable attorneys’ fees) arising out of the discovery of such hazardous waste or hazardous substances; (Q) the portion of any wages, salaries, fees, or fringe benefits paid to personnel above the level of regional property manager; (R) costs of extraordinary services provided to tenants of the Building or services to which Tenant is not entitled (including, without limitation, costs specially billed to and paid by specific tenants); (S) all costs relating to activities for the solicitation and execution of leases of space in the Building, including legal fees, real estate brokers’ commissions, expenses, fees, and advertising, moving expenses, design fees, rental concessions, rental credits, tenant improvement allowances, lease assumptions or any other cost and expenses incurred in the connection with the leasing of any space in the Building; (T) costs representing an amount paid to an affiliate of Landlord (exclusive of any management fee permitted under the Operating Expense inclusions) to the extent in excess of market rates for comparable services if rendered by unrelated third parties; (U) costs arising from Landlord’s default under this Lease or any other lease for space in the Building; (V) costs of selling the Project or any portion thereof or interest therein; (W) costs or expenses arising from the gross negligence or willful misconduct of Landlord or its agents or
employees; (X) costs incurred to remedy, repair, or otherwise correct violations of Laws that exist on the Commencement Date; (Y) ground rents or rentals payable by Landlord pursuant to any over-lease; (Z) cost of any HVAC, janitorial or other services provided to tenants on an extra cost basis after regular business hours; (AA) with the exception of the cafeteria and fitness facility, cost of installing, operating and maintaining any specialty service not available to Tenant, such as an observatory, broadcasting facilities, child or daycare; (BB) cost of correcting defects in the design, construction or equipment of, or latent defects in, the Building or the Project; (CC) cost of any work or services performed for any facility other than the Building; (DD) any cost of painting or decorating any interior parts of the Building other than common areas; (EE) costs of relamping all light fixtures in non-public areas of the Building including, without limitation, labor materials for light tubes, bulbs, starters and their equivalents; (FF) cost of initial cleaning and rubbish removal from the Building to be performed before final completion of the Building or tenant space; (GG) cost of initial landscaping of the Project; (HH) except as expressly provided above, cost of any item that, under generally accepted accounting principles, is properly classified as capital expenses; (II) lease payments for rental equipment (other than equipment for which depreciation is properly charged as an expense) that would constitute a capital expenditure if the equipment were purchased; (JJ) cost of the initial stock of tools and equipment for operation, repair, and maintenance of the Building or the Project; (KK) cost of acquiring, securing cleaning or maintaining sculptures, paintings and other works of art in excess of class A standards or not required by applicable Laws; (LL) direct costs or allocable costs (such as real estate taxes) associated with parking operations if there is a separate charge to Tenant, other than tenants or the public for parking; (MM) all other items for which another party compensates or pays so that Landlord shall not recover any item of cost more than once; (NN) costs of mitigation or impact fees or subsidies (however characterized), imposed or incurred prior to the date of the Lease or imposed or incurred solely as a result of another tenant’s or tenants’ use of the Building or their respective premises; (OO) costs associated with the initial construction of Drexel Square; or (PP) except as expressly set forth above, any charge for depreciation. Landlord shall not collect or be entitled to collect Operating Expenses from all of its tenants an amount in excess of 100% of the Operating Expenses actually incurred by Landlord. “ Drexel Square” means the Park Easement (and commonly referred to as Drexel Square) as defined in the Declaration of Easements, Covenants and Restrictions dated October 11, 2017.

(iv) “Taxes” means all taxes, assessments, and other governmental charges, including without limitation business improvement district charges, improvement contributions paid to business improvement districts or similar organizations, and special assessments for public improvements or traffic districts, that are levied or assessed against, or with respect to the ownership of, all or any portion of the Project during the Term or, if levied or assessed prior to the Term, are properly allocable to the Term, business property operating license charges, and reasonable real estate tax appeal expenditures incurred by Landlord. “Taxes” shall not include: (i) any inheritance, estate, succession, transfer, gift, franchise, corporation, net income or profit tax or capital levy that is or may be imposed upon Landlord; or (ii) any transfer tax or recording charge resulting from a transfer of the Building or the Project; provided, however, if at any time during the Term the method of taxation prevailing at the commencement of the Term shall be altered such that in lieu of or as a substitute in whole or in part for any Taxes now levied, assessed or imposed on real estate there shall be levied, assessed or imposed: (A) a tax on the rents received from such real estate; or (B) a license fee measured by the rents receivable by Landlord from the Premises or any portion thereof; or (C) a tax or license fee imposed upon the Premises or any portion thereof, then the same shall be included in Taxes. Tenant may not file or participate in any Tax appeals for any tax lot in the Project; provided that Landlord shall engage professionals to biennially review the Taxes and Landlord shall exercise prudent business judgment in deciding to appeal and pursue appeals of Taxes. Further, “Taxes” shall not include any sales, use, use and occupancy, transaction privilege, gross receipts, or other excise tax that may at any time be levied or imposed upon Tenant, or measured by any amount payable by Tenant under this Lease, whether such tax exists on the date of this Lease or is adopted hereafter (collectively, “Other Taxes”). As Additional Rent, Tenant shall pay all Other Taxes monthly or otherwise when due, whether collected by Landlord or collected directly by the applicable governmental agency.

(v) “Tenant’s Share” means the rentable square footage of the Premises divided by the rentable square footage of the Building on the date of calculation, which on the date of this Lease is stipulated to be 21.05% (and which shall be recalculated as of the Suite 300 Commencement Date). Tenant’s Share will change during the Term if the rentable square footage of the Premises and/or the Building changes.

(b) Commencing on the Commencement Date and continuing thereafter during the Term, Tenant shall pay to Landlord in advance on a monthly basis, payable pursuant to Section 5(c) below, Tenant’s Share of Operating
Expenses. To the extent that any Operating Expenses are incurred by Landlord (or Landlord’s affiliate(s)) for multiple buildings or uses, Landlord shall allocate such Operating Expenses to the Building on a commercially reasonable basis. If the Building is operated as part of a complex of buildings or in conjunction with other buildings or parcels of land, then Landlord may prorate the common expenses and costs with respect to each such building or parcel of land in such manner as Landlord, in its sole but reasonable judgment, shall determine. Landlord shall calculate Operating Expenses using generally accepted accounting principles, and may allocate certain categories of Operating Expenses to the applicable tenants on a commercially reasonable basis. Notwithstanding anything herein to the contrary, Operating Expenses associated with the repair, maintenance, replacement or operation of the Park shall be allocated among the buildings comprising Schuylkill Yards from time to time and Tenant’s Share of such costs shall be the rentable square footage of the Premises divided by the rentable square footage of all buildings in Schuylkill Yards, which shall be adjusted from time to time. “Schuylkill Yards” has the same meaning as such term in the Declaration of Easements, Covenants and Restrictions dated October 11, 2017. The “Park” is the park in Schuylkill Yards.

(c) For each calendar year (or portion thereof) for which Tenant has an obligation to pay any Operating Expenses, Landlord shall send to Tenant a statement of the monthly amount of projected Operating Expenses due from Tenant for such calendar year (“Estimated Operating Expenses”), and Tenant shall pay to Landlord such monthly amount of Estimated Operating Expenses as provided in Section 5(b), without further notice, demand, setoff, deduction, or counterclaim, except as otherwise expressly set forth in this Lease. As soon as administratively available after each calendar year but no later than 150 days following the end of such calendar year, Landlord shall send to Tenant a reconciliation statement of the actual Operating Expenses for the prior calendar year (“Reconciliation Statement”). If the amount actually paid by Tenant as Estimated Operating Expenses exceeds the amount due per the Reconciliation Statement, Tenant shall receive a credit in an amount equal to the overpayment, which credit shall be applied towards future Rent until fully credited. If the credit exceeds the aggregate future Rent owed by Tenant, and there is no Event of Default, Landlord shall pay the excess amount to Tenant within 30 days after delivery of the Reconciliation Statement. If Landlord has undercharged Tenant, then Landlord shall send Tenant an invoice setting forth the additional amount due, which amount shall be paid in full by Tenant within 30 days after receipt of such invoice.

(d) If, during the Term, less than 95% of the rentable area of the Building is or was occupied by tenants, Project Expenses, Janitorial Expenses, and Project Utility Costs (other than metered electric costs separately billed to a tenant) shall be deemed for such year to be an amount equal to the costs that would have been incurred had the occupancy of the Building been at least 95% throughout such year, as reasonably determined by Landlord and taking into account that certain expenses fluctuate with the Building’s occupancy level (e.g., Janitorial Expenses) and certain expenses do not so fluctuate (e.g., landscaping). In addition, if Landlord is not obligated or otherwise does not offer to furnish an item or a service to a particular tenant or portion of the Building (e.g., if a tenant separately contracts with an office cleaning firm to clean such tenant’s premises) and the cost of such item or service would otherwise be included in Project Expenses, Janitorial Expenses, and/or Project Utility Costs, Landlord shall equitably adjust the Project Expenses, Janitorial Expenses, or Project Utility Costs so the cost of the item or service is shared only by tenants actually receiving such item or service. All payment calculations under this Section shall be prorated for any partial calendar years during the Term and all calculations shall be based upon Project Expenses, Janitorial Expenses, and Project Utility Costs as grossed-up in accordance with the terms of this Lease. Tenant’s obligations under this Section shall survive the Expiration Date.

(e) If Landlord or any affiliate of Landlord has elected to qualify as a real estate investment trust (“REIT”), any service required or permitted to be performed by Landlord pursuant to this Lease, the charge or cost of which may be treated as impermissible tenant service income under the laws governing a REIT, may be performed by an independent contractor of Landlord, Landlord’s property manager, or a taxable REIT subsidiary that is affiliated with either Landlord or Landlord’s property manager (each, a “Service Provider”). If Tenant is subject to a charge under this Lease for any such service, then at Landlord’s direction Tenant shall pay the charge for such service either to Landlord for further payment to the Service Provider or directly to the Service Provider and, in either case: (a) Landlord shall credit such payment against any charge for such service made by Landlord to Tenant under this Lease; and (b) Tenant’s payment of the Service Provider shall not relieve Landlord from any obligation under this Lease concerning the provisions of such services.
Provided there is no outstanding Event of Default by Tenant under this Lease, Tenant shall have the right, at its sole cost and expense, to cause Landlord’s records related to a Reconciliation Statement to be audited provided: (i) Tenant provides notice of its intent to audit such Reconciliation Statement within 120 days after receipt of the Reconciliation Statement; (ii) the audit is performed by a certified public accountant that has not been retained on a contingency basis or other basis where its compensation relates to the cost savings of Tenant; (iii) any such audit may not occur more frequently than once during each 12-month period of the Term, nor apply to any year prior to the year of the then-current Reconciliation Statement being reviewed; (iv) the audit is completed within 2 months after the date that Landlord makes all of the necessary and applicable records available to Tenant or Tenant’s auditor; (v) the contents of Landlord’s records shall be kept confidential by Tenant, its auditor, and its other professional advisors, other than as required by applicable Law, or in the event of a judicial proceeding, but solely limited to information that is required to be disclosed in the judicial proceeding; and (vi) if Tenant’s auditor determines that an overpayment is due Tenant, Tenant’s auditor shall produce a detailed report addressed to both Landlord and Tenant, which report shall be delivered within 30 days after Tenant’s auditor’s completion of the audit. During completion of Tenant’s audit, Tenant shall nonetheless timely pay all of Tenant’s Share of Operating Expenses without setoff or deduction. If Tenant’s audit report discloses any discrepancy, Landlord and Tenant shall use good faith efforts to resolve the dispute. If the parties are unable to reach agreement within 20 days after Landlord’s receipt of the audit report, Tenant shall have the right to refer the matter to a mutually acceptable independent certified public accountant, who shall work in good faith with Landlord and Tenant to resolve the discrepancy; provided if Tenant does not so do within such 20-day period, Landlord’s calculations and the Reconciliation Statement at issue shall be deemed final and accepted by Tenant. The fees and costs of such independent accountant to which such dispute is referred shall be borne by the unsuccessful party. Within 30 days after resolution of the dispute, whether by agreement of the parties or a final decision of an independent accountant, Landlord shall pay or credit to Tenant, or Tenant shall pay to Landlord, as the case may be, all unpaid Operating Expenses due and owing, and if it is determined that Tenant was overcharged by more than 5% of the amount of Tenant’s Share of the Project Expenses for such year, Landlord shall reimburse Tenant the actual, reasonable cost of Tenant’s audit (including legal and accounting costs), not to exceed $5,000.

6. UTILITIES.

(a) Commencing on the Commencement Date, and continuing throughout the Term, Tenant shall pay for utility services as follows without setoff, deduction, or counterclaim (except as otherwise expressly set forth in this Lease): (i) Tenant shall pay directly to the applicable utility service provider for any utilities that are separately metered to the Premises; (ii) Tenant shall pay Landlord for any utilities that are separately submetered to the Premises based upon Tenant’s submetered usage, as well as for any maintenance and replacement costs associated with such submeters (provided such replacement costs shall only apply to submeters utilized to measure Tenant’s supplemental HVAC); (iii) Tenant shall pay Landlord for its proportionate share of any utilities serving the Premises that are not separately metered or submetered based upon its share of the area served by the applicable meter or submeter; and (iv) Tenant shall pay Landlord for Tenant’s Share of all utilities serving the Project, excluding the costs of utilities that are directly metered or submetered to Building tenants or paid separately by such tenants (“Project Utility Costs”). As of the date hereof, to Landlord’s actual knowledge, but without prejudice to Landlord’s right to make modifications from time to time:

• Electric for the lights and plugs of the Premises is currently separately submetered. As part of the Leasehold Improvements, Tenant shall install submeters to measure its electric usage associated with HVAC for both office and lab space, as well as for any steam and chilled water usage. Notwithstanding anything to the contrary in this Lease, Landlord shall have the right to install meters, submeters, or other energy-reducing systems in the Premises at any time to measure any or all utilities serving the Premises, the costs of which shall be included in Project Expenses. For those utilities set forth in subsections (ii) – (iv) above, Landlord shall have the right to either invoice Tenant for such utilities separately as Additional Rent, or include such utilities in amounts due as Operating Expenses. Landlord shall have the right to reasonably estimate the utility charge, which estimated amount shall be payable to Landlord within 30 days after receipt of an invoice therefor and may be included along with the invoice for Project Expenses, provided Landlord shall be required to reconcile on an annual basis based on utility invoices received for such period. The cost of utilities payable by Tenant under this Section shall include all applicable taxes and Landlord’s then-current charges for reading the applicable meters, provided Landlord shall have the right to engage a third party to read the submeters, and Tenant shall reimburse Landlord for both the utilities.
consumed as evidenced by the meters plus the reasonable market costs for reading the meters within 30 days after receipt of an invoice therefor. Tenant shall pay such rates as Landlord may establish from time to time, which shall not be in excess of any applicable rates chargeable by Law, or in excess of the general service rate or other such rate that would apply to Tenant’s consumption if charged by the utility or municipality serving the Building or general area in which the Building is located. If Tenant fails to pay timely any direct-metered utility charges from the applicable utility provider, Landlord shall have the right but not the obligation to pay such charges on Tenant’s behalf and bill Tenant for such costs plus the Administrative Fee (as defined in Section 17), which amount shall be payable to Landlord as Additional Rent within 30 days after receipt of an invoice therefor.

(b) For any separately metered utilities, Landlord is hereby authorized to request and obtain, on behalf of Tenant, Tenant’s utility consumption data from the applicable utility provider for informational purposes and to enable Landlord to obtain full building Energy Star scoring for the Building. Landlord, with reasonable prior written notice to Tenant shall have the right to shut down the Building systems (including electricity and HVAC systems) for required maintenance, safety inspections, or any other reason, including without limitation in cases of emergency (for which notice shall be practicable under the circumstances). Landlord shall coordinate the scheduling of any maintenance and safety inspections with Tenant to provide ample time for Landlord and Tenant to minimize any interference with Tenant’s use and occupancy of the Premises and the operation of Tenant’s business therefrom. Landlord shall use commercially reasonable efforts to schedule routine maintenance that will materially and adversely interfere with Tenant’s operations to occur during non-Business Hours. Landlord shall not be liable for any interruption in providing any utility that Landlord is obligated to provide under this Lease, unless such interruption or delay: (i) renders the Premises or any material portion thereof untenantable for the normal conduct of Tenant’s business at the Premises, and Tenant has ceased using such untenantable portion, provided Tenant shall first endeavor to use any generator that serves the Premises or of which Tenant has the beneficial use; (ii) results from Landlord’s negligence or willful misconduct; and (iii) extends for a period longer than 3 consecutive days, in which case, Tenant’s obligation to pay Fixed Rent shall be abated with respect to the untenantable portion of the Premises that Tenant has ceased using for the period beginning on the 4th consecutive day after such conditions are met and ending on the earlier of: (A) the date Tenant recommences using the Premises or the applicable portion thereof; or (B) the date on which the service(s) is substantially restored. The rental abatement described above shall be Tenant’s sole remedy in the event of a utility interruption, and Tenant hereby waives any other rights against Landlord in connection therewith. Landlord shall have the right to change the utility providers to the Project at any time. In the event of a casualty or condemnation affecting the Building and/or the Premises, the terms of Sections 14 and 15, respectively, shall control over the provisions of this Section.

(c) If Landlord reasonably determines that: (i) Tenant exceeds the design conditions for the heating, ventilation, and air conditioning (“HVAC”) system serving the Premises, introduces into the Premises equipment that overloads such system, or causes such system to not adequately perform its proper functions; or (ii) the heavy concentration of personnel, motors, machines, or equipment used in the Premises, including telephone and computer equipment, or any other condition in the Premises caused by Tenant (for example, more than one shift per day or 24-hour use of the Premises), adversely affects the temperature or humidity otherwise maintained by such system, then Landlord shall notify Tenant in writing and Tenant shall have 30 days to remedy the situation to Landlord’s reasonable satisfaction. If Tenant fails to timely remedy the situation to Landlord’s reasonable satisfaction, Landlord shall have the right to install one or more supplemental air conditioning units in the Premises with the cost thereof, including the cost of installation, operation and maintenance, being payable by Tenant to Landlord within 30 days after Landlord’s written demand. Tenant shall not change or adjust any closed or sealed thermostat or other element of the HVAC system serving the Premises without Landlord’s express prior written consent. Landlord may install and operate meters or any other reasonable system for monitoring or estimating any services or utilities used by Tenant in excess of those required to be provided by Landlord (including a system for Landlord’s engineer reasonably to estimate any such excess usage). If such system indicates such excess services or utilities, Tenant shall pay Landlord’s reasonable charges for installing and operating such system and any supplementary air conditioning, ventilation, heat, electrical, or other systems or equipment (or adjustments or modifications to the existing Building systems and equipment), and Landlord’s reasonable charges for such amount of excess services or utilities used by Tenant. All supplemental HVAC systems and equipment serving the Premises (including without limitation Tenant’s Supplemental HVAC, as defined in Section 11(a) below) shall be separately metered to the Premises at Tenant’s cost, and Tenant shall be solely responsible for all electricity registered by, and the maintenance and replacement of, such meters. Landlord has no obligation to
keep cool any of Tenant’s information technology equipment that is placed together in one room, on a rack, or in any similar manner (“ IT Equipment ”), and Tenant waives any claim against Landlord in connection with Tenant’s IT Equipment. Landlord shall have the option to require that the computer room and/or information technology closet in the Premises shall be separately submetered at Tenant’s expense, and Tenant shall pay Landlord for all electricity registered in such submeter. Within 1 month after written request, Tenant shall provide to Landlord electrical load information reasonably requested by Landlord with respect to any computer room and/or information technology closet in the Premises.

7. LANDLORD SERVICES.

(a) Subject to Tenant’s payment of Operating Expenses under Section 5 and utilities under Section 6, Landlord shall provide the following to the Premises 24 hours per day, 7 days per week during the entire Term: (i) HVAC service in the respective seasons during Business Hours in a manner consistent with the furnishing of same by other landlords of first class mixed use office and laboratory buildings in Philadelphia and providing a temperature range of 72º Fahrenheit (+/- 2 º); (ii) electricity for lighting and equipment for comparable mixed use office and laboratory buildings in the market in which the Project is located; (iii) water, sewer, and, to the extent applicable to the Building, gas service; (iv) steam during the period of October 15 through April 15 of each year during the Term; and (v) cleaning services meeting the minimum specifications set forth in Exhibit D attached hereto. Tenant, at Tenant’s expense, shall make arrangements with the applicable utility companies and public bodies to provide, in Tenant’s name, telephone, cable, and any other utility service not provided by Landlord that Tenant desires at the Premises.

(b) Landlord shall not be obligated to furnish any services, supplies, or utilities other than as set forth in this Lease; provided, however, upon Tenant’s prior request sent in accordance with Section 25(o) below, Landlord may furnish additional services, supplies, or utilities, in which case Tenant shall pay to Landlord, immediately upon demand, Landlord’s then-current charge for such additional services, supplies, or utilities, or Tenant’s pro rata share thereof, if applicable, as reasonably determined by Landlord.

(c) Notwithstanding anything to the contrary in this Lease, at its sole cost and expense Tenant shall cause all laboratory areas of the Premises to be cleaned and ensure the proper disposal of all Hazardous Materials in compliance with all applicable Laws, and Landlord shall have no responsibility for any of the foregoing.

8. USE; SIGNS; PARKING; COMMON AREAS.

(a) Tenant may use the Premises for general office use (non-medical) and storage incidental thereto, typical research and development use, and laboratory use for a pharmaceutical or biopharmaceutical company, and for no other purpose (“ Permitted Use ”). Tenant’s use of the Premises for the Permitted Use shall be subject to all applicable Laws, and to all reasonable requirements of the insurers of the Building. Tenant represents and warrants to Landlord, for informational purposes only, that Tenant’s current NAICS Code is set forth in Section 1 hereof, provided the foregoing shall not be construed in any manner as a restriction on the Permitted Use.

(b) Landlord shall provide Tenant with Building-standard identification signage on all Building lobby directories (to the extent installed by Landlord).

(c) Subject to the Building rules and regulations, Tenant shall have the nonexclusive right in common with others to use the Common Areas for their intended purposes. Not in limitation of the foregoing, Tenant shall have the right throughout the Term to obtain permits, up to a number equal to the Parking Permit Number (as defined below) for unreserved parking of standard-size automobiles of Tenant and its employees and business visitors within the Landlord Parking Facility (as defined below): (i) by entering from time to time into the parking garage operator’s standard agreement covering the use of parking spaces in such garage; (ii) upon the terms and subject to the conditions set forth in such agreements; and (iii) subject to Tenant’s monthly payment to such operator of its standard fee for the right to such parking spaces. To the extent not included in the fee (if any) charged for parking in the parking facility for the Building, Tenant shall be solely liable for all parking taxes (if any) imposed by the applicable governmental authority with respect to Tenant’s parking spaces. If Landlord elects (in its sole and absolute discretion) to operate the parking facility, Tenant shall pay Landlord such taxes within 15 days after receipt of an invoice therefor and Landlord.
shall then remit such taxes to the applicable governmental authority. If the parking facility is not operated by Landlord, Tenant shall pay the operator such taxes and the operator shall then remit such taxes to the applicable governmental authority. The “Landlord Parking Facility” means the parking garage or lot owned or controlled by Landlord or an affiliate of Landlord in University City, as determined by Landlord from time to time by written notice to Tenant, but in no event shall the Landlord Parking Facility be a distance from the Building that is greater than the distance from the garage at FMC Tower. The “Parking Permit Number” means 1 multiplied by the total rentable square footage of the Premises, and then divided by 2,500. Notwithstanding the foregoing, Landlord shall have the right, by written notice to Tenant, (i) to adjust the Parking Permit Number with respect to the rentable square footage of the Lower Level Space and Suite 200 after December 1, 2019 (the “First Parking Adjustment Date”) to equal Tenant’s average monthly utilization of the Landlord Parking Facility during the prior 12-month period of occupancy of the Premises (provided the First Parking Adjustment Date shall be pushed back on a day-for-day basis for each day that the Delivery Date is delayed beyond December 1, 2017); and (ii) to adjust the Parking Permit Number with respect to the rentable square footage of Suite 300 only after December 1, 2020 (the “Second Parking Adjustment Date”) to equal Tenant’s average monthly utilization of the Landlord Parking Facility with respect to Suite 300 only (i.e. exclude from Tenant’s average monthly utilization of the Landlord Parking Facility the Parking Permit Number determined in accordance with (i) above) during the prior 12-month period of occupancy of the Premises (provided the Second Parking Adjustment Date shall be pushed back on a day-for-day basis for each day that the Suite 300 Delivery Date is delayed beyond May 1, 2019). Notwithstanding anything herein to the contrary, if Tenant expands the Premises at any time during the Term, the Parking Permit Number shall increase in accordance with the ratio provided above with respect to the expansion space and Landlord shall have the right, by written notice to Tenant to adjust the Parking Permit Number with respect to such additional space on the date that is one (1) year following the date Tenant occupies the expanded space for the operation of Tenant’s business, to equal Tenant’s average monthly utilization of the Landlord Parking Facility with respect to such expanded space only during the prior 12-month period of occupancy of the Premises.

(d) Landlord shall have the right in its sole discretion to, from time to time, construct, maintain, operate, repair, close, limit, take out of service, alter, change, and modify all or any part of the Common Areas, provided, however, Landlord shall exercise such right in a commercially reasonable manner intended to minimize interference with Tenant’s use and occupancy of the Premises and the Common Areas, and to not adversely affect the number of parking spaces available for Tenant’s use. Landlord shall maintain the Common Areas in a manner consistent with the furnishing of same by other landlords of first class office buildings in Center City Philadelphia. Landlord, Landlord’s agents, contractors, and utility service providers shall have the right to install, use, and maintain ducts, pipes, wiring, and conduits in and through the Premises provided such use does not cause the usable area of the Premises to be reduced beyond a de minimis amount.

(e) Subject to Landlord’s security measures and Force Majeure Events (as defined in Section 25(g), Landlord shall provide Tenant with access to the Building and, if applicable, passenger elevator service for use in common with others for access to and from the Premises 24 hours per day, 7 days per week, except during emergencies. Landlord shall have the right to limit the number of elevators (if any) to be operated during repairs and during Non-Business Hours. During the Term, Landlord shall provide Tenant with access to the freight elevator(s) of the Building during Business Hours on a first-come, first-served basis at no charge for the delivery and handling of laboratory materials, consumables and hazardous materials and waste. Notwithstanding the foregoing, during construction of the Leasehold Improvements, Tenant shall have the right to use the building freight elevators from 7:00 a.m. to 3:00 p.m. on a nonexclusive, first-come, first-served basis at no charge except if Landlord reasonably determines that it is necessary for Landlord, Landlord’s contractor, or Tenant’s contractor, to employ an operating engineer to manage such nonexclusive use of the freight elevator (currently at a charge of $125 per hour), then the costs incurred by Landlord will be shared equitably among users, without markup. Landlord acknowledges and agrees that Tenant shall be permitted to reserve the freight elevators (subject to the payment of Landlord’s actual costs incurred as hereinafter provided) in one (1)-hour increments.

(f) Provided all of the Monument Signage Conditions are fully satisfied, Landlord shall install a new monument sign (“Monument Sign”) at the Building and install a panel sign for Tenant (“Panel”) on the Monument Sign on or before December 31, 2018, subject to applicable Laws and satisfaction of all of the following terms and conditions: (i) the size and location and Tenant’s specifications and design of the Panel shall be subject to Landlord’s prior written consent and generally consistent with the aesthetic standards of the Building and compatible with the
signage at Schuylkill Yards; (ii) Landlord shall obtain the Panel on Tenant’s behalf and at Tenant’s sole cost and expense at market rates; (iii) Landlord shall install the Panel, at Tenant’s sole cost and expense; (iv) Landlord shall maintain and repair the Monument Sign, the costs of which shall be proportionately paid by the tenants having panel signs on such Monument Sign; (v) Landlord shall maintain and repair the Panel, at Tenant’s sole cost and expense; (vi) if the Monument Sign is illuminated, Tenant shall pay its proportionate share of the costs of such illumination (equitably allocated in Landlord’s reasonable determination); and (vii) if the Panel requires replacement, such replacement shall be at Tenant’s sole cost and expense. The “Monument Signage Conditions” are that: (a) there has been no Event of Default which remains unsecured; and (b) this Lease is in full force and effect. Prior to the Surrender Date (as defined in Section 18(a)), or immediately upon any of the Monument Signage Conditions no longer being satisfied, Landlord shall have the right, at Tenant’s sole but reasonable cost and expense, to remove the Panel and repair and restore the Monument Sign to its prior existing condition. With respect to clause (i) above, Landlord’s determination and selection of the size, location, specifications, and design of the Panel may take into account the necessity to reserve or reallocate space for signage for existing and future tenants of the Building and in furtherance of the foregoing, Landlord shall have the right to require that the Panel be replaced with a Panel of a different size, configuration, or design, from time to time, and the Panel’s placement on the Monument Sign may be equitably relocated on such sign by Landlord, from time to time based upon the relative sizes of the premises leased by the tenants with a panel on the Monument Sign. Tenant shall pay Landlord for all costs due under this paragraph as Additional Rent within 30 days after receipt of Landlord’s invoice therefor.

(g) To the extent permitted by applicable Laws, and provided all of the Exterior Signage Conditions are fully satisfied, the originally named Tenant shall have the nonexclusive right, at its sole cost and expense (including without limitation with respect to installation, maintenance, and removal), to place signage on one side of the exterior Building façade displaying Tenant’s corporate name and logo (“Exterior Signage”). The “Exterior Signage Conditions” are that: (a) the originally named Tenant is paying full Rent and Landlord is able to recognize revenue on a GAAP basis on at least 100% of the rentable area of the second, third and fourth floors of the Building; (b) there has been no Event of Default which remains unsecured; and (c) this Lease is in full force and effect. Notwithstanding the foregoing, Tenant shall have the immediate right to install the Exterior Signage upon Tenant’s exercise of the Expansion Option or Tenant’s ROFO Notice with respect to the entire fourth floor of the Building. The Exterior Signage shall be subject to Landlord’s reasonable approval in writing as to the location, placement, color, size, design, construction, and architectural compatibility of the Exterior Signage with the exterior of the Building and the signage at Schuylkill Yards. Landlord’s approval of the Exterior Signage shall create no responsibility or liability on the part of Landlord for the completeness, design, or sufficiency thereof, or the compliance of the Exterior Signage with the requirements of applicable Laws. On or prior to the Surrender Date, or immediately if any of the Exterior Signage Conditions are no longer true, Tenant shall remove the Exterior Signage, at Tenant’s sole cost and expense, and restore and repair all parts of the Building affected by the installation or removal of the Exterior Signage, to the condition existing prior to its installation or to a condition reasonably acceptable to Landlord. Landlord shall have the right to remove the Exterior Signage at Tenant’s expense if Tenant fails to comply with the preceding sentence. Tenant understands and agrees that it is solely responsible to ensure the upkeep and condition of the Exterior Signage to its original status, normal wear and tear excepted. Specifically, any missing letters, whether by loss, destruction, wear, act of God, or otherwise, will be replaced at the full expense of Tenant and shall be repaired or replaced within 10 days after the occurrence of such deficiency. In addition to any other rights or remedies provided to Landlord in this Lease, if Tenant shall fail to complete such repair and/or replacement within such 10-day period, Landlord shall have the right, but not the obligation, to start to complete such repair and/or replacement at Tenant’s sole cost and expense, which sums shall constitute Additional Rent and be reimbursed by Tenant within 5 days following demand therefor by Landlord. Prior to constructing or installing the Exterior Signage, Tenant shall have obtained and must continue to maintain all permits and/or approvals required by applicable Laws with respect to the construction, installation, and maintenance of the Exterior Signage, and shall have provided Landlord with sufficient evidence of the existence of such permits and/or approvals and that the construction and installation of the Exterior Signage will comply in all respects with all applicable Laws. Tenant shall be solely responsible for ensuring that the Exterior Signage is in compliance with all present and future applicable Laws. Tenant, at its sole cost and expense, shall insure the Exterior Signage as part of Tenant’s Property, and shall also carry liability insurance with respect to the Exterior Signage. Tenant shall protect, defend, indemnify, and hold harmless Landlord and all Landlord Indemnitees (as defined in Section 13(a)) from and against any and all claims, damages, judgments, suits, causes of action, losses, liabilities, penalties, fines, expenses, and costs (including, without limitation,
sums paid in settlement of claims, attorneys' fees, consultant fees, and expert fees and court costs) arising out of or from or related to the construction, installation, maintenance, use, or removal of the Exterior Signage.

9. **TENANT’S ALTERATIONS.** Tenant shall not cut, drill into, or secure any fixture, apparatus, or equipment, or make alterations, improvements, or physical additions of any kind to any part of the Premises (collectively, “Alterations”) without first obtaining the written consent of Landlord, which consent shall not be unreasonably withheld, conditioned, or delayed. All Alterations shall be completed in compliance with all applicable Laws, and Landlord’s reasonable rules and regulations for construction, and sustainable guidelines and procedures. Notwithstanding the foregoing, Landlord’s consent shall not be required for any Alteration costing less than $75,000.00 in the aggregate per calendar year, and that: (i) is nonstructural; (ii) does not impact any of the Building systems, involve electrical work, require a building permit, or materially affect the air quality in the Building; and (iii) is not visible from outside of the Premises. Tenant shall be solely responsible for the installation and maintenance of its data, telecommunication, and security systems and wiring at the Premises, which shall be done in compliance with all applicable Laws, and Landlord’s reasonable rules and regulations. With respect to all improvements and Alterations made after the date hereof, other than those made by Landlord pursuant to the express provisions of this Lease, Tenant acknowledges that: (A) Tenant is not, under any circumstance, acting as the agent of Landlord; (B) Landlord did not cause or request such Alterations to be made; (C) Landlord has not ratified such work; and (D) Landlord did not authorize such Alterations within the meaning of applicable State statutes. Nothing in this Lease or in any consent to the making of Alterations or improvements shall be deemed or construed in any way as constituting a request by Landlord, express or implied, to any contractor, subcontractor, or supplier for the performance of any labor or the furnishing of any materials for the use or benefit of Landlord. Tenant shall not overload any floor or part thereof in the Premises or the Building, including any public corridors or elevators, by bringing in, placing, storing, installing or removing any large or heavy articles, and Landlord may prohibit, or may direct and control the location and size of, safes and all other heavy articles, and may require, at Tenant’s sole cost and expense, supplementary supports of such material and dimensions as Landlord may deem necessary to properly distribute the weight.

10. **ASSIGNMENT AND SUBLETTING.**

   (a) Except as expressly permitted pursuant to Section 10(e), neither Tenant nor Tenant’s legal representatives or successors-in-interest by operation of law or otherwise, shall sell, assign, transfer, hypothecate, mortgage, encumber, grant concessions or licenses, sublet, or otherwise dispose of all or any interest in this Lease or the Premises, or permit any person or entity other than Tenant to occupy any portion of the Premises (each of the foregoing is a “Transfer” to a “Transferee”), without Landlord’s prior written consent, which consent shall not be unreasonably withheld, conditioned, or delayed. Any Transfer undertaken without Landlord’s prior written consent (other than pursuant to Section 10(e)) shall constitute an Event of Default and shall, at Landlord’s option, be void and/or terminate this Lease. For purposes of this Lease, a Transfer shall include, without limitation, any assignment by operation of law, and any merger, consolidation, or asset sale involving Tenant, any direct or indirect transfer of control of Tenant, and any transfer of a majority of the ownership interests in Tenant (other than through the ownership of voting securities listed on a recognized securities exchange). Consent by Landlord to any one Transfer shall be held to apply only to the specific Transfer authorized, and shall not be construed as a waiver of the duty of Tenant, or Tenant’s legal representatives or assigns, to obtain from Landlord consent to any other or subsequent Transfers pursuant to the foregoing, or as modifying or limiting the rights of Landlord under the foregoing covenant by Tenant.

   (b) Without limiting the bases upon which Landlord may reasonably withhold its consent to a proposed Transfer, it shall not be unreasonable for Landlord to withhold its consent if: (i) the proposed Transferee shall have a net worth that is not acceptable to Landlord in Landlord’s reasonable discretion; (ii) the proposed Transferee, in Landlord’s reasonable opinion, is not reputable and of good character; (iii) the portion of the Premises requested to be subleased renders the balance of the Premises unleaseable as a separate area; (iv) Tenant is proposing to Transfer to an existing tenant of the Building or another property owned by Landlord or Landlord’s affiliate(s), or to another prospect with whom Landlord or Landlord’s affiliate(s) are then negotiating in the market of which the Building is a part; or (v) the nature of such Transferee’s proposed business operation would or might reasonably violate the terms of this Lease or of any other lease for the Building (including any exclusivity provisions), or would, in Landlord’s reasonable judgment, otherwise be incompatible with other tenancies in the Building.
(c) Notwithstanding the foregoing, Tenant shall have the right without the prior consent of Landlord, but after at least 10 days’ prior written notice to Landlord, to make a Transfer to any Affiliate (as defined below), or an entity into which Tenant merges or that acquires substantially all of the assets or stock of Tenant (“Surviving Entity”)(the Surviving Entity or Affiliate are also referred to as a “Permitted Transferee”); provided: (i) Tenant delivers to Landlord the Transfer Information (as defined below); (ii) if the Lease will be Transferred to a Surviving Entity, the Surviving Entity shall have a tangible net worth at least equal to the net worth of Tenant on the date of this Lease; (iii) the originally named Tenant shall not be released or discharged from any liability under this Lease by reason of such Transfer; and (iv) if the Transfer is to an Affiliate, such Transferee shall remain an Affiliate throughout the Term and if such Transferee shall cease being an Affiliate, Tenant shall notify Landlord in writing of such change and such Transfer shall be deemed an Event of Default if Landlord’s consent thereto is not given in writing within 10 business days after such notification. An “Affiliate” means a corporation, limited liability company, partnership, or other registered entity, 50% or more of whose equity interest is owned by the same persons or entities owning 50% or more of Tenant’s equity interests, a subsidiary, or a parent entity.

(d) If at any time during the Term Tenant desires to complete a Transfer, Tenant shall give written notice to Landlord of such desire together with the Transfer Information. If: (i) Tenant desires to assign this Lease or to sublease the entire Premises other than pursuant to Section 10(c), Landlord shall have the right to accelerate the Expiration Date so that the Expiration Date shall be the date on which the proposed assignment or sublease would be effective; or (ii) Tenant desires to sublease less than the entire Premises other than to an Affiliate, Landlord shall have the right to accelerate the Expiration Date with respect to the portion of the Premises that Tenant proposes to sublease. If Landlord elects to accelerate the Expiration Date pursuant to this paragraph, Tenant shall have the right to rescind its request for Landlord’s consent to the proposed assignment or sublease by giving written notice of such rescission to Landlord within 10 days after Tenant’s receipt of Landlord’s acceleration election notice. If Tenant does not so rescind its request: (A) Tenant shall deliver the Premises or the applicable portion thereof to Landlord in the same condition as Tenant is, by the terms of this Lease, required to deliver the Premises to Landlord upon the Expiration Date; and (B) Fixed Rent and Tenant’s Share shall be reduced on a per rentable square foot basis for the area of the Premises that Tenant no longer leases. If Landlord elects to accelerate the Expiration Date for less than the entire Premises, the cost of erecting any demising walls, entrances, and entrance corridors, and any other improvements required in connection therewith shall be performed by Landlord, with the cost thereof being divided evenly between Landlord and Tenant.

(e) The “Transfer Information” means the following information: (i) a copy of the fully executed assignment and assumption agreement, or sublease agreement, as applicable (with respect to a Permitted Transfer, such agreement to be delivered to Landlord within 10 business days after the transaction closes and with respect to all other Transfers, such agreement shall be provided in draft form and shall not be executed, or the effectiveness of such agreement shall be conditioned upon the receipt of Landlord’s consent, until Landlord’s consent has been given); (ii) a copy of the then-current financials of the Transferee (either audited or certified by the chief financial officer of the Transferee) (except no financials shall be required for a Transfer to an Affiliate); (iii) a copy of the formation certificate and good standing certificate of the Transferee; and (iv) such other reasonably requested information by Landlord needed to confirm or determine Tenant’s compliance with the terms and conditions of this Section.

(f) Any sums or other economic consideration received by Tenant as a result of any Transfer (except rental or other payments received that are attributable to the amortization of the cost of leasehold improvements made to the transferred portion of the Premises by Tenant for the Transferee, and other reasonable expenses incident to the Transfer, including standard leasing commissions and attorneys’ fees) whether denominated rentals under the sublease or otherwise, that exceed, in the aggregate, the total sums which Tenant is obligated to pay Landlord under this Lease (prorated to reflect obligations allocable to that portion of the Premises subject to such Transfer) shall, at Landlord’s option, be divided evenly between Landlord and Tenant, with Landlord’s portion being payable to Landlord as Additional Rent without affecting or reducing any other obligation of Tenant hereunder. This subsection (f) shall not apply to any Permitted Transfers.

(g) Regardless of Landlord’s consent to a proposed Transfer, no Transfer shall release Tenant from Tenant’s obligations or alter Tenant’s primary liability to fully and timely pay all Rent when due from time to time under this Lease and to fully and timely perform all of Tenant’s other obligations under this Lease, and the originally named Tenant and all assignees shall be jointly and severally liable for all Tenant obligations under this Lease. The
acceptance of rental by Landlord from any other person shall not be deemed to be a waiver by Landlord of any provision hereof. If a Transferee defaults in the performance of any of the terms of this Lease, Landlord may proceed directly against the originally named Tenant without the necessity of exhausting remedies against such Transferee. If there has been a Transfer and an Event of Default occurs, Landlord may collect Rent from the Transferee and apply the net amount collected to the Rent herein reserved; but no such collection shall be deemed a waiver of the provisions of this Section, an acceptance of such Transferee as tenant hereunder or a release of Tenant from further performance of the covenants herein contained.

11. REPAIRS AND MAINTENANCE.

(a) Except with respect to Landlord Repairs (as defined below), Tenant, at Tenant’s expense, shall keep and maintain the Premises in good order and condition including promptly making all repairs necessary to keep and maintain such in good order and condition. When used in this Lease, “repairs” shall include repairs and any reasonably necessary replacements. Tenant shall have the option of replacing lights, ballasts, tubes, ceiling tiles, outlets and similar equipment itself or advising Landlord of Tenant’s desire to have Landlord make such repairs, in which case Tenant shall pay to Landlord for such repairs at Landlord’s then-standard rate. To the extent that Tenant requests that Landlord make any other repairs that are Tenant’s obligation to make under this Lease, Landlord may elect to make such repairs on Tenant’s behalf, at Tenant’s expense, and Tenant shall pay to Landlord such expense along with the Administrative Fee. If Tenant shall have committed a monetary Event of Default under this Lease, Landlord may elect to require that Tenant prepay the amount of such repair. All repairs made by Landlord or Tenant shall utilize materials and equipment that are at least equal in quality, number, and usefulness to those originally used in constructing the Building and the Premises. In addition, Tenant shall maintain, at Tenant’s expense, Tenant’s Supplemental HVAC, Premises Hot Water Heaters, and/or Alterations in a clean and safe manner and in proper operating condition throughout the Term. “Tenant’s Supplemental HVAC” means any supplemental HVAC system serving the Premises (regardless of who installed it). “Premises Hot Water Heater” means any hot water heater serving the Premises (regardless of who installed it), including without limitation expansion tanks and any associated piping. Tenant shall maintain Tenant’s Supplemental HVAC under a service contract with a firm and upon such terms as may be reasonably satisfactory to Landlord, including inspection and maintenance on at least a semiannual basis, and provide Landlord with a copy thereof. Within 5 days after Landlord’s request, Tenant shall provide Landlord with evidence that such contract is in place. Tenant shall ensure that all Premises Hot Water Heaters have a working automatic water shut-off device. All repairs to the Building and/or the Project made necessary by reason of the installation, maintenance, and operation of Tenant’s Supplemental HVAC, Premises Hot Water Heaters, and Alterations shall be Tenant’s expense. In the event of an emergency, such as a burst waterline or act of God, Landlord shall have the right to make repairs for which Tenant is responsible hereunder (at Tenant’s cost) without giving Tenant prior notice, but in such case Landlord shall provide notice to Tenant as soon as practicable thereafter, and Landlord shall take commercially reasonable steps to minimize the costs incurred. Further, Landlord shall have the right to make repairs for which Tenant is responsible hereunder (at Tenant’s cost) with prior notice to Tenant if Landlord believes in its sole and absolute discretion that the repairs are necessary to prevent imminent harm or material damage to the Building, and Landlord shall take commercially reasonable steps to minimize the costs incurred.

(b) Landlord, at Landlord’s expense (except to the extent such expenses are includable in Project Expenses), shall make all necessary repairs to: (i) the footings and foundations and the structural elements of the Building; (ii) the roof of the Building; (iii) the HVAC, plumbing, elevators (if any), electric, fire protection and fire alert systems within the Building (except to the extent such systems are solely located within and solely serve the Premises), but specifically excluding Tenant’s Supplemental HVAC and Alterations; (iv) the Building exterior; and (v) the Common Areas (collectively, “Landlord Repairs”). Any provision of this Lease to the contrary notwithstanding, any repairs to the Project or any portion thereof made necessary by the negligent or willful act or omission of Tenant or any employee, agent, subtenant, contractor or invitee of Tenant shall be made at Tenant’s expense, subject to the waivers set forth in Section 12(c).

(c) If Landlord defaults in the performance of any of its maintenance or repair obligations under this Lease, Tenant may send to Landlord written notice thereof, which notice must identify with reasonable specificity the default and Tenant’s remedies under this paragraph (“Reminder Notice”). If Landlord fails to either: (a) dispute the existence of such default within 5 business days; or (b) cure such default within Landlord’s Cure Period, then Tenant
will have all rights and remedies available at law or in equity for a landlord default. “Landlord’s Cure Period” means 30 days after Landlord’s receipt of a Reminder Notice, provided if cure cannot be reasonably effected by Landlord within such 30-day period, Landlord’s Cure Period includes such additional time as may be reasonably necessary for Landlord to cure, provided Landlord commences to cure within such 30-day period and diligently prosecutes such cure to completion.

(d) The parties agree it is in their mutual best interest that the Building and Premises be operated and maintained in a manner that is environmentally responsible, fiscally prudent, and provides a safe and productive work environment. Accordingly, Tenant shall use commercially reasonable efforts, at no additional cost to Tenant, to conduct its operations in the Building and within the Premises to: (1) minimize to the extent reasonably feasible: (i) direct and indirect energy consumption and greenhouse gas emissions; (ii) water consumption; (iii) the amount of material entering the waste stream; and (iv) negative impacts upon the indoor air quality of the Building; and (2) permit the Building to maintain its LEED rating and an Energy Star label, to the extent applicable. Landlord shall use commercially reasonable efforts to operate and maintain the Common Areas of the Building to: (1) minimize to the extent reasonably feasible: (i) direct and indirect energy consumption and greenhouse gas emissions; (ii) water consumption; (iii) the amount of material entering the waste stream; and (iv) negative impacts upon the indoor air quality of the Building; and (2) permit the Building to maintain its LEED rating and an Energy Star label, to the extent applicable, the costs of which shall be included in Project Expenses (except to the extent otherwise not permitted).

12. INSURANCE; SUBROGATION RIGHTS.

(a) Tenant, at Tenant’s expense, shall obtain and keep in force at all times as of the Commencement Date (or Tenant’s earlier accessing of the Premises) commercial general liability insurance including contractual liability and personal injury liability and all similar coverage, with a combined single limit of $3,000,000 on account of bodily injury to or death of one or more persons as the result of any one accident or disaster and on account of damage to property, or in such other amounts as Landlord may from time to time reasonably require, which shall be primary and noncontributory. Such limit can be achieved by a primary policy or a combination of primary and umbrella/excess policies. Tenant shall, at its sole cost and expense, maintain in full force and effect a policy of “special form” property insurance on Tenant’s Property for full replacement value and with coinsurance waived. “Tenant’s Property” means Tenant’s trade fixtures, equipment, personal property, and Specialty Alterations (as defined in Section 18(b)). Tenant shall neither have, nor make, any claim against Landlord for any loss or damage to Tenant’s Property, regardless of the cause of the loss or damage. Tenant shall require its movers to procure and deliver to Landlord a certificate of insurance naming Landlord as an additional insured. All liability insurance required hereunder shall name Tenant as insured, and Landlord, Landlord’s property manager, and Brandywine Realty Trust as additional insureds, and, if requested in writing by Landlord, shall also name any mortgagee or holder of any mortgage that may be or become a lien upon any part of the Premises as its interests may appear. Each additional insured shall be afforded coverage as broad as if this Lease had expressly covered the claim against the additional insured, and for the greater of the minimum amount called for by this Lease or Tenant’s actual policy limit. Prior to the Commencement Date, Tenant shall provide Landlord with certificates that evidence that all insurance coverages required under this Lease are in place for the policy periods. Tenant shall also furnish to Landlord and/or Landlord’s designated agent throughout the Term replacement certificates at least 5 days prior to the expiration dates of the then-current policy or policies or, upon request by Landlord and/or its agent from time to time, sufficient information to evidence that the insurance required under this Section is in full force and effect. All insurance required under this Lease shall be issued by an insurance company that has been in business for at least 5 years, is authorized to do business in the State, and has a financial rating of at least an A-X as rated in the most recent edition of Best’s Insurance Reports. The limits of any such required insurance shall not in any way limit Tenant’s liability under this Lease or otherwise. If Tenant fails to maintain such insurance and such failure continues for 5 days after written notice of such failure from Landlord, Landlord may, but shall not be required to, procure and maintain the same, at Tenant’s expense, which expense shall be reimbursed by Tenant as Additional Rent within 10 days after written demand. Any deductible under such insurance policy in excess of $25,000 shall be approved by Landlord in writing prior to the issuance of such policy. Tenant shall not self-insure without Landlord’s prior written consent.

(b) Landlord shall obtain and maintain the following insurance during the Term: (i) replacement cost insurance including “all risk” property insurance on the Building, including without limitation leasehold
improvements (exclusive of Tenant’s Property); (ii) commercial general liability insurance (including bodily injury and property damage) covering Landlord’s operations at the Project in amounts reasonably required by Landlord or any Mortgagor (as defined in Section 16); and (iii) such other insurance as reasonably required by Landlord or any Mortgagee.

(c) Landlord and Tenant shall each procure an appropriate clause in or endorsement to any property insurance covering the Project or any portion thereof and personal property, fixtures, and equipment located therein, wherein the insurer waives subrogation and consents to a waiver of right of recovery pursuant to the terms of this paragraph. Both Landlord and Tenant agree to immediately give each insurance company which has issued to it policies of property insurance written notice of the terms of such mutual waivers and to cause such insurance policies to be properly endorsed, if necessary, to prevent the invalidation thereof by reason of such waivers. Notwithstanding anything to the contrary in this Lease, Landlord and Tenant hereby waive, and agree not to make, any claim against, or seek to recover from, the other for any loss or damage to its property or the property of others resulting from conditions to the extent of proceeds received after application of any commercially reasonable deductible (or would have been received if the party had obtained and maintained the insurance it was required to carry under this Lease or if Tenant did not elect to self-insure) by the property insurance that was required to be carried by that party under the terms of this Lease.

(d) If Tenant deals with or uses, stores, handles, processes or disposes of any Hazardous Materials in the ordinary course of its business pursuant to the Permitted Use, other than such cleaning supplies and products normally found in modern offices of which are permitted in accordance with the terms set forth in Section 20(a) hereof, Tenant shall obtain and maintain throughout the Term, pollution legal liability insurance, with limits of $2,000,000 per occurrence and $2,000,000 annual aggregate for losses caused by pollution conditions (including, without limitation, any actual, alleged or threatened emission, discharge, dispersal, seepage, release or escape of Hazardous Materials) that arise from the operations of Tenant, its contractors, or their subcontractors, such coverage to include: (w) bodily injury, sickness, disease, mental anguish or shock sustained by any person or death; (x) property damage, including physical injury to or destruction or tangible property, including the resulting loss of use thereof; (y) clean-up costs and the loss of use of tangible property that has not been physically damaged or destroyed; and (z) defense, including costs, charges and expenses incurred in the investigation, adjustment, settlement or defense of claims for damages asserted against Landlord and/or the additional insureds.

13. INDEMNIFICATION.

(a) Subject to Section 12(c), Tenant shall defend, indemnify, and hold harmless Landlord, Landlord’s property manager, Brandywine Realty Trust, and each of Landlord’s directors, officers, members, partners, trustees, employees, and agents (collectively, “Landlord Indemnitees”) from and against any and all third-party claims, actions, damages, liabilities, and expenses (including all reasonable costs and expenses (including reasonable attorneys’ fees)) to the extent arising out of or from or related to: (i) Tenant’s breach of this Lease; (ii) any negligence or willful act of Tenant, any Tenant Indemnitees (as defined below), or any of Tenant’s invitees, subtenants, licensees, or contractors; and (iii) any acts or omissions occurring at, or the condition, use or operation of, the Premises, except to the extent arising from Landlord’s negligence or willful misconduct. If Tenant fails to promptly defend a Landlord Indemnitee following written demand by the Landlord Indemnitee, the Landlord Indemnitee shall defend the same at Tenant’s expense, by retaining or employing counsel reasonably satisfactory to such Landlord Indemnitee.

(b) Subject to Section 12(c), Landlord shall defend, indemnify, and hold harmless Tenant and each of Tenant’s directors, officers, members, partners, trustees, employees, and agents (collectively, “Tenant Indemnitees”) from and against any and all third-party claims, actions, damages, liabilities, and expenses (including all reasonable costs and expenses (including reasonable attorneys’ fees)) to the extent arising out of or from or related to: (i) Landlord’s breach of this Lease; and (ii) any negligence or willful misconduct of Landlord or any Landlord Indemnitees. If Landlord fails to promptly defend a Tenant Indemnitee following written demand by the Tenant Indemnitee, the Tenant Indemnitee shall defend the same at Landlord’s expense, by retaining or employing counsel reasonably satisfactory to such Tenant Indemnitee.
Landlord’s and Tenant’s obligations under this Section shall not be limited by the amount or types of insurance maintained or required to be maintained under this Lease. The provisions of this Section shall survive the Expiration Date.

14. **CASUALTY DAMAGE.** If there occurs any casualty to the Project (other than to the Premises) and: (i) insurance proceeds are unavailable to Landlord or are insufficient to restore the Project to substantially its pre-casualty condition; or (ii) more than 30% of the total area of the Building is damaged, Landlord shall have the right to terminate this Lease and all the unaccrued obligations of the parties hereto, by sending written notice of such termination to Tenant within 60 days after such casualty. Such notice shall specify a termination date not fewer than 30 nor more than 90 days after such notice is given to Tenant. If there occurs any casualty to the Premises and: (i) in Landlord’s reasonable judgment, the repair and restoration work would require more than 210 consecutive days to complete after the casualty (assuming normal work crews not engaged in overtime); or (ii) the casualty occurs during the last 12 months of the Term, then Landlord shall promptly deliver to Tenant Landlord’s written estimate (“Landlord’s Repair Estimate”) of the time it would take to repair and restore the Premises, and Landlord and Tenant shall each have the right to terminate this Lease and all the unaccrued obligations of the parties hereto, by sending written notice of such termination to the other party within 60 days after Tenant’s receipt of Landlord’s Repair Estimate. Such notice shall specify a termination date not fewer than 30 nor more than 90 days after such notice is given to the other party, but in no event shall the termination date be after the last day of the Term. If this Lease is terminated pursuant to this Section 14, Tenant’s obligation to pay Rent shall terminate as of the date of such casualty. If this Lease is not terminated pursuant to this paragraph and Landlord fails to complete the repair or restoration work within 30 days after Landlord’s estimated date for completion of the repair and restoration work (subject to extension for delays caused by Tenant and Force Majeure Events) (however in no event shall such date be extended more than sixty (60) days due to Force Majeure Events), then Tenant shall have the right to terminate this Lease by sending at least 30 days’ prior written notice to Landlord within 60 days after such estimated date of completion. If there occurs any casualty to the Premises and neither party terminates this Lease, then Landlord shall use commercially reasonable efforts to cause the damage to be repaired (exclusive of Tenant’s Property) to a condition as nearly as practicable to that existing prior to the damage, with commercially reasonable speed and diligence, subject to delays that may arise by reason of adjustment of the loss under insurance policies, Laws, and Force Majeure Events. Landlord shall not be liable for any inconvenience or annoyance to Tenant or Tenant Indemnitees, injury to Tenant’s business, or pain and suffering, resulting in any way from such damage or the repair thereof. Notwithstanding the foregoing, Tenant’s obligation to pay Fixed Rent and Additional Rent shall be equitably adjusted or abated during the period (if any) during which Tenant is not reasonably able to use the Premises or an applicable portion thereof as a result of such casualty. Tenant shall have no right to terminate this Lease as a result of any damage or destruction of the Premises, except as expressly provided in this Section. The provisions of this Lease, including this Section, constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, and any Law with respect to any rights or obligations concerning damage or destruction in the absence of an express agreement between the parties, and any other statute or regulation, now or hereafter in effect, shall have no application to this Lease or any damage or destruction to all or any part of the Premises.

15. **CONDEMNATION.** If a taking renders the Building reasonably unsuitable for the Permitted Use, this Lease shall, at either party’s option exercised by written notice to the other within 30 days after such taking, terminate as of the date title to condemned real estate vests in the condemnor, the Rent herein reserved shall be apportioned and paid in full by Tenant to Landlord to such date, all Rent prepaid for period beyond that date shall forthwith be repaid by Landlord to Tenant, and neither party shall thereafter have any liability for any unaccrued obligations hereunder; provided, however, a condition to the exercise by Tenant of such right to terminate shall be that the portion of the Premises taken shall be of such extent and nature as materially to handicap, impede, or impair Tenant’s use of the balance of the Premises for its normal business operations. If this Lease is not terminated after a condemnation, then notwithstanding anything to the contrary in this Lease, Fixed Rent and Additional Rent shall be equitably reduced in proportion to the area of the Premises that has been taken for the balance of the Term. Tenant shall have the right to make a claim against the condemnor for moving expenses and business dislocation damages, including personal property, fixtures and equipment, to the extent that such claim does not reduce the sums otherwise payable by the condemnor to Landlord.

16. **SUBORDINATION; ESTOPPEL CERTIFICATE; GROUND LEASE.**
(a) This Lease shall be subordinate at all times to the lien of any mortgages and deeds of trust now or hereafter placed upon the Premises, Building, and/or Project and land of which they are a part (a “Mortgage”) without the necessity of any further instrument or act on the part of Tenant to effectuate such subordination provided the holder (the “Mortgagee”) of any such Mortgage shall be deemed to recognize the rights of Tenant as tenant under all of the terms of this Lease and to agree not to disturb Tenant’s possession of the Premises so long as there is no Event of Default, without the necessity of any further instrument or act on the part of Tenant or such Mortgagee to effectuate such subordination, recognition, and non-disturbance. Tenant further agrees to execute and deliver within 10 business days after written demand such further commercially reasonable instrument evidencing such subordination and attornment as shall be reasonably required by any Mortgagee. If Landlord shall be or is alleged to be in default of any of its obligations owing to Tenant under this Lease, Tenant shall give to the holder of any mortgage or deed of trust now or hereafter placed upon the Premises, Building and/or Project whose name and address has been furnished to Tenant in writing, notice by overnight mail of any such default that Tenant shall have served upon Landlord. Tenant shall not be entitled to exercise any right or remedy as there may be because of any default by Landlord without having given such notice to the Mortgagee. If Landlord shall fail to cure such default, the Mortgagee shall have 45 additional days within which to cure such default. Notwithstanding the foregoing, any Mortgagee may at any time subordinate its mortgage to this Lease, without Tenant’s consent, by notice in writing to Tenant, and thereupon this Lease shall be deemed prior to such Mortgagee without regard to their respective dates of execution and delivery, and in that event the Mortgagee shall have the same rights with respect to this Lease as though it had been executed prior to the execution and delivery of the Mortgage. Provided there is no outstanding Event of Default and the Premises comprise at least one full floor of the Building, Landlord shall use commercially reasonable efforts to obtain a subordination, non-disturbance, and attornment agreement from any future Mortgagee on such Mortgagee’s then-current form therefor upon Tenant’s written request and at Tenant’s cost. Landlord represents that there is no Mortgage recorded against the Project as of the date hereof.

(b) Tenant shall attorn to any foreclosing mortgagee, purchaser at a foreclosure sale or by power of sale, or purchaser by deed in lieu of foreclosure. If the holder of a superior mortgage shall succeed to the rights of Landlord, then at the request of such party so succeeding to Landlord’s rights (herein sometimes called successor landlord) and upon such successor landlord’s written agreement to accept Tenant’s attornment, Tenant shall attorn to and recognize such successor landlord as Tenant’s landlord under this Lease and shall promptly, without payment to Tenant of any consideration therefor, execute and deliver any commercially reasonable instrument that such successor landlord may request to evidence such attornment. Upon such attornment, this Lease shall continue in full force and effect as, or as if it were, a direct lease between the successor landlord and Tenant upon all of the terms, conditions, and covenants as are set forth in this Lease and shall be applicable after such attornment. With respect to any assignment by Landlord of Landlord’s interest in this Lease, or the rents payable hereunder, conditional in nature or otherwise, which assignment is made to any Mortgagee, Tenant agrees that the execution thereof by Landlord, and the acceptance thereof by the Mortgagee, shall never be deemed an assumption by such Mortgagee of any of the obligations of Landlord hereunder, unless such Mortgagee shall, by written notice sent to Tenant, specifically elect, or unless such Mortgagee shall foreclose the Mortgage and take possession of the Premises. Tenant, upon receipt of written notice from a Mortgagee that such Mortgagee is entitled to collect Rent hereunder may in good faith remit such Rent to Mortgagee without incurring liability to Landlord for the non-payment of such Rent. The provisions for attornment set forth in this Section 16(b) shall be self-operative and shall not require the execution of any further instrument. However, if Landlord reasonably requests a further instrument confirming such attornment, Tenant shall execute and deliver such instrument within 10 business days after receipt of such request.

(c) Tenant must at any time and from time to time, within 10 days after receipt of Landlord’s written request, execute and deliver to Landlord an estoppel certificate certifying all reasonably requested information pertaining to this Lease.

(d) Reference is hereby made to the Ground Lease Agreement dated October 13, 2017 (as amended, “Ground Lease”) between Academic Properties, Inc. (“Ground Lessor”) and Landlord, as may be amended, pursuant to which Landlord ground leases the land under the Building from Ground Lessor. Except to the extent prohibited by applicable Laws: (i) this Lease shall be expressly subject to the terms and conditions of the Ground Lease (including, without limitation, the use restrictions contained therein); (ii) provided Tenant is not disturbed in its
possession of the Premises, Tenant will be required to attorn (A) to Ground Lessor in the event of the termination of the Ground Lease, or (B) to any mortgagee of the Ground Lease that becomes the ground lessee prior to the expiration date of this Lease; (iii) Ground Lessor shall have no obligation to pay, perform, or observe any of the obligations of Landlord under this Lease, and this Lease shall not purport to bind the interest of Ground Lessor in the ground leased premises, or in any other real property, to any exclusive or restrictive covenant or similar restriction upon the use or occupancy of any other real property of Ground Lessor, nor shall this Lease impose upon Ground Lessor any obligation to construct or alter any portion of the ground leased premises or of any other real property of Ground Lessor, or to provide any duty or services not expressly required of Ground Lessor under the Ground Lease; (iv) this Lease shall not permit any use of the Premises or any portion thereof that is not permitted under the Ground Lease or under any applicable Laws; (v) Ground Lessor shall not be obligated to commence or complete construction of any alterations or improvements required to be constructed or made by Landlord under this Lease; (vi) Ground Lessor shall not be required to pay any improvement allowance or other sum to be made or contributed by Landlord to or for the benefit of Tenant under this Lease; (vii) Ground Lessor shall not be liable for any act or omission of any prior landlord under this Lease (including Landlord), except that Tenant shall retain all rights and remedies available to Tenant against such prior landlord under this Lease; (viii) Ground Lessor shall not be subject to any offsets or defenses which Tenant might have against any prior landlord hereunder; (ix) Ground Lessor shall not be bound by any prepayment of rent or additional rent which Tenant might have paid, except as the same may actually have been paid directly to or actually received by Ground Lessor; (x) Ground Lessor shall not be bound to return any security deposit under this Lease unless Ground Lessor has actually received that security deposit; (xi) Ground Lessor shall not be liable on account of any breach or violation of any restrictive covenant contained in this Lease that may have occurred or be existing at the time of any event of default occurring under the Ground Lease or thereafter, or bound by any restrictive covenant pertaining to or binding any property other than the ground leased premises; and (xii) the Permitted Use shall be commensurate with a class A building. Landlord shall use commercially reasonable efforts to obtain a non-disturbance and recognition agreement from Ground Lessor in favor of Tenant.

17. DEFAULT AND REMEDIES.

(a) An “Event of Default” shall be deemed to exist and Tenant shall be in default hereunder if: (i) Tenant fails to pay any Rent when due and such failure continues for more than 5 business days after Landlord has given Tenant written notice of such failure; provided, however, in no event shall Landlord have any obligation to give Tenant more than 2 such notices in any 12-month period, after which there shall be an Event of Default if Tenant fails to pay any Rent when due, regardless of Tenant’s receipt of notice of such non-payment; (ii) Tenant fails to bond over a mechanic’s or materialmen’s lien filed in connection with any work performed by or on behalf of Tenant within 30 days after Landlord’s demand; (iii) there is any assignment or subletting (regardless of whether the same might be void under this Lease) in violation of the terms of this Lease; (iv) Tenant fails to deliver any Landlord-requested estoppel certificate or subordination agreement within 5 business days after receipt of notice that such document was not received within the time period required under this Lease; (v) Tenant’s or any Guarantor’s filing of a voluntary petition for relief, or the filing of a petition against Tenant or any Guarantor in a proceeding under the federal bankruptcy or other insolvency laws that is not withdrawn or dismissed within 60 days thereafter, or Tenant’s rejection of this Lease after such a filing, or, under the provisions of any law providing for reorganization or winding up of corporations, the assumption by any court of competent jurisdiction of jurisdiction, custody, or control of Tenant or any substantial part of its property, or of any Guarantor, where such jurisdiction, custody, or control remains in force, unrelinquished, unsecured, or in the hands of a receiver; (vi) Tenant fails to observe or perform any of Tenant’s other agreements or obligations under this Lease and such failure continues for more than 30 days after Landlord gives Tenant written notice of such failure, or the expiration of such additional time period as is reasonably necessary to cure such failure (not to exceed 60 days), provided Tenant immediately commences and thereafter proceeds with all due diligence and in good faith to cure such failure.

(b) Upon the occurrence of an Event of Default, Landlord, in addition to the other rights or remedies it may have under this Lease, at law, or in equity, and without prejudice to any of the same, shall have the option, without any notice to Tenant and with or without judicial process, to pursue any one or more of the following remedies:
(i) Landlord shall have the right to terminate this Lease, in which event Tenant shall immediately surrender the Premises to Landlord, and Tenant shall pay Landlord upon demand for all losses and damages that Landlord suffers or incurs by reason of such termination, including damages in an amount equal to the total of: (A) the costs of repossessing the Premises and all other expenses incurred by Landlord in connection with Tenant’s default, plus the Administrative Fee; (B) the unpaid Rent earned as of the date of termination; (C) all Rent for the period that would otherwise have constituted the remainder of the Term, discounted to present value at a rate of 4% per annum; and (D) all other sums of money and damages owing by Tenant to Landlord.

(ii) Landlord shall have the right to terminate Tenant’s right of possession (but not this Lease) and may repossess the Premises by forcible detainer or forcible entry and detainer suit or otherwise, without demand or notice of any kind to Tenant and without terminating this Lease. If Tenant receives written notice of a termination of its right to possession, such notice will serve as both a notice to vacate, notice to pay or quit, and a demand for possession of, the Premises, and Landlord may immediately thereafter initiate a forcible detainer action without any further demand or notice of any kind to Tenant.

(iii) Landlord shall have the right to enter and take possession of all or any portion of the Premises without electing to terminate this Lease, in which case Landlord shall have the right to relet all, or any portion of the Premises on such terms as Landlord deems advisable. Landlord will not be required to incur any expenses to relet all or any portion of the Premises, although Landlord may at its option incur customary leasing commissions or other costs for the account of Tenant as Landlord shall deem necessary or appropriate to relet. In no event will the failure of Landlord to relet all or any portion of the Premises reduce Tenant’s liability for Rent or damages.

(iv) Landlord shall have the right to enter the Premises without terminating this Lease and without being liable for prosecution or any claim for damages therefor and maintain the Premises and repair or replace any damage thereto or do anything for which Tenant is responsible hereunder. Tenant shall reimburse Landlord immediately upon demand for any reasonable and actual out-of-pocket costs which Landlord incurs in thus effecting Tenant’s compliance under this Lease, and Landlord shall not be liable to Tenant for any damages with respect thereto.

(v) Landlord shall have the right to continue this Lease in full force and effect, whether or not Tenant shall have abandoned the Premises. If Landlord elects to continue this Lease in full force and effect pursuant to this Section, then Landlord shall be entitled to enforce all of its rights and remedies under this Lease, including the right to recover Rent as it becomes due. Landlord’s election not to terminate this Lease pursuant to this Section or pursuant to any other provision of this Lease, at law or in equity, shall not preclude Landlord from showing the Premises to potential tenants, subsequently electing to terminate this Lease, or pursuing any of its other remedies.

(vi) Landlord shall have the right to cure any default on behalf of Tenant and Tenant shall reimburse Landlord upon demand for any sums paid or costs incurred by Landlord in curing such default, including attorneys’ fees and other legal expenses, plus the Administrative Fee. The “Administrative Fee” means 10% of the costs incurred by Landlord in curing Tenant’s default or performing Tenant’s obligations hereunder.

(c) Upon the occurrence of an Event of Default, Tenant shall be liable to Landlord for, and Landlord shall be entitled to recover: (i) all Rent accrued and unpaid; (ii) all costs and expenses incurred by Landlord in recovering possession of the Premises, including reasonable legal fees, and removal and storage of Tenant’s property; (iii) the reasonable costs and expenses of restoring the Premises to the condition in which the same were to have been surrendered by Tenant as of the Expiration Date; (iv) the costs of reletting commissions; (v) all reasonable legal fees and court costs incurred by Landlord in connection with the Event of Default; and (vi) the unamortized portion (as reasonably determined by Landlord) of brokerage commissions and consulting fees incurred by Landlord, and tenant concessions including free rent given by Landlord, in connection with this Lease.

(d) Any amount payable by Tenant under this Lease that is not paid when due shall bear interest at the rate of 1% per month until paid by Tenant to Landlord. If Tenant fails to pay Rent when due on 3 or more occasions during the Term, Landlord shall have the right to require Tenant to pay all future Rent by ACH debit of funds, in which case Tenant shall complete Landlord’s then-current forms authorizing Landlord to automatically debit Tenant’s bank account.
Neither any delay or forbearance by Landlord in exercising any right or remedy hereunder nor Landlord’s undertaking or performing any act that Landlord is not expressly required to undertake under this Lease shall be construed to be a waiver of Landlord’s rights or to represent any agreement by Landlord to thereafter undertake or perform such act. Landlord’s waiver of any breach by Tenant of any covenant or condition herein contained (which waiver shall be effective only if so expressed in writing by Landlord) or Landlord’s failure to exercise any right or remedy in respect of any such breach shall not constitute a waiver or relinquishment for the future of Landlord’s right to have any such covenant or condition duly performed or observed by Tenant, or of Landlord’s rights arising because of any subsequent breach of any such covenant or condition nor bar any right or remedy of Landlord in respect of such breach or any subsequent breach.

The rights granted to Landlord in this Section shall be cumulative of every other right or remedy provided in this Lease or which Landlord may otherwise have at law or in equity or by statute, and the exercise of one or more rights or remedies shall not prejudice or impair the concurrent or subsequent exercise of other rights or remedies or constitute a forfeiture or waiver of Rent or damages accruing to Landlord by reason of any Event of Default under this Lease. Landlord shall have all rights and remedies now or hereafter existing at law or in equity with respect to the enforcement of Tenant's obligations hereunder and the recovery of the Premises. No right or remedy herein conferred upon or reserved to Landlord shall be exclusive of any other right or remedy, but shall be cumulative and in addition to all other rights and remedies given hereunder or now or hereafter existing at law or in equity. Landlord shall be entitled to injunctive relief in case of the violation, or attempted or threatened violation, of any covenant, agreement, condition or provision of this Lease, or to a decree compelling performance of any covenant, agreement, condition or provision of this Lease.

No payment by Tenant or receipt by Landlord of a lesser amount than any payment of Fixed Rent or Additional Rent herein stipulated shall be deemed to be other than on account of the earliest stipulated Fixed Rent or Additional Rent due and payable hereunder, nor shall any endorsement or statement or any check or any letter accompanying any check or payment as Rent be deemed an accord and satisfaction. Landlord may accept such check or payment without prejudice to Landlord’s right to recover the balance of such Rent or pursue any other right or remedy provided for in this Lease, at law or in equity, and acceptance of such partial payment shall be deemed subject to Landlord’s reservation of all rights.

If there is an Event of Default, Landlord shall use commercially reasonable efforts to mitigate its damages. However, Landlord shall not be required to give any special preference or priority to reletting the Premises over other vacant space in the Building, Landlord shall be deemed to have used commercially reasonable efforts if it uses the same efforts in marketing the Premises as used in marketing other vacant space at the Building, and in no event shall Landlord be responsible or liable for any failure to relet the Premises or any part thereof, or for any failure to collect any rent due upon a reletting. Landlord’s rejection of a prospective replacement tenant based on an offer of rentals below Landlord’s published rates for new leases of comparable space at the Building at the time in question, or below the rates provided in this Lease or containing terms less favorable than those contained herein, shall not give rise to a claim by Tenant that Landlord failed to mitigate its damages.

Tenant further waives the right to any notices to quit as may be specified in the Landlord and Tenant Act of Pennsylvania, Act of April 6, 1951, as amended, or any similar or successor provision of law, and agrees that 10 days’ notice shall be sufficient in any case where a longer period may be statutorily specified.

In addition to, and not in lieu of any of the foregoing rights granted to Landlord, provided Landlord provides a second notice of the Event of Default and such Event of Default is not cured within five (5) business days after such second notice, then:

1. WHEN THIS LEASE OR TENANT’S RIGHT OF POSSESSION SHALL BE TERMINATED BY COVENANT OR CONDITION BROKEN, OR FOR ANY OTHER REASON, EITHER DURING THE TERM OF THIS LEASE OR ANY RENEWAL OR EXTENSION THEREOF, AND ALSO WHEN AND AS SOON AS THE TERM HEREBY CREATED OR ANY EXTENSION THEREOF SHALL HAVE EXPIRED, IT SHALL BE LAWFUL FOR ANY ATTORNEY AS ATTORNEY FOR TENANT TO FILE AN AGREEMENT FOR ENTERING IN ANY COMPETENT COURT AN ACTION TO CONFESS JUDGMENT IN EJECTMENT AGAINST
TENANT AND ALL PERSONS CLAIMING UNDER TENANT, WHEREUPON, IF LANDLORD SO DESIRES, A WRIT OF EXECUTION OR OF POSSESSION MAY ISSUE FORTHWITH, WITHOUT ANY PRIOR WRIT OF PROCEEDINGS, WHATSOEVER, AND PROVIDED IF FOR ANY REASON AFTER SUCH ACTION SHALL HAVE BEEN COMMENCED THE SAME SHALL BE DETERMINED AND THE POSSESSION OF THE PREMISES HEREBY DEMISED REMAIN IN OR BE RESTORED TO TENANT, LANDLORD SHALL HAVE THE RIGHT UPON ANY SUBSEQUENT DEFAULT OR Defaults, OR UPON THE TERMINATION OF THIS LEASE AS HEREINBEFORE SET FORTH, TO BRING ONE OR MORE ACTION OR ACTIONS AS HEREINBEFORE SET FORTH TO RECOVER POSSESSION OF THE SAID PREMISES.

(2) In any action to confess judgment in ejectment, Landlord shall first cause to be filed in such action an affidavit made by it or someone acting for it setting forth the facts necessary to authorize the entry of judgment, of which facts such affidavit shall be conclusive evidence, and if a true copy of this Lease (and of the truth of the copy such affidavit shall be sufficient evidence) be filed in such action, it shall not be necessary to file the original as a warrant of attorney, any rule of Court, custom or practice to the contrary notwithstanding.

TENANT WAIVER. TENANT SPECIFICALLY ACKNOWLEDGES THAT TENANT HAS VOLUNTARILY, KNOWINGLY, AND INTELLIGENTLY WAIVED CERTAIN DUE PROCESS RIGHTS TO A PREJUDGMENT HEARING BY AGREEING TO THE TERMS OF THE FOREGOING PARAGRAPHS REGARDING CONFESSION OF JUDGMENT. TENANT FURTHER SPECIFICALLY AGREES THAT IN THE EVENT OF DEFAULT, LANDLORD MAY PURSUE MULTIPLE REMEDIES INCLUDING OBTAINING POSSESSION PURSUANT TO A JUDGMENT BY CONFESSION AND ALSO OBTAINING A MONEY JUDGMENT FOR PAST DUE AND ACCELERATED AMOUNTS AND EXECUTING UPON SUCH JUDGMENT. IN SUCH EVENT AND SUBJECT TO THE TERMS SET FORTH HEREBIN, LANDLORD SHALL PROVIDE FULL CREDIT TO TENANT FOR ANY MONTHLY CONSIDERATION WHICH LANDLORD RECEIVES FOR THE LEASED PREMISES IN MITIGATION OF ANY OBLIGATION OF TENANT TO LANDLORD FOR THAT MONEY. FURTHERMORE, TENANT SPECIFICALLY WAIVES ANY CLAIM AGAINST LANDLORD AND LANDLORD’S COUNSEL FOR VIOLATION OF TENANT’S CONSTITUTIONAL RIGHTS IN THE EVENT THAT JUDGMENT IS CONFESSED PURSUANT TO THIS LEASE.

TENANT:
SPARK THERAPEUTICS, INC.

By: 
Name: 
Title: 
Date:

18. SURRENDER; HOLDOVER.

(a) No later than upon the Expiration Date or earlier termination of Tenant’s right to possession of the Premises (such earlier date, the “Surrender Date”), Tenant shall vacate and surrender the Premises to Landlord in good order and condition, vacant, broom clean, and in conformity with the applicable provisions of this Lease, including without limitation Sections 9 and 11. Tenant shall have no right to hold over beyond the Surrender Date, and if Tenant does not vacate as required such failure shall be deemed an Event of Default and Tenant’s occupancy shall not be construed to effect or constitute anything other than a tenancy at sufferance. During any period of occupancy beyond the Surrender Date, the amount of Rent owed by Tenant to Landlord will be the Holdover Percentage of the Rent that would otherwise be due under this Lease, and except that any provisions in this Lease that limit the amount or defer the payment of Additional Rent are null and void. The “Holdover Percentage” equals: (i) 150% for the first 2 months of holdover; and (ii) 200% for any period of holdover beyond 2 months. The acceptance of Rent by Landlord or the failure or delay of Landlord in notifying or evicting Tenant following the Surrender Date shall not create any tenancy rights in Tenant and any such payments by Tenant may be applied by Landlord against its costs and expenses, including reasonable attorneys’ fees, incurred by Landlord as a result of such holdover. The provisions of this Section shall not constitute a waiver by Landlord of any right of reentry as set forth in this Lease; nor shall receipt of any Rent
or any other act in apparent affirmance of the tenancy operate as a waiver of Landlord’s right to terminate this Lease for a breach of any of the terms, covenants, or obligations herein on Tenant’s part to be performed. No option to extend this Lease shall have been deemed to have occurred by Tenant’s holdover, and any and all options to extend this Lease or expand the Premises shall be deemed terminated and of no further effect as of the first date that Tenant holds over. In addition, if Tenant fails to vacate and surrender the Premises as herein required for a period that continues longer than 15 days, Tenant shall indemnify, defend, and hold harmless Landlord from and against any and all costs, losses, expenses, or liabilities incurred as a result of or related to such failure, including without limitation, claims made by any succeeding tenant and real estate brokers’ claims and reasonable attorneys’ fees. Tenant’s obligation to pay Rent and to perform all other Lease obligations for the period up to and including the Surrender Date, and the provisions of this Section, shall survive the Expiration Date. In no way shall the remedies to Landlord set forth above be construed to constitute liquidated damages for Landlord’s losses resulting from Tenant’s holdover.

(b) Prior to the Surrender Date, Tenant, at Tenant’s expense, shall remove from the Premises Tenant’s Property and all telephone, security, and communication equipment system wiring and cabling, and restore in a good and workmanlike manner any damage to the Premises and/or the Building caused by such removal or replace the damaged component of the Premises and/or the Building if such component cannot be restored as aforesaid as reasonably determined by Landlord. Notwithstanding the foregoing, Tenant shall not be required to remove a Specialty Alteration if at the time Tenant requests Landlord’s consent to such Specialty Alteration, Tenant provides Landlord with written notification that Tenant desires not to be required to remove such Specialty Alteration and Landlord consents in writing to Tenant’s non-removal request. A “Specialty Alteration” means an Alteration that: (i) Landlord required to be removed in connection with Landlord’s consent to making such Alteration; or (ii) is not Building standard, including without limitation kitchens (other than a pantry installed for the use of Tenant’s employees only), executive restrooms, computer room installations, supplemental HVAC equipment and components, safes, vaults, libraries or file rooms requiring reinforcement of floors, internal staircases, slab penetrations, non-Building standard life safety systems, security systems, specialty door locks (such as cipher locks) or lighting, and any demising improvements done by or on behalf of Tenant after the Commencement Date. If Tenant fails to remove any of Tenant’s Property, wiring, or cabling as required herein, the same shall be deemed abandoned and Landlord, at Tenant’s expense, may remove and dispose of same and repair and restore any damage caused thereby, or, at Landlord’s election, such Tenant’s Property, wiring, and cabling shall become Landlord’s property. Tenant shall have the right, at Tenant’s option, prior to the Surrender Date and at Tenant’s expense, to remove any Alteration (including Specialty Alterations and Leasehold Improvements) from the Premises without the prior consent of Landlord, provided Tenant shall restore in a good and workmanlike manner any damage to the Premises and/or the Building caused by such removal.

19. RULES AND REGULATIONS.

(a) Tenant covenants that Tenant and its employees, agents, invitees, subtenants, and licensees shall comply with the rules and regulations set forth on Exhibit E attached hereto. Landlord shall have the right to rescind and/or augment any of the rules and regulations and to make such other and further written rules and regulations, provided such rules apply to all tenants of the Project, as in the reasonable judgment of Landlord shall from time to time be needed for the safety, protection, care, and cleanliness of the Project, the operation thereof, the preservation of good order therein, and the protection and comfort of its tenants, their agents, employees, and invitees, which when delivered to Tenant shall be binding upon Tenant in a like manner as if originally prescribed. In the event of an inconsistency between the rules and regulations and this Lease, the provisions of this Lease shall control. Landlord shall use commercially reasonable efforts to enforce the Rules and Regulations and terms, covenants or conditions in any other lease against all tenants in the Building, as applicable, provided, however, Landlord shall not be liable to Tenant for violation of the same by any other tenant, its employees, agents, visitors or licensees, provided Landlord shall enforce the Rules or Regulations against all tenants in a nondiscriminatory fashion.

(b) Notwithstanding the rules and regulations set forth in Exhibit E, where appliance, break room and kitchen is referred to, those words shall be understood to include multiple of such items; Tenant shall be permitted to maintain small refrigerators in the Premises. With respect to Rule #32 and the last paragraph of Exhibit E, Tenant shall be responsible for the conduct of its invitees inasmuch that Tenant controls being able to remove such invitees from the Building, to direct them to leave the Premises, and to demand that they cease conduct that is in violation of the rules and regulations.
20. **GOVERNMENTAL REGULATIONS.**

(a) Tenant shall not use, generate, manufacture, refine, transport, treat, store, handle, dispose, bring, or otherwise cause to be brought or permit any of its agents, employees, subtenants, contractors, or invitees to bring in, on, or about any part of the Project, any hazardous waste, solid waste, hazardous substance, toxic substance, petroleum product or derivative, asbestos, polychlorinated biphenyl, hazardous material, pollutant, contaminant, or similar material or substance as defined by the Comprehensive Environmental Response Compensation and Liability Act, 42 U.S.C. Sections 9601 et seq., as the same may from time to time be amended, and the regulations promulgated pursuant thereto (CERCLA), or now or hereafter defined or regulated as such by any other Law (“Hazardous Material”). Notwithstanding the foregoing, Tenant shall be permitted to bring onto the Premises office cleaning supplies and products normally found in modern offices or used by Tenant in connection with its Permitted Use, provided: (i) Tenant only brings a reasonable quantity of such supplies and products onto the Premises; (ii) Tenant shall at all times comply with all Laws pertaining to the storage, handling, use, disposal, and application of such supplies and products, and all Laws pertaining to the communication to employees and other third parties of any hazards associated with such supplies and products; (iii) the use and presence of Hazardous Materials is strictly and properly monitored and maintained according to all Laws. As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with the Permitted Use, Tenant shall deliver to Landlord (and, if directed by Landlord, Ground Lessors), at such times as are required by any applicable Law or other governmental requirement or whenever otherwise requested by Landlord for a non-arbitrary, bona-fide business purpose, a list identifying each type of Hazardous Materials to be present on the Premises in any material quantities and setting forth any and all governmental approvals or permits required in connection with the presence of such Hazardous Materials on the Premises. Tenant also shall, when requested by Landlord for a non-arbitrary, bona-fide business purpose, deliver to Landlord (and, if directed by Landlord, Ground Lessor) true and correct copies of the following documents relating to the handling, storage, disposal, and emission of Hazardous Materials concurrently with the receipt from or submission thereof to a governmental agency: permits, approvals, reports, and material correspondence; written storage and management plans; and notice of violations of any Laws. Tenant shall not install any underground or above ground tanks on the Premises. Tenant shall not cause or permit to exist any release, spillage, emission, or discharge of any Hazardous Material on or about the Premises in violation of applicable Law (“Release”). In the event of a Release, Tenant shall immediately notify Landlord both orally and in writing, report such Release to the relevant government agencies as required by applicable Law, and promptly remove the Hazardous Material and otherwise investigate and remediate the Release in accordance with applicable Law and to the reasonable satisfaction of Landlord. Landlord shall have the right, but not the obligation, to enter upon the Premises to investigate and/or remediate the Release in lieu of Tenant, and Tenant shall reimburse Landlord as Additional Rent for the costs of such remediation and investigation. Tenant shall promptly notify Landlord if Tenant acquires knowledge of the presence of any Hazardous Material on or about the Premises, except as Tenant is permitted to bring onto the Premises under this Lease. Landlord shall have the right to inspect and assess the Premises for the purpose of determining whether Tenant is handling any Hazardous Material in violation of this Lease or applicable Law, or to ascertain the presence of any Release. This subsection shall survive the Expiration Date.

(b) Tenant shall, and shall cause its employees, agents, contractors, licensees, subtenants, and assignees to, use the Premises in compliance with all applicable Laws. Tenant shall, at its sole cost and expense, promptly comply with each and all of such Laws, except in the case of required structural changes not triggered by Tenant’s particular use or manner of use or change in use of the Premises, or Tenant’s alterations, additions, or improvements therein. Without limiting the generality of the foregoing, Tenant shall: (i) obtain, at Tenant’s expense, before engaging in Tenant’s business or profession within the Premises, all necessary licenses and permits including, but not limited to, state and local business licenses, and permits; and (ii) remain in compliance with and keep in full force and effect at all times all licenses, consents, and permits necessary for the lawful conduct of Tenant’s business or profession at the Premises. Tenant shall pay all personal property taxes, income taxes, and other taxes, assessments, duties, impositions, and similar charges that are or may be assessed, levied, or imposed upon Tenant or Tenant’s Property. Tenant shall also comply with all applicable Laws that do not relate to the physical condition of the Premises and with which only the occupant can comply, such as laws governing maximum occupancy, workplace smoking, VDT regulations, and illegal business operations, such as gambling. The judgment of any court of competent jurisdiction or the admission of Tenant in any judicial, governmental or regulatory action, regardless of whether Landlord is a party thereto, that Tenant has violated any of such Laws shall be conclusive of that fact as between Landlord and Tenant.
Notwithstanding anything to the contrary in this Section, if the requirement of any public authority obligates either Landlord or Tenant to expend money in order to bring the Premises and/or any area of the Project into compliance with Laws as a result of: (i) Tenant’s particular use or alteration of the Premises; (ii) Tenant’s change in the use of the Premises; (iii) the manner of conduct of Tenant’s business or operation of its installations, equipment, or other property therein; (iv) any cause or condition created by or at the instance of Tenant, other than by Landlord’s performance of any work for or on behalf of Tenant; or (v) breach of any of Tenant’s obligations hereunder, then Tenant shall bear all costs of bringing the Premises and/or Project into compliance with Laws, whether such costs are related to structural or nonstructural elements of the Premises or Project.

Except to the extent Tenant shall comply as set forth above, during the Term Landlord shall comply with all applicable Laws regarding the Project (including the Premises), including without limitation compliance with Title III of the Americans with Disabilities Act of 1990, 42 U.S.C. §12181 et seq. and its regulations as to the design and construction of the Common Areas.

Each party hereto hereby acknowledges and agrees that it will not knowingly violate any applicable Laws regarding bribery, corruption, and/or prohibited business practices as they concern each such party’s respective activities under or in connection with this Lease, and each such party will be solely responsible for and will hold harmless the other party from and against any claims or liabilities in connection with any of such responsible party’s own violations of any such Laws.

21. **NOTICES.** Wherever in this Lease it is required or permitted that notice or demand be given or served by either party to this Lease to or on the other party, such notice or demand will be duly given or served if in writing and either: (i) personally served; (ii) delivered by prepaid nationally recognized courier service (e.g., Federal Express, UPS, and USPS) with evidence of receipt required for delivery; (iii) delivered by registered or certified mail, return receipt requested, postage prepaid; or (iv) emailed with evidence of receipt; in all such cases addressed to the parties at the addresses set forth below. Each such notice will be deemed to have been given to or served upon the party to which addressed on the date the same is delivered or delivery is refused. Each party has the right to change its address for notices (provided such new address is in the continental United States) by a writing sent to the other party in accordance with this Section, and each party will, if requested, within 10 days confirm to the other its notice address. Notices may be given by either an agent or attorney acting on behalf of the respective party. Notwithstanding the foregoing: (a) any notice from Landlord to Tenant regarding ordinary business operations (e.g., exercise of a right of access to the Premises, notice of maintenance activities or Landlord access, changes in rules and regulations, etc.) may be given by written notice left at the Premises or delivered by regular mail, facsimile, or electronic means (such as email) to any person at the Premises whom Landlord reasonably believes is authorized to receive such notice on behalf of Tenant without copies; and (b) invoices, notices of change in billing or notice address, and statements of estimated or reconciliation of Operating Expenses and/or utilities, may be sent by regular mail or electronic means (such as email) to Tenant’s billing contact without copies.
Tenant: Spark Therapeutics, Inc.
Attn: Corporate Facilities
3737 Market Street, 13th Floor
Philadelphia, PA 19104
Phone No.: 215-220-9300
Email for billing contact: AP@sparktx.com

Spark Therapeutics, Inc.
Attn: Corporate Facilities
2929 Walnut Street, Suite 1000
Philadelphia, PA 19104
Phone No. 215-220-9300
Email for billing contact: AP@sparktx.com

Landlord: Brandywine 3025 Market, LP
c/o Brandywine Realty Trust
FMC Tower at Cira Centre South
2929 Walnut Street, Suite 1700
Philadelphia, PA 19104
Attn: Jeff DeVuono, Executive Vice President & Senior Managing Director
Phone No. 610-325-5600
Email: jeff.devuono@bdnreit.com

With a copy to:
Email: Legal.Notices@bdnreit.com

22. BROKERS. Landlord and Tenant each represents and warrants to the other that such representing party has had no dealings, negotiations, or consultations with respect to the Premises or this transaction with any broker or finder other than a Landlord affiliate and Broker. Each party shall indemnify, defend, and hold harmless the other from and against any and all liability, cost, and expense (including reasonable attorneys’ fees and court costs), arising out of or from related to its misrepresentation or breach of warranty under this Section. Landlord shall pay Broker a commission in connection with this Lease pursuant to the terms of a separate written agreement between Landlord and Broker. This Section shall survive the Expiration Date.

23. LANDLORD’S LIABILITY. Landlord’s obligations hereunder shall be binding upon Landlord only for the period of time that Landlord is in ownership of the Building, and upon termination of that ownership, and the transfer of any Security Deposit to such successor-in-interest, Tenant, except as to any obligations that are then due and owing, shall look solely to Landlord’s successor-in-interest in ownership of the Building for the satisfaction of each and every obligation of Landlord hereunder. Upon request and without charge, Tenant shall attorn to any successor to Landlord’s interest in this Lease and, at the option of any Mortgagees, to such Mortgagees. Landlord shall have no personal liability under any of the terms, conditions or covenants of this Lease and Tenant shall look solely to the equity of Landlord in the Building and/or the rent, profits and proceeds therefrom for the satisfaction of any claim, remedy or cause of action of any kind whatsoever arising from the relationship between the parties or any rights and obligations they may have relating to the Project, this Lease, or anything related to either, including without limitation as a result of the breach of any Section of this Lease by Landlord. In addition, no recourse shall be had for an obligation of Landlord hereunder, or for any claim based thereon or otherwise in respect thereof or the relationship between the parties, against any past, present, or future Landlord Indemnitee (other than Landlord), whether by virtue of any statute or rule of law, or by the enforcement of any assessment or penalty or otherwise, all such other liability being expressly waived and released by Tenant with respect to the Landlord Indemnitees (other than Landlord).

24. RELOCATION. [INTENTIONALLY DELETED]

25. GENERAL PROVISIONS.

(a) Provided no Event of Default is then outstanding, Tenant shall peaceably and quietly hold and enjoy the Premises for the Term, without hindrance from Landlord or anyone lawfully or equitably claiming by, through, or under Landlord, under and subject to the terms and conditions of this Lease and of any deeds of trust now or hereafter affecting all or any portion of the Premises.
(b) Subject to the terms and provisions of Section 10, the respective rights and obligations provided in this Lease shall bind and inure to the benefit of the parties hereto, their successors and assigns.

(c) This Lease shall be governed in accordance with the Laws of the State, without regard to choice of law principles. Landlord and Tenant hereby consent to the exclusive jurisdiction of the state and federal courts located in the jurisdiction in which the Project is located.

(d) In connection with any litigation or arbitration arising out of this Lease, Landlord or Tenant, whichever is the prevailing party as determined by the trier of fact in such litigation, shall be entitled to recover from the other party all reasonable costs and expenses incurred by the prevailing party in connection with such litigation, including reasonable attorneys’ fees. If, in the context of a bankruptcy case, Landlord is compelled at any time to incur any expense, including attorneys’ fees, in enforcing or attempting to enforce the terms of this Lease or to enforce or attempt to enforce any actions required under the Bankruptcy Code to be taken by the trustee or by Tenant, as debtor-in-possession, then the reasonable sum so paid by Landlord shall be awarded to Landlord by the Bankruptcy Court and shall be immediately due and payable by the trustee or by Tenant’s bankruptcy estate to Landlord in accordance with the terms of the order of the Bankruptcy Court.

(e) This Lease, which by this reference incorporates all exhibits, riders, schedules, and other attachments hereto, supersedes all prior discussions, proposals, negotiations and discussions between the parties and this Lease contains all of the agreements, conditions, understandings, representations, and warranties made between the parties hereto with respect to the subject matter hereof, and may not be modified orally or in any manner other than by an agreement in writing signed by both parties hereto or their respective successors-in-interest. Except to the extent expressly set forth otherwise in this Lease, neither Landlord, nor anyone acting on Landlord’s behalf, has made any representation, warranty, estimation, or promise of any kind or nature whatsoever relating to the physical condition of the Building or the land under the Building or suitability, including without limitation, the fitness of the Premises for Tenant’s intended use.

(f) TIME IS OF THE ESSENCE UNDER ALL PROVISIONS OF THIS LEASE, INCLUDING ALL NOTICE PROVISIONS.

(g) Except for the payment of Rent, each party hereto shall be excused for the period of any delay and shall not be deemed in default with respect to the performance of any of its obligations when prevented from so doing by a cause beyond such party’s reasonable control, including, without limitation, strikes or other labor disputes, orders or regulations of any federal, state, county or municipal authority, embargoes, non-issuance of a governmental permit, fire or other casualty (or reasonable delays in the adjustment of insurance claims), acts of terrorism or war, inability to obtain any materials or services, or acts of God (each, a “Force Majeure Event”). Except as expressly set forth herein, no such inability or delay due to a Force Majeure Event shall constitute an actual or constructive eviction, in whole or in part, or entitle Tenant to any abatement or diminution of Rent, or relieve the other party from any of its obligations under this Lease, or impose any liability upon such party or its agents, by reason of inconvenience or annoyance to the other party, or injury to or interruption of the other party’s business, or otherwise.

(h) Excepting payments of Fixed Rent, Operating Expenses, and utilities (which are to be paid as set forth in Sections 4, 5 and 6) and unless a specific time is otherwise set forth in this Lease for any Tenant payments, all amounts due from Tenant to Landlord shall be paid by Tenant to Landlord within 30 days after receipt of an invoice therefor. As Additional Rent and to the extent not included in Taxes, Tenant shall pay monthly or otherwise when due, whether collected by Landlord or collected directly by the applicable governmental agency, any and all sales, use, use and occupancy, transaction privilege, gross receipts, or other excise tax that may at any time be levied or imposed upon Tenant, or measured by any amount payable by Tenant under this Lease, whether such tax exists on the date of this Lease or is adopted hereafter.

(i) Unless Tenant’s financials are publicly available online at no cost to Landlord, within 10 business days after written request by Landlord (but not more than once during any 12-month period unless an Event of Default has occurred under this Lease, or in the event of a sale, financing, or refinancing by Landlord of all or any portion of the Project), Tenant shall furnish to Landlord, Landlord’s Mortgagee, prospective Mortgagee or purchaser,
reasonably requested financial information as such information is then available. Tenant shall have no obligation to provide any financial or other information to Landlord in violation of Law or the regulations of the U.S. Securities and Exchange Commission. In connection therewith and upon Tenant’s request, Landlord and Tenant shall execute a mutually acceptable confidentiality agreement on Landlord’s form therefor.

(j) Tenant represents and warrants to Landlord that: (i) Tenant was duly organized and is validly existing and in good standing under the Laws of the jurisdiction set forth for Tenant in the first sentence of this Lease; (ii) Tenant is legally authorized to do business in the State; (iii) the person(s) executing this Lease on behalf of Tenant is(are) duly authorized to do so; and (iv) Tenant has the full corporate or partnership power and authority to enter into this Lease and has taken all corporate or partnership action, as the case may be, necessary to carry out the transaction contemplated herein, so that when executed, this Lease constitutes a valid and binding obligation enforceable in accordance with its terms. Landlord represents and warrants to Tenant that: (i) Landlord was duly organized and is validly existing and in good standing under the Laws of the State; (ii) Landlord is legally authorized to do business in the State; and (iii) the person(s) executing this Lease on behalf of Landlord is(are) duly authorized to do so.

(k) Each party hereto represents and warrants to the other that such party is not a party with whom the other is prohibited from doing business pursuant to the regulations of the Office of Foreign Assets Control (“OFAC”) of the U.S. Department of the Treasury, including those parties named on OFAC’s Specially Designated Nationals and Blocked Persons List. Each party hereto is currently in compliance with, and shall at all times during the Term remain in compliance with, the regulations of OFAC and any other governmental requirement relating thereto. Each party hereto shall defend, indemnify, and hold harmless the other from and against any and all claims, damages, losses, risks, liabilities, and expenses (including reasonable attorneys’ fees and costs) incurred by the other to the extent arising from or related to any breach of the foregoing certifications. The foregoing indemnity obligations shall survive the Expiration Date.

(l) Landlord shall have the right, to the extent required to be disclosed by Landlord or Landlord’s affiliates in connection with filings required by applicable Laws, including without limitation the Securities and Exchange Commission (“SEC”), without notice to Tenant to include in such securities filings general information relating to this Lease, including, without limitation, Tenant’s name, the Building, and the square footage of the Premises. Except as set forth in the preceding sentence, neither Tenant nor Landlord shall issue, or permit any broker, representative, or agent representing either party in connection with this Lease to issue, any press release or other public disclosure regarding the specific terms of this Lease (or any amendments or modifications hereof), without the prior written approval of the other party. The parties acknowledge that the transaction described in this Lease and the terms thereof (but not the existence thereof) are of a confidential nature and shall not be disclosed except to such party’s employees, attorneys, accountants, consultants, advisors, affiliates, and actual and prospective purchasers, lenders, investors, subtenants and assignees (collectively, “Permitted Parties”), and except as, in the good faith judgment of Landlord or Tenant, may be required to enable Landlord or Tenant to comply with its obligations under Law or under laws and regulations of the SEC or to the extent necessary in connection with a dispute with respect to this Lease. Neither party may make any public disclosure of the specific terms of this Lease, except as required by Law, including without limitation SEC laws and regulations, or as otherwise provided in this paragraph. In connection with the negotiation of this Lease and the preparation for the consummation of the transactions contemplated hereby, each party acknowledges that it will have had access to confidential information relating to the other party. Each party shall treat such information and shall cause its Permitted Parties to treat such confidential information as confidential, and shall preserve the confidentiality thereof, and not duplicate or use such information, except by Permitted Parties.

(m) Neither Tenant, nor anyone acting through, under, or on behalf of Tenant, shall have the right to record this Lease, nor any memorandum, notice, affidavit, or other writing with respect thereto.

(n) Provided there is no Event of Default at the time of Tenant’s request and at the time of the execution of such agreement, Landlord agrees to execute, from time to time after receipt of Tenant’s written request therefor, an agreement subordinating Landlord’s lien in Tenant’s personal property, furniture, fixtures, equipment, leasehold improvements and other assets, on Landlord’s customary form, with such modifications that are reasonably acceptable to Landlord, Tenant and Tenant’s lender(s).
All requests made to Landlord to perform repairs or furnish services, supplies, utilities, or freight elevator usage (if applicable), shall be made online to the extent available (currently such requests shall be made via http://etenants.com/, as the same may be modified by Landlord from time to time) otherwise via email or written communication to Landlord’s property manager for the Building. Whenever Tenant requests Landlord to take any action not required of Landlord under this Lease or give any consent required or permitted to be given by Landlord under this Lease (for example, a request for a Transfer consent, a consent to an Alteration, or a subordination of Landlord’s lien, but other than a request for services, supplies, or utilities which is governed by Section 7(b)), Tenant shall pay to Landlord for Landlord’s administrative and/or professional costs in connection with each such action or consent Landlord’s reasonable costs incurred by Landlord in reviewing and taking the proposed action or consent, including reasonable attorneys’, engineers’ and/or architects’ fees (as applicable), plus the Administrative Fee, but no more than $1,500 with respect to a Transfer request. The foregoing amount shall be paid by Tenant to Landlord within 30 days after Landlord’s delivery to Tenant of an invoice for such amount. Tenant shall pay such amount without regard to whether Landlord takes the requested action or gives the requested consent.

Tenant acknowledges and agrees that Landlord shall not be considered a “business associate” for any purpose under the Health Insurance Portability and Accountability Act of 1996 and all related implementing regulations and guidance.

Tenant shall cause any work performed on behalf of Tenant to be performed by contractors who work in harmony, and shall not interfere, with any labor employed by Landlord or Landlord’s contractors. If at any time any of the contractors performing work on behalf of Tenant does not work in harmony or interferes with any labor employed by Landlord, other tenants, or their respective mechanics or contractors, then the permission granted by Landlord to Tenant to do or cause any work to be done in or about the Premises may be withdrawn by Landlord with 48 hours’ written notice to Tenant.

This Lease may be executed in any number of counterparts, each of which when taken together shall be deemed to be one and the same instrument. This Lease shall not be binding nor shall either party have any obligations or liabilities or any rights with respect hereto, or with respect to the Premises, unless and until both parties have executed and delivered this Lease. The parties acknowledge and agree that notwithstanding any law or presumption to the contrary, the exchange of copies of this Lease and signature pages by electronic transmission shall constitute effective execution and delivery of this Lease for all purposes, and signatures of the parties hereto transmitted and/or produced electronically shall be deemed to be their original signature for all purposes.

Landlord and persons authorized by Landlord may enter the Premises at all reasonable times upon reasonable advance notice or, in the case of an emergency, at any time with such notice as is reasonable under the circumstances. Landlord shall not be liable for inconvenience to or disturbance of Tenant by reason of any such entry; provided, however, in the case of repairs or work, such shall be done, so far as practicable, so as to not unreasonably interfere with Tenant’s use of the Premises. Notwithstanding, the foregoing, except in an emergency, Landlord shall not enter any “clean space” or laboratory space within the Premises without Tenant’s prior consent.

If more than one person executes this Lease as Tenant, each of them is jointly and severally liable for the keeping, observing, and performing of all of the terms, covenants, conditions, provisions, and agreements of this Lease to be kept, observed, and performed by Tenant.

TO THE EXTENT PERMITTED BY APPLICABLE LAW, LANDLORD AND TENANT HEREBY WAIVE TRIAL BY JURY IN ANY ACTION, PROCEEDING, OR COUNTERCLAIM BROUGHT BY EITHER AGAINST THE OTHER ON ANY MATTER ARISING OUT OF OR IN ANY WAY CONNECTED WITH THIS LEASE, THE RELATIONSHIP OF LANDLORD AND TENANT, OR TENANT’S USE OR OCCUPANCY OF THE BUILDING, ANY CLAIM OR INJURY OR DAMAGE, OR ANY EMERGENCY OR OTHER STATUTORY REMEDY WITH RESPECT THERETO.

26. EXPANSION OPTION.
Provided no Event of Default then exists, this Lease is in full force and effect, Tenant is Spark Therapeutics, Inc. or a Permitted Transferee, and Tenant and/or a Permitted Transferee is then occupying at least 90% of the Premises, Tenant shall have the one-time right ("Expansion Option") to lease all of the Expansion Space on the terms set forth herein by delivering Tenant’s written expansion election notice (" Expansion Notice") to Landlord no later than September 1, 2018, with time being of the essence. The "Expansion Space" means all of the fourth floor of the Building. If Tenant timely exercises the Expansion Option and there is no Event of Default, then the Expansion Space shall be leased under all of the same terms and conditions as set forth in this Lease except that the Term for Expansion Space shall commence on December 1, 2019 (the “Expansion Space Commencement Date”), including at the same Fixed Rent per rentable square foot and for the same Term as for the then-current Premises, with a pro rata Improvement Allowance, restroom renovation allowance and Abatement Period, the “Premises” shall include the Expansion Space and, except as otherwise set forth in this Section, all computations made under this Lease based upon or affected by the rentable area of the Premises shall be recomputed to include the Expansion Space; provided, however, the Expansion Space Commencement Date shall be pushed back on a day-for-day basis for: (i) each day (if any) that Substantial Completion of the initial improvements in the Expansion Space is delayed due to a Force Majeure Event or Landlord Delay (as defined in Exhibit C); and (ii) each day Landlord fails to deliver the Expansion Space to Tenant for the construction of Tenant’s initial improvements beyond May 1, 2019. Upon Tenant’s delivery of the Expansion Notice, Tenant may not thereafter revoke its exercise of the Expansion Option. Effective on Landlord’s delivery of possession of the Expansion Space to Tenant, for purposes of all insurance and indemnity provisions in this Lease, the term “Premises” shall include the Expansion Space.

27. RIGHT OF FIRST OFFER.

(a) Provided no Event of Default then exists, this Lease is in full force and effect, Tenant or a Permitted Transferee, and Tenant and/or a Permitted Transferee is then occupying at least 90% of the Premises, then from and after September 1, 2018 Landlord shall notify Tenant in writing (“Landlord’s ROFO Notice”) when any rentable space located on the fourth floor of the Building (exclusive of any Expansion Space leased under the Expansion Option) or any other non-retail space on the garden level of the Building becomes available for lease (as defined below) from Landlord or Landlord reasonably anticipates that such space will become available for lease from Landlord during the Initial Term (“ROFO Space”). Landlord’s ROFO Notice shall include the anticipated availability date and basic fair market economic terms for the lease of the ROFO Space (as reasonably determined by Landlord and, subject to the terms and provisions of this Section, Tenant shall have the right (“ROFO”) to lease all (but not less than all) of the ROFO Space by delivering Tenant’s written notice of such election to Landlord (“Tenant’s ROFO Notice”) within 10 days after Tenant’s receipt of Landlord’s ROFO Notice. Upon Tenant's delivery of Tenant’s ROFO Notice, Tenant may not thereafter revoke Tenant’s exercise of the ROFO. Space is “available to lease” if and when: (i) the lease for any current tenant of all or a portion of the space expires or is otherwise terminated, provided space shall not be deemed to be or become available if the space is assigned or subleased by the current tenant of the space, or relet by the current tenant or subtenant of the space by renewal, extension, or new lease; and (ii) to the extent that all or a portion of the ROFO Space is available for lease from Landlord as of the date of this Lease, Landlord has entered into a lease with a third-party tenant for such space. Notwithstanding the foregoing, during the period from September 1, 2018 through February 28, 2019, space is “available to lease” if and when Landlord identifies a potential new tenant for such space.

(b) Notwithstanding anything to the contrary in this Lease, the ROFO shall be subject to the following: (i) Tenant shall not have the right to lease the ROFO Space under this article if upon the commencement
date of the leasing of the ROFO Space there would not then be at least thirty-six (36) months remaining in the Term (provided if less than thirty-six (36) months remain in the Term, Landlord shall deliver Landlord’s ROFO Notice to Tenant and Tenant shall be permitted to exercise an available Extension Option so that at least 36 months remain in the Term); (ii) if Tenant notifies Landlord that Tenant elects not to lease the ROFO Space or if Tenant fails to timely deliver Tenant’s ROFO Notice to Landlord with respect thereto, then Landlord shall have the right to enter into a lease for the ROFO Space under one or more leases containing such terms as Landlord deems acceptable in Landlord’s sole discretion (including, without limitation, any right of first offer or other expansion rights that Landlord might grant such tenant(s) for such ROFO Space) and the ROFO shall be void and have no further force or effect with respect to such space (but Tenant shall retain Tenant’s ROFO for such portions of the ROFO Space not previously offered to Tenant in Landlord’s ROFO Notice); provided, however, if Landlord does not lease the ROFO Space within 12 months after offering it to Tenant, Tenant’s ROFO shall be revoked and reinstated with respect to such ROFO Space; and (iii) the ROFO shall be subject, subordinate, and in all respects inferior to the rights of any existing third-party tenant leasing space at the Building as of the date of this Lease (including, without limitation, any lease term extension period(s) contained in such tenant’s lease, regardless of whether the extension right or agreement is contained in such lease or is agreed to at any time by Landlord and the tenant under such lease). If an Event of Default exists at any time after Landlord receives Tenant’s ROFO Notice but before the first day that Tenant commences to lease the ROFO Space, Landlord, at Landlord’s option, shall have the right to nullify Tenant’s exercise of the ROFO with respect to the ROFO Space.

32. Extension Option.

(a) Provided no Event of Default then exists, this Lease is in full force and effect, and Tenant is the originally named Tenant or a Permitted Transferee, and Tenant and/or a Permitted Transferee is then occupying at least 1 full floor of the Building, Tenant shall have the right to extend the Term with respect to the Extension Premises (“Extension Premises”) by delivering Tenant’s written extension election notice to Landlord no later than the Extension Deadline, with time being of the essence. The “Extension Premises” means, at Tenant’s election as set forth in its extension election notice, either all of the Premises or all of the Premises excluding all or some portion of the Expansion Premises and ROFO Space so long as the Extension Premises consist of entire contiguous floors of the Building. The “Extension Deadline” means: (i) if Tenant and/or a Permitted Transferee is then occupying 3 or more full floors of the Building, the date that is 30 months prior to the expiration of the then-current Term; or (ii) if Tenant and/or a Permitted Transferee is then occupying less than 3 full floors of the Building, the date that is 24 months prior to the expiration of the then-current Term. The terms and conditions of this Lease during each Extension Term shall remain unchanged.
except Tenant shall only be entitled to the 3 Extension Terms provided above, the annual Fixed Rent for the Extension Term shall be the Extension Rent (as defined below), the Expiration Date shall be the last day of the Extension Term (or such earlier date of termination of this Lease pursuant to the terms hereof), and, except to the extent reflected in the Extension Rent, Landlord shall have no obligation to perform any tenant improvements to the Premises or provide any tenant improvement allowance to Tenant. Upon Tenant’s timely delivery of its written extension election notice, Tenant may not thereafter revoke its exercise of the Extension Option. Notwithstanding anything to the contrary in this Lease, Tenant shall have no right to extend the Term other than or beyond the applicable Extension Terms described in this paragraph.

(b) “Extension Rent” means, with respect to the first 12 months of an Extension Term, the greater of: (i) the fair market extension term base rent for space comparable to the Extension Premises in comparable buildings in the market in which the Project is located (“Fair Market Rent”); or (ii) 102.5% of the Fixed Rent in effect for the Extension Premises for the calendar month immediately prior to the start of such Extension Term. In determining the Fair Market Rent, Landlord, Tenant and any broker shall take into account all relevant factors including, without limitation, prevailing market allowances and concessions for renewing tenants, space measurement methods and loss factors, the lease term, the size of the space, the location of the building(s), parking charges, the amenities offered at the building(s), the age of the building(s), and whether Project Expenses and other pass-through expenses are on a triple net, base year, expense stop or other basis. In lieu of directly providing any prevailing market allowances and/or concessions, Landlord may elect to reduce the Extension Rent by the economic equivalent thereof to reflect the fact that such allowances and concessions were not provided directly to Tenant. During the Extension Term, Tenant shall not be entitled to any tenant improvement allowances, free rent periods or other economic concessions (if any) that Tenant was entitled to during the Initial Term, except to the extent such items are indirectly incorporated into the Fair Market Rent as set forth in this Section. When the Extension Rent is being determined for the first year of the Extension Term, the Extension Rent for the second and all subsequent years of the Extension Term shall also be determined in accordance with the same procedures as are set forth herein and based upon either: (I) if the first year of the Extension Term is determined to be the Fair Market Rent, then the then-prevailing annual rent escalation factor in the applicable leasing market; or (II) if the first year of the Extension Term is determined to be 102.5% of the Fixed Rent in effect for the calendar month immediately prior to the start of such Extension Term, then the Fixed Rent in effect for each 12-month period of the Extension Term shall equal 102.5% of the Fixed Rent in effect for the prior 12-month period.

(c) If Tenant timely exercises an Extension Option and Landlord and Tenant do not agree upon the Fair Market Rent in writing by the date that is the later of 20 days after Landlord’s receipt of Tenant’s extension notice or 3 months prior to the Extension Deadline, then within 15 days after either party notifies the other in writing that such notifying party desires to determine the Fair Market Rent in accordance with the procedures set forth in this Section, Landlord and Tenant shall each deliver to the other party a written statement of such delivering party’s determination of the Fair Market Rent, together with such supporting documentation as the delivering party desires to deliver. Within 10 days after such 15-day period, Landlord and Tenant shall appoint a real estate broker having a minimum of 10 years’ experience in the market in which the Project is located who shall select either Landlord’s determination or Tenant’s determination, whichever the broker finds more accurately reflects the Fair Market Rent. The broker shall be instructed to notify Landlord and Tenant of such selection within 10 days after such broker’s appointment. The broker shall have no power or authority to select any Fair Market Rent other than the Fair Market Rent submitted by Landlord or Tenant nor shall the broker have any power or authority to modify any of the provisions of this Lease, and the decision of the broker shall be final and binding upon Landlord and Tenant. If Landlord and Tenant do not timely agree in writing upon the appointment of the broker, Landlord shall submit to Tenant the names of 3 qualified brokers (i) with a minimum of 10 years’ experience in the market in which the Project is located and (ii) who have not been employed or retained by either Landlord or Tenant or any affiliate of either for a period of at least 10 years prior to appointment pursuant hereto, and Tenant shall have 10 days after receiving such names to notify Landlord of which of the 3 brokers Tenant selects to determine the Fair Market Rent. If Tenant fails to timely notify Landlord of Tenant’s selection, Landlord shall have the right to unilaterally appoint the broker. The fee and expenses of the broker shall be shared equally by Landlord and Tenant.

(d) Upon Tenant’s timely and proper exercise of an Extension Option pursuant to the terms above and satisfaction of the above conditions: (i) the “Term” shall include the Extension Term, subject only to the determination of Extension Rent; (ii) the “Premises” during the Extension Term means the Extension Premises; and

34
(iii) upon Landlord’s request, Tenant shall execute prior to the expiration of the then-expiring Term, an appropriate amendment to this Lease, in form and content reasonably satisfactory to both Landlord and Tenant, memorializing the extension of the Term for the ensuing Extension Term (provided Tenant’s failure to execute such amendment shall not negate the effectiveness of Tenant’s exercise of the Extension Option).

29. **TERMINATION OPTION.** Provided: (i) no Event of Default then exists; (ii) this Lease is in full force and effect; and (iii) Tenant is the originally named Tenant or a Permitted Transferee, Tenant has the right to terminate this Lease with respect to one or more contiguous floors of the Premises effective at 11:59 p.m. on the Termination Date, in accordance with and subject to each of the following terms and conditions ("Termination Option."). The “Termination Date” means the last day of the 127th full calendar month after the Commencement Date. If Tenant desires to exercise the Termination Option, Tenant must give to Landlord irrevocable written notice of Tenant’s exercise of the Termination Option ("Termination Notice."), together with the Termination Payment (as defined below), which notice shall specify which floor(s) are being terminated (provided if Tenant does not specify, then the Termination Option shall be for all of the Premises). The Termination Notice and the Termination Payment must be received by Landlord no later than the Termination Deadline, failing which the Termination Option is deemed waived (provided Landlord reserves the right to waive in writing the requirement that Tenant fully and/or timely pay the Termination Payment). The “Termination Deadline” means: (i) if Tenant and/or a Permitted Transferee is then occupying 3 or more full floors of the Building, the date that is 30 months prior to the Termination Date; or (ii) if Tenant and/or a Permitted Transferee is then occupying less than 3 full floors of the Building, the date that is 24 months prior to the Termination Date. The “Termination Payment” means the sum of the unamortized (amortized on a straight-line basis with interest at 8%) amount as of the Termination Date of the following in connection with this Lease and any amendment to this Lease with respect to the portion of the Premises being terminated: (i) brokerage commissions and attorneys’ fees paid by Landlord; (ii) rent concessions; and (iii) total cost incurred by Landlord for improvements to the Premises, including without limitation the Leasehold Improvements and any Building Improvements (as defined in Section 30) and Total Façade Costs (as defined in Section 30), plus any and all allowances to Tenant, including without limitation the Improvement Allowance and the Additional Allowance used by Tenant. Promptly following the Commencement Date, and within 30 days after Landlord’s receipt of Tenant’s written request therefor, the parties shall execute and deliver a statement confirming the amount of the Termination Payment. Tenant’s payment of the Termination Payment is a condition precedent to the termination of this Lease on the Termination Date, and such obligation survives the Expiration Date. Tenant acknowledges and agrees that the Termination Payment is not a penalty and is fair and reasonable compensation to Landlord for the loss of expected rentals from Tenant. The Termination Payment is payable only by wire transfer or cashier’s check. Time is of the essence with respect to the dates and deadlines set forth herein. Notwithstanding the foregoing, if at any time during the period on or after the date of the Termination Notice, up to and including the Termination Date, Tenant is in default of this Lease, beyond all applicable notice, cure and grace periods, then Landlord may elect, by written notice to Tenant to cancel and declare null and void Tenant’s exercise of the Termination Option, in which case this Lease shall continue in full force and effect for the full Term unaffected by Tenant’s exercise of the Termination Option. As of the date Tenant delivers the Termination Notice, any and all unexercised rights or options of Tenant to extend the Term or expand the Premises (whether expansion options, rights of first refusal, rights of first offer, or otherwise), and any and all outstanding tenant improvement allowance not properly claimed by Tenant in accordance with this Lease immediately terminate and are automatically, without further action required by any party, null and void and of no force or effect. If Tenant timely and properly exercises the Termination Option in accordance with this paragraph and Landlord has not negated the effectiveness of Tenant’s exercise of the Termination Option pursuant to the foregoing, this Lease and the Term for the terminated Premises shall come to an end on the Termination Date with the same force and effect as if the Term were fixed to expire on such date, the Expiration Date shall be the Termination Date, and the terms and provisions of Section 18 shall apply with respect to the terminated premises. If the terminated Premises are less than all of the Premises, then this Lease shall remain in full force and effect with respect to the balance of the Premises, and all provisions in this Lease based on the square footage of the Premises, including without limitation Rent and Tenant’s Share, shall be adjusted accordingly effective on the day immediately following the Termination Date.

30. **BUILDING IMPROVEMENTS.**
(a) Landlord covenants to spend or have spent, or cause its affiliates to spend or have spent, on or before June 30, 2020, no less than $25,000,000.00 in the aggregate on improvements to the Building and/or Drexel Square as it exists on the date of this Lease (collectively, “Building Improvements”).

(b) If this Lease is amended to expand the Premises to include at least 3 full floors of the Building above street level, and provided the originally named Tenant or a Permitted Transferee is paying Rent on at least 3 full floors of the Building above street level, there is no Event of Default which remains uncured, this Lease is in full force and effect, and the Building Improvements that have been completed include improvements to the east façade of the Building, then Tenant shall have the right to request that Landlord review north and south façade improvements proposed by Tenant. If such façade improvements are approved by Landlord, which approval Landlord may give or deny in its sole and absolute discretion (“Approved Façade Improvements”), Landlord shall provide Tenant with a written estimate of the total design and construction costs therefor. Within 30 days after Tenant’s receipt of such estimate, Tenant shall notify Landlord in writing as to whether Tenant approves or disapproves of the estimate, which approval shall not be unreasonably withheld, conditioned, or delayed, provided if no response is received within such 30-day period, then Tenant shall be deemed to have disapproved the estimate and Landlord shall have no further obligation with respect to the Approved Façade Improvement. However, if Tenant approves the estimate within such 30-day period, Landlord shall cause the Approved Façade Improvements to be completed in a commercially reasonable manner, provided the actual total design and construction costs of the Approved Façade Improvements (“Total Façade Costs”) shall be borne by Tenant and paid as follows: (i) Landlord shall advise Tenant in writing of the Total Façade Costs, and the date that is 30 days after the later of Tenant’s receipt of such writing and Landlord’s commencement of such Approved Façade Improvements is the “Payback Period Start Date.”; (ii) Landlord shall amortize the Total Façade Costs on a straight-line basis with interest at 8% over the number of months in the Term from and after the Payback Period Start Date, and the resulting monthly amortized amount is referred to herein as the “Monthly Façade Increase”; (iii) commencing on the Payback Period Start Date, Tenant shall pay the Monthly Façade Increase as Additional Rent on the first day of each month of the Term; and (iv) Landlord may prepare and deliver to Tenant an amendment to this Lease reflecting the foregoing. Tenant shall promptly execute and return to Landlord the amendment for Landlord’s counter-signature, together with a check for the initial Monthly Façade Increase. If Tenant fails to execute or object to the amendment within 10 days after receipt, the amendment shall be deemed accepted by Tenant. Notwithstanding the foregoing, Tenant shall have the option, by providing written notice of such when Tenant approves the estimate, to elect to directly pay Landlord the Total Façade Costs within 30 days following Landlord’s invoice therefor, together with copies of reasonable supporting documentation evidencing such costs.

31. ZONING. In the event that Tenant desires to pursue zoning relief in connection with its use of the Premises, Landlord shall, at no cost to Landlord, support and assist Tenant with such pursuit, including, but not limited to, signing and submitting applications. The foregoing shall not be deemed to modify the Permitted Use.

[SIGNATURES ON FOLLOWING PAGE]
TENANT CONFESSION CERTIFICATION: Tenant acknowledges and agrees that any failure of Tenant to execute Section 17 of this Lease shall be an absolute bar from Tenant (or Tenant’s successors or assigns) claiming, alleging or petitioning, including, but not limited to, in any petition to open said confession, that such Section is invalid and not binding upon Tenant (or Tenant’s successors or assigns).

IN WITNESS WHEREOF, the parties hereto have executed this Lease under seal as of the day and year first-above stated.

BRANDYWINE 3025 MARKET, LP, a Delaware limited partnership
By: Brandywine 3025 Market Holdings, LLC, its general partner
By: National Safe Harbor Exchanges, its sole member

By: ______________________
Name: _____________________
Title: _______________________
Date: _______________________

TENANT:
SPARK THERAPEUTICS, INC., a Delaware corporation
By: _______________________
Name: _____________________
Title: _______________________
Date: _______________________

Exhibits:
Exhibit A: Location Plan of Premises
Exhibit B: Form of COLT
Exhibit C: Leasehold Improvements
Exhibit D: Janitorial Specifications
Exhibit E: Rules and Regulations

[Signature Page]
EXHIBIT A
LOCATION PLAN OF PREMISES (NOT TO SCALE)
CONFIRMATION OF LEASE TERM

THIS CONFIRMATION OF LEASE TERM ("COLT") is made as of ______________________ between ____________________________________________ ("Landlord") and ____________________________________________ ("Tenant").

1. Landlord and Tenant are parties to that certain lease dated ________________ ("Lease Document"), with respect to the premises described in the Lease Document, known as State __________ consisting of approximately _______ rentable square feet ("Premises"), located at ________________________________.

2. All capitalized terms, if not defined in this COLT, have the meaning given such terms in the Lease Document.

3. Tenant has accepted possession of the Premises in their "AS IS" "WHERE IS" condition and all improvements required to be made by Landlord per the Lease Document have been completed.

4. The Lease Document provides for the commencement and expiration of the Term of the lease of the Premises, which Term commences and expires as follows:
   a. Commencement of the Term of the Premises: ________________
   b. Expiration of the Term of the Premises: ________________

5. The required amount of the Security Deposit and/or Letter of Credit per the Lease Document is $ __________. Tenant has delivered the Security Deposit and/or Letter of Credit per the Lease Document in the amount of $ __________.

6. The Building Number is __________ and the Lease Number is __________. This information must accompany every payment of Rent made by Tenant to Landlord per the Lease Document.

TENANT: ________________________________

__________________________________________________________________________
By: ___________________________ Name: ___________________________
Title: __________________________

LANDLORD: ________________________________

__________________________________________________________________________
By: ___________________________ Name: ___________________________
Title: __________________________

B- 1
EXHIBIT C
LEASEHOLD IMPROVEMENTS

This Exhibit C - Leasehold Improvements (this “Exhibit”) is a part of the Lease to which this Exhibit is attached. Capitalized terms not defined in this Exhibit shall have the meanings set forth for such terms in the Lease. Notwithstanding anything to the contrary herein, it is contemplated that the Leasehold Improvements will be completed in two phases, the first with respect to the Lower Level Space and Suite 200, and the second with respect to Suite 300.

1. Definitions.

1.1 “Architect” means the licensed architect engaged by Tenant, subject to Landlord’s reasonable approval, to prepare the Architectural Plans.

1.2 “Architectural Plans” means 100% fully coordinated and complete, Permittable and accurate architectural working drawings and specifications for the Leasehold Improvements prepared by the Architect including all architectural dimensioned plans showing wall layouts, wall and door locations, power and telephone locations and reflected ceiling plans and further including elevations, details, specifications and schedules according to accepted AIA standards.

1.3 “Building Standard” means the quality and quantity of materials, finishes, ways and means, and workmanship specified from time to time by Landlord as being standard for leasehold improvements at the Building or for other areas at the Building, as applicable.

1.4 “Central Systems” means any Building system or component within the Building core servicing the tenants of the Building or Building operations generally (such as base building plumbing, electrical, heating, ventilation and air conditioning, fire protection and fire alert systems, elevators, structural systems, building maintenance systems or anything located within the core of the Building or central to the operation of the Building).

1.5 “Construction Costs” means all costs in the permitting, demolition, construction, acquisition, and installation of the Leasehold Improvements, including, without limitation, contractor fees, overhead and profit, and the cost of all labor and materials supplied by Contractor, suppliers, independent contractors, and subcontractors arising in connection with the Leasehold Improvements.

1.6 “Contractor” means the general contractor selected by Tenant in accordance with the terms of this Exhibit to construct and install the Leasehold Improvements, subject to Section 3.1.

1.7 “Improvement Allowance” means, collectively, the Leasehold Improvement Allowance and the Restroom Improvement Allowance.

1.8 “Improvement Costs” means the sum of: (i) the Planning Costs; and (ii) the Construction Costs.

1.9 “Landlord’s Designer” means the architect, space planner, or engineer, if any, engaged by Landlord to review the Plans for the Leasehold Improvements as contemplated by Section 2 below.

1.10 “Leasehold Improvement Allowance” means: (i) with respect to the Lower Level Space and Suite 200, an amount equal to the product of $65.00 multiplied by the rentable square footage of the Lower Level Space plus Suite 200, which product equals $3,868,410.00; and (ii) with respect to Suite 300, an amount equal to the product of $58.74 multiplied by the rentable square footage of Suite 300, which product equals $2,828,624.70.

1.11 “Leasehold Improvements” means the improvements, alterations, and other physical additions to be made or provided to; constructed, delivered or installed at, or otherwise acquired for, all of the Premises in accordance with the Plans, or otherwise approved in writing by Landlord or paid for in whole or in part from the Improvement Allowance. Any provision of this Exhibit to the contrary notwithstanding, the Leasehold Improvements shall not include Tenant’s Equipment.
1.12 “MEP Engineer” means the engineer engaged by Tenant, subject to Landlord’s reasonable approval, to prepare the MEP Plans.

1.13 “MEP Plans” means 100% fully coordinated and complete, Permittable and accurate mechanical, electrical and plumbing plans, schedules and specifications for the Leasehold Improvements prepared by the MEP Engineer in accordance and in compliance with the requirements of applicable building, plumbing, and electrical codes and the requirements of any authority having jurisdiction over or with respect to such plans, schedules and specifications, which are complete, accurate, consistent, and fully coordinated with and implement and carry out the Architectural Plans.

1.14 “Permittable” means that the applicable plan meets the requirements necessary to obtain a building permit from the county in which the Building is located.

1.15 “Planning Costs” means all costs related to the design of the Leasehold Improvements including, without limitation, the professional fees of the Architect and other professionals preparing and/or reviewing the Plans.

1.16 “Plans” means the Architectural Plans together with the MEP Plans, copies of all permit applications required for the Leasehold Improvements, all related documents, and if applicable, the Structural Plans.

1.17 “Restroom Improvement Allowance” means an amount equal to the product of $5.00 multiplied by the rentable square footage of the Premises, which product with respect to Suite 200 equals $263,275.00, and with respect to Suite 300 equals $240,775.00 (there is no Restroom Improvement Allowance with respect to the Lower Level Suites).

1.18 “Structural Engineer” means the engineer engaged by Tenant, subject to Landlord’s reasonable approval, to prepare the Structural Plans.

1.19 “Structural Plans” means 100% fully coordinated and complete, Permittable, and accurate structural plans, schedules and specifications, if any, for the Leasehold Improvements prepared by the Structural Engineer in accordance and in compliance with the requirements of any authority having jurisdiction over or with respect to such plans, schedules and specifications, which are complete, accurate, consistent, and fully coordinated with and implement and carry out the Architectural Plans.

1.20 “Substantial Completion” means the later of the date on which the Leasehold Improvements have been completed except for punch list items as determined by Landlord’s architect or space planner, and Tenant has obtained a certificate permitting the lawful occupancy of the Premises issued by the appropriate governmental authority.

1.21 “Tenant’s Equipment” means any telephone, telephone switching, data, and security cabling and systems, cabling, furniture, computers, servers, Tenant’s trade fixtures, and other personal property installed (or to be installed) by or on behalf of Tenant in the Premises.

2. Plans.

2.1 Access. Following the full execution and delivery of this Lease, Tenant and its authorized agents, employees and Contractor shall have the right, at Tenant’s own risk, expense, and responsibility, to enter the Premises for the purpose of designing and constructing the Leasehold Improvements, provided that Tenant acknowledges that all provisions of the Lease shall then be in full force and effect (except the obligation to pay Fixed Rent, Project Expenses, Taxes, and Project Utility Costs (except for electricity used by Tenant at the Premises)). Tenant and its authorized agents, employees, and contractors shall have the right to enter the Building core areas on every floor, including existing pipe and duct chases connecting and continuing from the Premises to the basement and to the penthouse and roof. Access to spaces adjacent to, or within space occupied by other tenants, shall be scheduled with the affected tenants at least 24 hours in advance.

Tenant work letter
2.2 Process. Tenant shall prepare and deliver to Landlord proposed Plans for Landlord’s review, stamped for permit filing, together with any underlying detailed information Landlord may require in order to evaluate the Plans no later than: (i) with respect to the Leasehold Improvements in the Lower Level Space and Suite 200, the later of 45 business days after full execution and delivery of the Lease and prior to commencement of the Leasehold Improvements in the Lower Level Space and Suite 200; and (ii) with respect to the Leasehold Improvements in Suite 300, the later of 45 business days after the Suite 300 Delivery Date and prior to commencement of the Leasehold Improvements in Suite 300. The design of the Leasehold Improvements must be consistent with sound architectural and construction practices in first-class office buildings comparable in size and market to the Building and must utilize only Building Standard items or such items as are approved by Landlord, such approval not to be unreasonably withheld. Within 10 business days after Landlord’s receipt of the Plans, Landlord shall notify Tenant in writing as to whether Landlord approves or disapproves such Plans, which approval shall not be unreasonably withheld, and may contain conditions. If Landlord disapproves of the Plans, or approves the Plans subject to modifications, Landlord shall state in its written notice to Tenant the reasons therefor, and Tenant, upon receipt of such written notice, shall revise and resubmit the Plans to Landlord for review and Landlord’s reasonable approval, which approval shall not be unreasonably withheld, and which response shall be given within 10 business days after Landlord’s receipt of such revised Plans. All design, construction, and installation in connection with the Leasehold Improvements shall conform to the requirements of applicable building, plumbing, and electrical codes and the requirements of any authority having jurisdiction over, or with respect to, such Leasehold Improvements. All reasonable third-party costs incurred by Landlord, including the professional fees of Landlord’s Designer, in reviewing the Plans shall be paid by Tenant to Landlord within 30 days after receipt by Tenant of a statement of such costs. Landlord’s approval of the Plans is not a representation that: (a) such Plans are in compliance with all applicable Laws; or (b) the Plans or design is sufficient for the intended purposes. Tenant shall be responsible for all elements of the design of the Plans (including, without limitation, compliance with law, functionality of design, the structural integrity of the design, the configuration of the Premises and the placement of Tenant’s furniture, appliances and equipment), and Landlord’s approval thereof or of Tenant’s plans therefor shall in no event relieve Tenant of the responsibility for such design.

2.3 Permit Application. Tenant shall deliver any and all Plans and all revisions thereto to Landlord and obtain Landlord’s approval of same prior to submitting any of such Plans for permits. Tenant shall promptly apply for and pay the cost of obtaining all permits and certificates for the Leasehold Improvements upon receiving Landlord’s approval of the Plans. Tenant agrees to pay for any charges levied by inspecting agencies as such charges are levied in connection with the Leasehold Improvements.

2.4 Plan Changes. If there are any material changes in the Leasehold Improvements or the Plans from the work or improvements shown in the Plans as approved by Landlord, each such change must receive the prior written approval of Landlord, and, in the event of any such approved change in the Plans, Tenant shall, upon completion of the Leasehold Improvements, furnish Landlord with an accurate “as built” plan of the Leasehold Improvements as constructed (hard copy and CAD/REVIT files), which plans shall be incorporated into this Exhibit by this reference for all intents and purposes.

2.5 Tenant’s and Landlord’s Representative. “Tenant’s Representative” means Jim White, whose email address is jim.white@sparktx.com. “Landlord’s Representative” means John Hill, whose email address is john.hill@bdnreit.com. Each party shall have the right to designate a substitute individual as Tenant’s Representative or Landlord’s Representative, as applicable, from time to time by written notice to the other. All correspondence and information to be delivered to Tenant with respect to this Exhibit shall be delivered to Tenant’s Representative, and all correspondence and information to be delivered to Landlord with respect to this Exhibit shall be delivered to Landlord’s Representative. Notwithstanding anything to the contrary in the Lease, communications between Landlord’s Representative and Tenant’s Representative in connection with this Exhibit may be given via electronic means such as email without copies.


3.1 Selection of Contractor. Tenant shall inform Landlord of the general contractors from whom Tenant desires to solicit bids for the Leasehold Improvements. Each general contractor from whom Tenant desires to solicit a bid and the terms of the selected contractor’s contract (the “Construction Contract”) shall be subject to Landlord’s
reasonable approval. Landlord shall have the right to specify one general contractor who, at Tenant’s option, shall either be the Contractor or one of the general contractors to whom Tenant bids the Leasehold Improvements. The Contractor shall contract for such work directly with Tenant, but shall perform such work in coordination with Landlord’s operation of the Building. Tenant shall provide Landlord with a list of all subcontractors the Contractor will use in connection with the performance of the Leasehold Improvements as such subcontractors are selected to assist in the performance of the Leasehold Improvements. Tenant’s contractors and subcontractors shall work in harmony and shall not interfere with labor employed by Landlord, or its contractors or subcontractors or by any other tenant or their contractors.

3.2 Construction in Accordance with Plans; Schedule. Tenant shall cause the Leasehold Improvements to be performed by the Contractor substantially in accordance with the approved Plans (including without limitation any Landlord conditions on such approval), Laws, and Landlord’s rules and regulations for construction, and sustainable guidelines and procedures. Tenant shall diligently pursue completion of the Leasehold Improvements, which shall expressly include improving all of the Premises. Within 30 days after execution of the Construction Contract, Tenant shall provide Landlord with a completed Sustainability Cost Detail Form, the form of which will be provided by Landlord. Prior to commencement of the Leasehold Improvements, Tenant shall provide Landlord with a schedule of the estimated dates and amounts for Tenant’s requests for disbursement from the Improvement Allowance pursuant to Section 4.6 below (the “Draw Schedule”). If during completion of the Leasehold Improvements there are any material changes to the dates or amounts on the Draw Schedule, Tenant shall promptly notify Landlord with the specifics of the changes. Within 30 days after receipt of request therefor from time to time, Tenant shall provide Landlord with an accounting of all costs incurred by or on behalf of Tenant in connection with the Leasehold Improvements, and/or a certificate of the percentage of completion from the Architect.

3.3 Tenant’s Equipment. Tenant shall be solely responsible for the ordering and time of ordering of Tenant’s Equipment.

3.4 Building Standards. Except to the extent that the Plans expressly provide for the construction or installation of improvements, items, materials, fixtures, finishes, quantities, specifications, etc. that are non-Building Standard, Tenant will cause the Leasehold Improvements to be constructed or installed to Building Standards or better.

3.5 Fire-Life Safety; Central Systems.

a. Any Leasehold Improvements relating to the Building fire and life safety systems shall be performed by Landlord’s fire and life safety subcontractor, at Tenant’s expense, or by Tenant’s fire and life safety subcontractor with Landlord’s prior written approval.

b. Neither Tenant nor any of its agents or contractors shall alter, modify, or in any manner disturb any of the Central Systems without Landlord’s prior written approval.


4.1 Improvement Allowance.

a. Landlord shall provide the Improvement Allowance to Tenant in accordance with the terms of this Exhibit.

b. Except as may be expressly provided to the contrary in this Exhibit, the Improvement Allowance shall be applied solely towards payment of the Improvement Costs (specifically excluding costs for Tenant’s Equipment, cabling, moving, utilities, and movable furniture, fixtures, or equipment that has no permanent connection to the structure of the Building), provided the Restroom Improvement Allowance shall be applied solely towards payment of Improvement Costs that are incurred with respect to the renovation of the restrooms to specifications comparable to that of FMC Tower restrooms and so that they are also in compliance with all applicable Laws.

c. If, as of the 18-month anniversary of the Commencement Date (or the 18-month anniversary of the Suite 300 Rent Commencement Date with respect to the Improvement Allowance allocated to the Suite 300

C-4
Leasehold Improvements), any portion of the Improvement Allowance remains undisbursed, the Improvement Allowance shall be deemed reduced by such undisbursed amount, and Landlord shall retain such undisbursed portion of the Improvement Allowance which shall be deemed waived by Tenant and shall not be paid to Tenant, credited against Rent, or applied to Tenant’s moving costs or prior lease obligations.

4.2 Additional Allowance Option. Provided there is no Event of Default, Tenant shall have the option (“Additional Allowance Option”) of being provided an additional allowance by Landlord in the amount equal to the product of $35.00 multiplied by the rentable square footage of the Premises ($2,082,990.00 for the Lower Level Space and Suite 200, and $1,685,425.00 for Suite 300) (“Additional Allowance”), to be applied against the Improvement Costs. In connection with Tenant exercising the Additional Allowance Option, the amount of the Additional Allowance shall increase the amount of Fixed Rent payable by Tenant as follows: the total amount of the Additional Allowance shall be amortized over the Initial Term of the Lease on a straight-line basis at the interest rate of 8% and Fixed Rent shall be increased by the resulting product of such calculation. In the event that Tenant elects to exercise the Additional Allowance Option, Tenant shall provide written notice to Landlord within 120 days after the execution of this Lease with respect to the Lower Level Space and Suite 200, or within 120 days following the Suite 300 Commencement Date, as applicable. If Tenant fails to so notify Landlord within the time period provided herein, then Tenant shall have no further Additional Allowance Option and such Additional Allowance shall be null and void. If Tenant timely elects to exercise the Additional Allowance Option, then Tenant and Landlord shall enter into an amendment to the Lease memorializing the amount of the Additional Allowance that Tenant elects to utilize pursuant to this paragraph and the corresponding increase in the amount of Fixed Rent consistent with the terms and conditions set forth in this Section.

4.3 Tenant’s Payment Responsibility. Tenant shall be responsible for the full and timely payment of all Improvement Costs.

4.4 Excess Costs. To the extent that the Improvement Costs exceed the Improvement Allowance, Tenant shall be solely responsible for payment of such excess amount.

4.5 Rent. If Tenant fails to make any payment to Landlord when due under this Exhibit, such failure shall be deemed a failure to make a Rent payment under the Lease. Landlord shall have no obligation to make a disbursement from the Improvement Allowance if, at the time such disbursement is to be made, there exists an Event of Default or a condition which with notice and/or the passage of time would constitute an Event of Default.

4.6 Disbursement of Improvement Allowance.

a. Subject to the terms of this Exhibit, Landlord shall disburse the Improvement Allowance to Tenant for payment or reimbursement to Tenant, as the case may be, of the Improvement Costs for work in place (but not for costs arising from an Event of Default or from any facts or circumstances that could become an Event of Default, such as legal fees or bonding costs arising in connection with a mechanic’s lien placed on the Premises or Tenant’s interest therein), and in no event will Landlord be required to disburse all or any portion of the Improvement Allowance prior to the Delivery Date. Landlord shall have the right to make Improvement Allowance disbursements to any party for whom Tenant has requested a disbursement or, following the occurrence of an Event of Default, directly to the Contractor.

b. Landlord shall be entitled to withhold from any requested disbursement for payment under the Construction Contract a retainage equal to the greater of the retainage set forth in the Construction Contract or 10% of amount due under the Construction Contract (the “Retainage”).

c. Any provision of this Exhibit to the contrary notwithstanding, Tenant agrees that Landlord shall not be obligated to make a disbursement from the Improvement Allowance unless the following conditions have been satisfied or waived in writing by Landlord:

(i) Intentionally Deleted.

C-5
With respect to amounts payable under the Construction Contract or any other contract under which a mechanic’s or materialmen’s lien could arise (as reasonably determined by Landlord), Landlord shall have received from Tenant a request for payment, which request includes: (A) a copy of a certificate signed by the Architect certifying the then-percentage completion of the Leasehold Improvements, and approving payment of an amount at least equal to the amount set forth in Tenant’s request for payment; (B) a submission by the Architect of AIA forms G-702 and G-703, or substantially similar forms (Landlord and Tenant agree that the retainage set forth in such forms is one and the same as the Retainage set forth above and that there will not be a separate or an additional retainage under such forms); (C) as applicable, proof of payment; and (D) partial releases of liens from the Contractor and any other relevant contractor or subcontractor for work for which Tenant requests a disbursement (collectively, the “Lien Waivers”).

Provided Landlord has received a disbursement request from Tenant, together with the other items, certifications, Lien Waivers, etc. required under this Exhibit in connection with such disbursement, Landlord shall make such disbursement within thirty (30) days following such disbursement request. Landlord shall not be required to make more than one (1) disbursement from the Improvement Allowance during any thirty (30)-day period.

Landlord shall have had the opportunity to inspect and approve the Leasehold Improvements performed for which disbursement has been requested, such approval not to be unreasonably withheld.

Landlord shall have no obligation to make a disbursement from the Improvement Allowance to the extent that there exists any unbonded lien against the Building or the Premises or Tenant’s interest therein (including the cost to bond over the lien to the reasonable satisfaction of Landlord, plus Landlord’s reasonable attorneys’ fees) by reason of work done, or claimed to have been done, or materials supplied, or claimed to have been supplied, to or for Tenant for the Premises, or if the conditions to advances of the Improvement Allowance are not satisfied. Landlord shall notify Tenant in writing of the reasons that Landlord disputes disbursing any portion of the Improvement Allowance. Landlord shall withhold only such amounts as Landlord disputes in good faith and only such amounts as Landlord deems reasonably necessary to protect Landlord’s interests. Landlord shall have no obligation to disburse any portion of the Improvement Allowance for the payment of any bond premiums required of Tenant under this Exhibit in connection with any liens filed or sought in connection with the Leasehold Improvements.

The Retainage shall be disbursed to Tenant 30 days after Substantial Completion of the Leasehold Improvements; provided, however, in no event shall the Retainage be disbursed to Tenant until such time as Tenant has complied with the requirements set forth in Section 3.2 and Section 5.3 hereof and the cost to correct punch list items would be less than $5,000.

With respect to Planning Costs incurred by Tenant, Landlord shall disburse to Tenant the amount requested by Tenant (not to exceed the Improvement Allowance, and subject to any limitations on soft cost disbursements set forth elsewhere in this Exhibit) within 30 days after Landlord receives a disbursement request from Tenant, which request shall include a reasonably detailed invoice from the professional for whom the disbursement is sought and a certification from Tenant that such professional has satisfactorily performed his/her or its services for which the disbursement is sought.

There shall exist no Event of Default.

Inspection of Leasehold Improvements. Landlord reserves the right to inspect and to be present during the performance of the Leasehold Improvements solely for the purpose of protecting Landlord’s interest in the Building, but Landlord will have no obligation to so inspect or be present and, if Landlord elects to so inspect, or to be present during the performance of all or any portion of the Leasehold Improvements, neither such inspection nor such presence shall give rise to any liability by Landlord to Tenant or to any other person or entity.

Landlord’s Warranty Work and Rules for Work.

Tenant work letter

C-6
5.1 **Landlord’s Warranty Work Complete.** Tenant accepts the Premises in “AS IS” condition. Except with respect to Landlord’s Warranty Work, Landlord shall have no obligation under the Lease, this Exhibit, or otherwise to make any improvements (including, without limitation, to perform any demolition, which shall be Tenant’s responsibility) to the Premises or to deliver, provide or install any materials in, to, or at the Premises.

5.2 **Conditions to Disbursement of Retainage.** Prior to Landlord’s disbursement of any portion of the Retainage, Tenant, at Tenant’s expense, shall:

   a. furnish evidence reasonably satisfactory to Landlord that the Leasehold Improvements have been paid for in full (other than any Leasehold Improvements to be paid for with the Retainage), that any and all liens therefor that have been or might be filed have been discharged of record (by payment, bond, order of a court of competent jurisdiction, or otherwise) or waived, and that no security interests relating to the Leasehold Improvements are outstanding and provide final Lien Waivers;

   b. furnish to Landlord a copy of the Certificate of Occupancy and all other certifications and approvals with respect to the Leasehold Improvements that may be required from any governmental authority and/or any board or fire underwriters or similar body for the use and/or occupancy of the Premises;

   c. furnish to Landlord proof of the insurance required by the Lease;

   d. furnish an affidavit from the Architect certifying that the Leasehold Improvements have been completed substantially in accordance with the Plans; and

   e. provide Landlord with the opportunity to inspect the Premises so that Landlord can be reasonably satisfied that Substantial Completion occurred in accordance with the Plans.

5.3 **Additional Deliveries.** Within 90 days after Substantial Completion, Tenant, at Tenant’s expense, shall furnish Landlord with:

   a. 1 set of reproducible “as built” blueprints of the Premises, together with CAD/REVIT files;

   b. an HVAC air balancing report reasonably satisfactory to Landlord;

   c. copies of all guarantees and/or warranties; and

   d. copies of all O&M information, manuals, etc.

5.4 **Interference with Others.** Tenant will make reasonable efforts not to materially obstruct or materially interfere with the rights of, or otherwise materially disturb or injure, other tenants of the Building during the performance of the Leasehold Improvements.

5.5 **Rules and Regulations for Construction.** Tenant shall cause the Contractor and each of the Contractor’s subcontractors to adhere to the rules and procedures set forth in Exhibit C-1 attached hereto. Landlord shall apply and enforce such rules and procedures against all contractors and tenants of the Project in a uniform and non-discriminatory manner.

5.5 **Insurance.** Tenant shall cause the Contractor, at no cost to Landlord, to maintain and keep in full force and effect, the insurance required under Exhibit C-2, with such companies, and in such form and amounts as Landlord may reasonably require. Tenant shall, at no cost to Landlord, maintain and keep in full force and effect, the insurance required of Tenant under the Lease and this Exhibit. Prior to commencement of construction of the Leasehold Improvements, Landlord shall be provided with copies of insurance certificates indicating coverages as required by Exhibit C-2, are in full force and effect, and a copy of the executed Construction Contract.
5.6 **Landlord Delay Defined.** A “Landlord Delay” is any delay in Substantial Completion to the extent caused by any of the following, provided written notice of such potential Landlord Delay is first given to Landlord’s Representative and the cause of such potential delay is not remedied within 48 hours:

a. Landlord’s failure to comply with the terms of the Lease, without limitation Landlord’s failure to comply with any of the deadlines specified in this Exhibit.

b. Delay caused by major or extensive revisions to the Plans requested by Landlord arising from circumstances other than circumstances beyond the control of Landlord or unforeseen at the time of Landlord’s approval of the Plans.

c. The nonperformance or the delay in performance of any work or activity including the Landlord’s Warranty Work if required to be performed by Landlord or any of its employees, agents, or separate contractors except by reason of Force Majeure Events.

d. Landlord’s interference with Tenant’s access to the Premises, including the unavailability of freight elevator service to all floors of the Premises due to the elevators being out of service (and not due to their being used for other purposes, provided access to the elevators is provided in accordance with Section 8(e) of the Lease) and other areas of the Building needed by Tenant in order to perform the Leasehold Improvements.
A. General

1. No work shall be permitted until the property management office is furnished with copies of all required permits.

2. All demolition, removal or other types of work, which may inconvenience other tenants or disturb building operations, must be scheduled and performed before or after normal working hours. The property management office shall be notified at least 24 hours prior to commencement of such work.

3. All fire alarm testing must be performed after normal working hours.

B. Prior to commencement of Leasehold Improvements

1. Tenant shall deliver to Landlord, for Landlord’s approval, which will not be unreasonably withheld, a list of all the contractors and subcontractors who will be performing the work. Landlord hereby approves Structuretone as an approved contractor.

2. The Contractor must obtain a performance and payment bond for the project. Bonding companies shall be licensed in the jurisdiction in which the Building is located. The bond premium shall be included in all bids. Bond form and agent shall be submitted for Landlord review prior to construction start.

3. Tenant shall deliver to Landlord 2 complete sets of permit plans and specifications properly stamped by a registered architect or professional engineer and shall deliver to Landlord any and all subsequent revisions to such plans and specifications.

4. It is Tenant’s responsibility to obtain approval of plans and required permits from jurisdictional agencies. Tenant must submit copies of all approved plans and permits to the property management office and post the original permit on the Premises prior to commencement of any work. All work performed by a contractor or subcontractor shall be subject to Landlord’s inspection.

C. Requirements and Procedures

1. At such time as other tenants shall occupy the Building, core drilling or cutting shall be permitted only between the hours of 7:00 p.m. and 7:00 a.m. Monday through Friday and 4:00 p.m. on Saturday through 7:00 a.m. on Monday. All core drilling/cutting must be approved by the Base Building structural engineer. X-rays of areas may be required at Landlord’s engineer’s discretion. The property management office must be notified at least 24 hours prior to commencement of such work.

2. Prior to the initiation of any construction activity in the Building, Tenant shall make arrangements for use of the loading dock and elevators with the property management office. Upon initiation of construction activity in the Building, Tenant shall make arrangements for use of the loading dock and elevators with the property management office 48 hours in advance. Notwithstanding the foregoing, Tenant shall not have a priority over future tenants and/or their contractors in the use of the elevators and loading dock. No material or equipment shall be carried under or on top of the elevators. If the building manager deems an elevator operator is required, such operator shall be provided by the general contractor at the general contractor’s expense.

3. Tie-in of either fire alarm or sprinkler/fire suppression systems shall not occur until all other work related to such systems has been completed.
4. If a shutdown of risers and mains for electric, HVAC, sprinkler, fire protection, and plumbing work is required, work shall be scheduled with 24-hour advance notice. Drain downs or fill-ups of the sprinkler system or any other work to the fire protection system which may set off an alarm, must be accomplished between the hours of 7:00 p.m. and 7:00 a.m. Monday through Friday and 4:00 p.m. on Saturday through 7:00 a.m. on Monday.

5. The general contractor must:
   a. Properly supervise construction on the Premises at all times.
   b. Police the job at all times, continually keeping the Premises and Project orderly. All Tenant materials are to be reasonably neatly stacked.
   c. Maintain cleanliness and protection of all areas, including elevator and lobbies.
   d. Distribute I.D. badges, provided by Landlord, to all construction workers. Any construction worker without a valid badge will be escorted from the building. I.D. badges will be changed at the discretion of the property management office.
   e. If other tenants occupy the building, provide the property management office with a list of those who are expected on the job after hours or during a weekend. Tenant shall use its best efforts to submit such list by noon on the day in which after hours work is scheduled.
   f. Arrange for telephone service if necessary. The property management and security telephones will not be available for use by contractors.
   g. Block off supply and return grills, diffusers and ducts to keep dust from entering into the Building air system.
   h. Avoid and prevent the disturbance of other tenants.
   i. Tenant’s contractors and subcontractors may only park in parking areas at the Project specifically designated by Landlord.

6. If Tenant’s general contractor is negligent in any of its responsibilities, Landlord shall give Tenant notice of such negligence and a reasonable opportunity to cure such negligence (except in the case of emergencies or potential harm to persons or damage to property), at Tenant’s sole expense. If Tenant fails to cure timely such negligence, Landlord may elect to correct the same and Tenant shall be charged for the corrective work.

7. All equipment and material installation must be equal to or exceed the standards of workmanship and quality established for the Building.

8. Upon completion of the work, Tenant shall submit to the property management office properly executed forms or other documents indicating approval by all relevant agencies of the local government having jurisdiction over the Building whose approval is required for Tenant’s use and occupancy of the Premises.

9. Tenant shall submit to the property management office a final “as-built” and/or record set of drawings, together with CAD/REVIT files, showing all items of work in full detail.

10. Contractors who require security for the Premises during construction shall provide same at their sole expense. Landlord will not be liable for any stolen items from Tenant’s work area. It is suggested
that the contractor and subcontractors use only tools and equipment bearing an identification mark denoting the contractor and subcontractor’s name.

11. All contractors/subcontractors/employees will enter and exit through the loading dock area, and use the freight elevator. Building passenger elevators may not be used.

12. Prior to the commencement of construction, Landlord and Tenant will inspect the Building, and Tenant will prepare and deliver to Landlord a memorandum setting forth any pre-construction damages to the Building. Any damage caused by the contractor to existing work of others shall be repaired or replaced at the sole cost and expense of the contractor to Landlord’s satisfaction.

13. The contractor shall be responsible for the protection of finished surfaces of public areas (floors, walls, ceiling, etc.).

14. Contractors will be permitted to use restroom facilities only on the floors on which construction services are being provided. Any damages to these facilities will be repaired by the contractor at its sole cost and expense. Landlord will provide no janitorial services to such restrooms.

15. Tenant shall pay all utility costs after the delivery of the Premises to Tenant, and during any construction period. If required by Landlord at any time during the completion of the Leasehold Improvements, Landlord may install, at Landlord’s sole cost and expense, electric submeters on each floor of the Premises. All electric power to Tenant’s contractor and subcontractors’ tools shall be powered through such submeters. Tenant shall pay Landlord for use of such electric power within 10 days after written demand. If Tenant requests that Landlord provide central heating or air conditioning, Tenant shall be charged the then-prevailing hourly rate for such central heating or air conditioning service.

16. The contractor must arrange to have freight or stock received by its own forces. Contractors and subcontractors are required to submit to the property management office a written request for dock space for offloading materials and/or equipment required to construct Tenant’s space. All requests are to include the name of the supplier/hauler, time of expected arrival and departure from Landlord’s dock facility, name of contractors and subcontractors designated to accept delivery, and the location that the materials/equipment will be transported by the contractor/subcontractor. Disregard for this requirement will result in those vehicles being moved at the vehicle owner’s expense. Under no circumstances will a vehicle be parked and left in the loading dock. The contractor must provide for storage and removal of all trash at the contractor’s expense. The contractor is not allowed to use the building trash dumpster under any circumstances. Any building materials left in loading dock, service corridor, stairwell, garage, on the site, etc. will be removed from the Project at the contractor’s expense. Upon delivery of materials to the loading dock, tools, supplies, equipment, etc., the transport vehicle must be removed from the loading dock prior to the materials being carried to the worksite.

17. The location of construction dumpsters, porta potties, and other items necessary to facilitate orderly execution of construction with minimal disruption to other tenants and the site shall be selected by the mutual agreement of Tenant and Landlord.
EXHIBIT C-2
INSURANCE REQUIREMENTS

The Contractor shall, throughout the duration of any contract or any work authorized under purchase order, at its expense, carry and from time to time renew worker’s compensation insurance, and commercial general liability insurance in the amount of $5,000,000, single limit covering both bodily injury and property damage, including any indemnity and hold harmless clause Landlord may reasonably require, in such amounts Landlord may approve. An insurance certificate in the customary form, naming Landlord and Landlord’s property manager as additional insureds and evidencing that premiums therefor have been paid, shall be delivered to Landlord simultaneously with the execution of any contract and prior to performing any work authorized under a purchase order and within 5 days prior to expiration of such insurance a like certificate shall be delivered to Landlord evidencing the renewal of such together with evidence satisfactory to Landlord of payment of the premium.
# JANITORIAL SPECIFICATIONS

## CLEANING SPECIFICATIONS

<table>
<thead>
<tr>
<th></th>
<th>DAILY</th>
<th>WEEKLY</th>
<th>AS NEEDED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Office</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Empty trash and recycle</td>
<td>Dust chairs nearly and cloth of personal effects, and tops of system furniture</td>
<td>Clean windows and doors</td>
</tr>
<tr>
<td></td>
<td>Spot clean carpet</td>
<td>Vacuum carpet</td>
<td>Clean light fixtures and windows</td>
</tr>
<tr>
<td></td>
<td>Remove visible spots/ litter from carpet</td>
<td>Clean telephones in common areas</td>
<td>Clean walls</td>
</tr>
<tr>
<td></td>
<td>Spot clean desks and tables</td>
<td>Cleanable tables</td>
<td>Dust shelves, cabinets and bookshelves</td>
</tr>
<tr>
<td></td>
<td>Straighten chair - furniture</td>
<td></td>
<td>Clean chokers</td>
</tr>
<tr>
<td></td>
<td>Turn off lights</td>
<td>Dust pictures and surfaces over 5'</td>
<td>Dust picture rails, blinds, drapes, and radiators</td>
</tr>
<tr>
<td><strong>Restroom</strong></td>
<td>Sinks</td>
<td>Dust lights</td>
<td>Geline vents</td>
</tr>
<tr>
<td></td>
<td>Showers</td>
<td>Clean surfaces over 5'</td>
<td>Clean sanitaris</td>
</tr>
<tr>
<td></td>
<td>Counters</td>
<td></td>
<td>Clean partitions</td>
</tr>
<tr>
<td></td>
<td>Trash receptacles</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toilet/urinals</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Floor</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spot clean walls</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spot clean partitions</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Floor Care</strong></td>
<td>Spot clean carpet</td>
<td>Sweep Kitchen floors</td>
<td>Run risk polished surfaces</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wet mop kitchen floors</td>
<td>Machine sweep restroom floors</td>
</tr>
</tbody>
</table>

These specifications are subject to change without notice. The cost for any cleaning over and above the standard cleaning specifications are to be paid by tenant.
RULES AND REGULATIONS

1. Sidewalks, entrance passages, elevators, vestibules, stairways, corridors, halls, lobby, and any other part of the Building shall not be obstructed or obstructed by Tenant or used for any purpose other than agents or agents of users and from the Premises. Landlord shall have the right to use and operate the common areas of the Building and common areas furnished for common use of the Building’s tenants (such as the eating, smoking, and parking areas) as such tenants or Landlord deem appropriate.

2. No awnings or other extensions may be attached to the exterior walls of the Building without the prior written consent of Landlord. All signs and window signs shall be of a quality type, design, color, and attached in a manner approved in writing by Landlord.

3. No displays, display cases, or other articles may be placed in front of or affixed to any part of the exterior of the Building, or placed in hallways or corridors without the prior written consent of Landlord. All signs shall be in the designated storage areas. Tenant shall not use or permit the use of any portion of the Premises for outdoor storage. No parts, tools, or other objects may be placed in the public corridors, hallways, stair, or other common areas of the Building.

4. Restrooms and other plumbing fixtures shall not be used for any purposes other than those for which they were intended and no soiled, disputed, rag, or other substances may be thrown therein. Only standard toilet tissue may be flushed in the toilets. All damage resulting from any misuse of these fixtures shall be the responsibility of the tenant who, or whose employees, agents, visitors, clients, or licensees, caused such damage. Bathing and hanging of clothes is permitted only in designated showers and areas, and is not permitted in restrooms.

5. Tenant shall not, without the prior written consent of Landlord, make, paint, drill into, burn, cut string, wires, or in any way deface any part of the Premises or the Building except the unavoidable hanging of decorations or institutional materials on the walls of the Premises. Tenant shall remove all marks, decorations, and any other fixtures that are visible outside of the Premises within 30 days after the end of the applicable tenancy.

6. Tenant shall not construct, install, maintain, use, or operate in any part of the Premises, any electrical device, wiring, or other apparatus in connection with any road, street, or other public communication systems that may be harmful either to the Premises.

7. No bicycles, horses, dogs, or other animals, except on a leash, shall be brought into, used, or kept in or about the Building or in the common areas of the Project, or in any other part of the Premises. No animals of any kind (other than dogs) shall be permitted to enter the Building, and no animal shall be left in the Building. No animals, pets, or pets shall be permitted in the Building. No animal shall be permitted in the common areas of the Project.

8. Tenant shall not cause or permit any unusual or objectionable odors to be produced upon or permitted from the Premises.

9. No signs in the Premises may be used for the manufacture of goods for sale in the ordinary course of business, or for the sale of merchandise, goods, or property at any time.

10. Tenant shall not cause or permit any unreasonably disturbing actions, or disturb or interfere with the occupants of the Building or neighboring buildings or residents by voice, musical instrument, radio, talking machine, whistling, singing, loud speaking, or in any other way. All passage through the Building’s hallways, stairways, and main lobby shall be conducted in a quiet, businesslike manner. Tenant shall not commit or suffer any nuisance upon the Premises, the Building, or the Project, or in any instance, or any other act or thing that may disturb the quiet enjoyment of any other tenant in the Building or Project.

11. Tenant shall not throw anything out of the doors, windows, or doorways, or other areas or stair of the Building.

12. Tenant shall not place, install, or operate in the Premises or in any part of the Project, any engine, steam,
machinery, or electrical equipment not directly related to its business, including without limitation space
heaters, coffee cup Warmers, and small refrigerators, unless mechanical operations, cause the con or
storage, or place or cause in or about the Premises or the Project any explosives, gasoline, television, radio,
chemical, or harmful, explosive, or hazardous material, without the prior written consent of Landlord. Notwithstanding the foregoing, Tenant shall have the right to install and use a
coffee machine, microwave oven, toaster, ice maker, refrigerator, and vending machine in compliance
with all applicable Laws in a kitchen or break room designated as such by Landlord, provided Tenant shall
use only standard steel hooded hobs. All supply water lines shall be of copper (not plastic) tubing.

13. No smoking (including without limitation of cigarettes, pipes, and electronic cigarettes) is permitted anywhere in
the Premises, the Building, or the Project, including but not limited to restrooms, kitchens, elevators, lobby,
and entrance vestibules, sidewalks, and parking lots areas. Provided smoking shall be permitted in any
Landlord-designated exterior smoking area. All cigarette ashes and butts shall be deposited in the
containers provided for such disposal, and shall not be disposed of on sidewalks, parking lot areas, or
buildings.

14. Tenant shall not install any additional locks or bolts of any kind upon any door or window of the Building
without the prior written consent of Landlord. Tenant shall, upon the termination of its tenancy, return
Landlord all keys for the Premises, either furnished or otherwise provided by Landlord, and all security
access cards to the Building.

15. Tenant shall keep all doors to the Building and corridors closed during Business Hours except as they may be
used for ingress or egress.

16. Tenant shall not use the name of the Building, Project, Landlord, or Landlord’s agents or affiliates in any
way in connection with its business, except as the address thereof. Landlord shall also have the right to
prohibit any advertising by Tenant that, in Landlord’s sole discretion, tends to injure the reputation of
the Building or is disparatory as a building for offices, and upon written notice from Landlord, Tenant shall
refrain from or discontinue such advertising.

17. Tenant shall be responsible for all security access cards issued to it and shall secure the return of all
security cards from all employees, not having employment with them. Lost cards shall cost $50.00 per card
to replace. In the event any other person other than regular tenants and their employees may have security
access cards issued Landlord grants prior written approval.

18. All delivery to the Building that involve the use of a hand cart, hand truck, or other heavy equipment or
device shall be made via the freight elevator, if such freight elevator exists in the Building. Tenant shall
be responsible for Landlord for any loss or damage resulting from any delivery made by or for Tenant to the
Building. Tenant shall procure and deliver to Landlord a certificate of insurance from its carriers, which
certificate shall name Landlord as an additional insured.

19. Landlord reserves the right to inspect all freight to be brought into the Building, and to evaluate the
Building it brings in other materials, that violate any of these rules and regulations.

20. Tenant shall refer all contractors, contractor’s representatives, and installers to Landlord for Landlord’s approval
and supervision before performance of any construction, or access to building. This provision shall apply to all work performed in the
Building including installation of telephones, telegraph equipment, electrical devices and attachments, and
installation of any nature affecting floors, walls, windows, trim, windows, ceilings, equipment, or any
other physical portion of the Building. Landlord reserves the right to require that all agents of contractors
and vendors sign and understand the Building.
22. Landlord reserves the right to exclude from the Building at all times any person who is not known or does not properly identify himself to Landlord's management or security personnel.

23. Landlord may require, at its sole option, all persons entering the Building outside of Business Hours to register at the time they enter and at the time they leave the Building.

24. No space within the Building, or in the common areas such as the parking lot, may be used at any time for the purpose of dancing, sleeping, or for any social or similar purposes.

25. Tenant shall use the hallways, stairs, lobby, or other common areas of the Building as lounging areas during breaks or during lunch periods.

26. No smoking, soliciting, or peddling is permitted in the Building or its common areas.

27. Tenant shall comply with all laws regarding the collection, sorting, segregation, and recycling of garbage, trash, rubbish, and other refuse, and Landlord's recycling policy for the Building.

28. Landlord does not maintain specific finishes that are non-standard, such as showers, bathtubs, wallpaper, suspended ceilings, etc. However, should the need arise for repair of items not maintained by Landlord, Landlord at its sole option may charge the tenant for the work to be done at tenant's expense.

29. Tenant shall clean at least once a year, at its expense, drapes in the Premises that are visible from the exterior of the Building.

30. No posters, signs, drawings, obscene, or other material may be placed in or on windows in such a manner as they are visible from the exterior, without the prior written consent of Landlord.

31. Tenant is prohibited at all times from eating or drinking in hallways, elevators, lobbies, or other common areas of the Premises. Food storage shall be limited to a Landlord-approved kitchen or break room.

32. Tenant shall be responsible to Landlord for any acts of vandalism performed in the Building by its employees, invitees, agents, contractors, licensees, subtenants, and assignees.

33. Tenant shall not permit the visit to the Premises of persons in such numbers or under such conditions as to interfere with the use and enjoyment by other tenants of the entrances, hallways, elevators, lobby, exterior common areas, or other public portions of the Building.

34. Landlord's employees shall perform any work or do anything outside of their regular duties under special instructions from Landlord. Requests for such requirements shall be submitted in writing to Landlord.

35. Tenant is prohibited from interfering in any manner with the installation, alteration, or maintenance of the heating, air conditioning, and ventilation facilities and equipment at the Premises.
Landlord shall not be responsible for lost or stolen personal property, equipment, money, or jewelry regardless of whether such loss occurs whenever an area is locked or against entry in or at.

Landlord shall not permit entrance to the Premises by use of pass key controlled by Landlord, to any person at any time without written permission of Tenant, except employees, contractors or service personnel supervised or employed by Landlord.

Tenant shall observe and comply with the driving and parking signs and markers on the Project grounds and surrounding areas. Tenant shall comply with all reasonable and uniformly applied parking regulations promulgated by Landlord from time to time for the orderly use of vehicle parking areas. Parked vehicles shall not be used for vending or any other purpose or other activity which is prohibited in the parking areas. Vehicles shall be parked only in striped parking spaces, except for loading and unloading, which shall be solely in zones marked for such purpose, and be so conducted as not to unreasonably interfere with traffic flow or with loading and unloading zones of other tenants. Tenant's trailers shall be parked in areas designated for trailer trailer parking. Employee and tenant vehicles shall be parked in spaces marked for visitor parking or other specific use. All vehicles entering or parking in the parking areas shall do so at owner's sole risk and Landlord assumes no responsibility for any damage, destruction, vandalism, or theft. Tenant shall cooperate with Landlord in any reasonable and uniformly applied measures implemented by Landlord to control abuse of the parking areas, including additional or alternate access control programs, tenant and guest vehicle identification programs, and validated parking programs. Parked vehicles, provided no such validated parking program shall result in Tenant being charged for spaces to which it has a right to free use under the Lease. Each vehicle owner shall promptly respond to any reasonable vehicle owner or lease, and failure to do so may result in temporary or permanent exclusion of such vehicle from the parking area. Any vehicle that violates the parking regulations may be towed, towed at the expense of the owner, temporarily or permanently excluded from the parking areas, or subject to other civil consequences.

Tenant shall not enter other separate tenants' hallways, restrooms, or premises except with prior written approval from Landlord's management.

Tenant shall not place weights anywhere beyond the load per square-foot carrying capacity of the Building.

Tenant shall comply with all laws, regulations, or other governmental requirements with respect to energy savings, not permit any waste of any utility services provided, and cooperate with Landlord only to ensure the most efficient and efficient operation of the Building.

The signboard, including signs and signs, and the furnishings and fixtures in any area of the Premises that are visible from the common areas of the Building are subject to Landlord's approval in its sole discretion. Requests for these items must be approved in writing by Landlord.

Power strips and extension cords shall not be combined (also known as daisy chaining).

Candles and open flames are prohibited in the Building.

Guns, firearms, and other dangerous weapons (amended or otherwise) are not allowed in the Project, subject to applicable laws (e.g., requiring Landlord to not permit at the Project.

Landlord reserves the right to rescind any of these rules and make such other and further rules and regulations as in the judgment of Landlord shall from time to time be needed for the safety, protection, care, and cleanliness of the Project. The Landlord, in addition to the preservation of good order therein, and make rules and regulations as to the premises, their agents, employees, and personnel, which rules and regulations shall be binding upon Tenant in the manner as is ordinarily prescribed. As used in these rules and regulations, capitalized terms shall have the respective meanings given to them in the Lease to which these rules and regulations are attached, provided Tenant shall be responsible for compliance hereunder by reason under Tenant's reasonable control, including without limitation all tenants, users, agents, contractors, invitees, subcontractors and assigns, and a violation of any of these rules and regulations by any of the foregoing is deemed a violation by Tenant.
AMENDMENT #2 TO LICENSE AGREEMENT

This Amendment #2 to License Agreement (the “Second Amendment”) is entered into and made effective as of November 6, 2017 (the “Second Amendment Effective Date”) and amends that certain License Agreement dated December 6, 2014 (as previously amended by the First Amendment dated June 9, 2016, the “License Agreement”), by and between Pfizer Inc., a corporation organized and existing under the laws of the State of Delaware with offices at 235 East 42nd Street, New York, New York 10017 (“Pfizer”) and Spark Therapeutics, Inc., a corporation organized and existing under the laws of the State of Delaware with offices at 3737 Market Street, Suite 1300, Philadelphia, Pennsylvania 19104 (“Spark”). Pfizer and Spark are referred to herein individually as a “Party” and collectively as the “Parties”.

WHEREAS, the Parties wish to amend the License Agreement to modify the rights, roles and responsibilities of the Parties under the License Agreement;

NOW THEREFORE, in consideration of the premises and for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged by each Party, the Parties hereby agree as follows.

1. Terms. Capitalized terms used in this Second Amendment (and in the License Agreement, as amended hereby) and not defined herein shall have the respective meanings given to such terms in the License Agreement.

1.1 “Companion Diagnostic Assay” means any in vitro, in vivo or cell based assay that is intended to (i) qualitatively or quantitatively measure neutralizing antibodies to any AAV capsid, or (ii) be used to otherwise assess whether a clinical trial subject or a patient is a candidate for treatment with a Licensed Product. For clarity, any such assay may, but need not necessarily, include as a component thereof any Compound or any component of any Compound or Licensed Product.

1.2 “Companion Diagnostic Assay Improvement” means, as to a Companion Diagnostic Assay that qualitatively or quantitatively measures neutralizing antibodies to any AAV capsid contained in a Licensed Product or can be used to otherwise assess whether a clinical trial subject or a patient is a candidate for treatment with a Licensed Product, any modification made by Pfizer or its Affiliates, or on any of their behalf by a Third Party contractor, to (a) any materials provided by Spark to Pfizer (or to an Affiliate or Third Party contractor designated by Pfizer) under the License Agreement that are incorporated into or otherwise used as part of such Companion Diagnostic Assay, or (b) Spark’s proprietary methods disclosed to Pfizer (or to an Affiliate or Third Party contractor designated by Pfizer),
which methods are incorporated into or otherwise used to perform such Companion Diagnostic Assay.

1.3 “Joint Companion Diagnostic Assay Know-How” means any Joint Know-How that is necessary or useful for the Development or use of any Companion Diagnostic Assay Developed for use in connection with the Development or Commercialization of any Licensed Product.

1.4 “Joint Companion Diagnostic Patent Rights” means any Joint Patent Right that claims or discloses any invention included in Joint Companion Diagnostic Assay Know-How.

1.5 “Joint Companion Diagnostic Technology” means the Joint Companion Diagnostic Assay Know-How and the Joint Companion Diagnostic Patent Rights.

1.6 “Manufacturing Technology Transfer Plan” shall have the meaning set forth in Section 4.5.3 of the License Agreement, as amended by the Second Amendment.

1.7 “Pfizer Companion Diagnostic Patent Rights” means any Patent Right, other than the Joint Companion Diagnostic Patent Rights, in any form and whether pending or issued, that both (a) is Controlled by Pfizer or any of its Affiliates as of the Second Amendment Effective Date or that comes into the Control of Pfizer or any of its Affiliates following the Second Amendment Effective Date and during the term of the Agreement (other than through the grant of a license by Spark) and (b) claims or discloses (i) any Companion Diagnostic Assay Improvement or (ii) any Companion Diagnostic Assay (including any component thereof) that comprises a Companion Diagnostic Assay Improvement.

1.8 “Second Amendment” is defined in the preamble above.

1.9 “Second Amendment Effective Date” is defined in the preamble above.

1.10 “Spark Companion Diagnostic Assay Know-How” means any Know-How, other than the Joint Companion Diagnostic Assay Know-How, that (a) is Controlled by Spark, or, subject to Section 2.5.1, any of its Affiliates as of the Second Amendment Effective Date or that comes into the Control of Spark or any of its Affiliates following the Second Amendment Effective Date and during the Term (in each case, other than through the grant of a license by Pfizer) and (b) is necessary or useful for the Development or use of any Companion Diagnostic Assay that qualitatively or quantitatively measures neutralizing antibodies to any AAV capsid contained in a Licensed Product or can be used to otherwise assess whether a clinical trial subject or a patient is a candidate for treatment with a Licensed Product.

1.11 “Spark Companion Diagnostic Patent Rights” means any Patent Right, other than the Joint Companion Diagnostic Patent Rights, in any form and whether pending or issued, that both (a) is Controlled by Spark or, subject to Section 2.5.1, any of its Affiliates as of
the Second Amendment Effective Date or comes into the Control of Spark or, subject to Section 2.5.1, any of its Affiliates following the Second Amendment Effective Date and during the Term (other than through the grant of a license by Pfizer) and (b) claims or discloses (i) any Spark Companion Diagnostic Assay Know-How, (ii) any Companion Diagnostic Assay (including any component thereof), or (iii) any method of making, using or otherwise exploiting any Companion Diagnostic Assay (including any component thereof). The Spark Companion Diagnostic Patent Rights as of the Second Amendment Effective Date are listed in Exhibit A attached to this Second Amendment.


2. Effects of Second Amendment. This Second Amendment amends the License Agreement solely to the extent expressly provided below as of the Second Amendment Effective Date. As so amended, the License Agreement continues in full force and effect and is ratified in all respects. Any references in the License Agreement to the “Agreement” will be deemed to mean the License Agreement as amended by this Second Amendment.

3. Amendments.

3.1 Collaboration Period.

3.1.1 The definition of “Collaboration Period” set forth in Section 1.1.30 of the License Agreement is hereby deleted and replaced with: “‘Collaboration Period’ means the date beginning on the Effective Date and ending, subject to the proviso below, [**] after the completion of [**] the Phase I/II Clinical Trial, provided, however, that in the event Pfizer determines and notifies Spark, in writing, that clinical comparability (as compared to patients dosed with Licensed Product containing Compound produced using the “Process 1” manufacturing process) is demonstrated [**] treated with Licensed Product containing Compound produced using the “Process 2” manufacturing process (based on the clinical comparability criteria set forth in Exhibit B attached to the Second Amendment of this License Agreement), the Collaboration Period will end upon the later of (i) such determination and notification if the [**], in which event the [**] or (ii) if the [**] prior to such determination and notification, the date that is [**]. For the avoidance of doubt, the Collaboration Period shall end automatically as set forth above in this Section 1.1.30 and, except as expressly provided above in this Section 1.1.30, shall not require Pfizer’s determination of clinical comparability.”

3.1.2 Both during and following the Collaboration Period, each Party shall conduct the activities assigned to it as and when provided under the Roles and Responsibilities Plan attached to this Second Amendment as Exhibit C (the “Roles and Responsibilities Plan”). Without limiting the generality of the foregoing, Spark shall use Commercially Reasonable Efforts (a) to conduct and complete [**] the Phase I/II Clinical Trial, [**], as soon as practicable
after the Second Amendment Effective Date, with the goal of completing the same by [**], and (b) if Pfizer has not concluded that the [**] or if Pfizer otherwise requests Spark to [**] in the Phase I/II Clinical Trial, [**], as soon as practicable after the Second Amendment Effective Date, with the goal of completing the same by [**]. Notwithstanding any provision in the License Agreement or this Second Amendment to the contrary, (i) the INDs for the Spark Phase I/II Clinical Trials shall not be transferred to Pfizer until each of the items in the Roles and Responsibilities Plan that are identified as being required prior to the transfer to Pfizer of the INDs have been completed and (ii) Spark shall remain responsible for conducting all activities that are necessary as part of the continuing conduct of the Phase I/II Clinical Trial (as defined below) until the INDs for the Phase I/II Clinical Trial have been transferred to and accepted by Pfizer, in each case, notwithstanding that the Collaboration Period may have ended prior to the time that such INDs are so transferred and accepted.

3.1.3 Following the Collaboration Period and the completion of the transfer to Pfizer of the INDs for the Phase I/II Clinical Trial:

(a) Pfizer shall assume responsibility for the conduct and completion of the Phase I/II Clinical Trial (including with respect to short-term and long-term following of patients after initial dosing by Spark), and Pfizer shall have final decision-making authority as to such activities;

(b) Pfizer shall become the sponsor for the Phase I/II Clinical Trial;

(c) Upon Pfizer’s request, Spark shall assign to Pfizer those applicable vendor agreements (as identified in such request) with respect to the Phase I/II Clinical Trial, including, without limitation, the [**];

(d) notwithstanding Section 4.4.2 of the License Agreement, Pfizer, as sponsor for the Phase I/II Clinical Trial, shall assume (and Spark shall not have) responsibility for the completion of the Phase I/II Clinical Data Package;

(e) Spark shall have no further obligation under Section 4.4.1 of the License Agreement, except to the extent that any such responsibilities are required of Spark to be conducted after the Collaboration Period as provided under the Roles and Responsibilities Plan; and

(f) in the event that Pfizer, despite having used its Commercially Reasonable Efforts to do so, has not entered into an agreement with a Third Party contractor such that such Third Party contractor can conduct [**], as applicable, beginning on or before [**], then, if requested by Pfizer, Spark and Pfizer shall negotiate, in good faith, a services agreement, under which Spark would continue to perform
3.2 Phase I/II Clinical Trial. The definition of “Phase I/II Clinical Trial” in Section 1.1.107 of the License Agreement is hereby replaced in its entirety with: “Phase I/II Clinical Trial’ means Spark’s first in human clinical trials involving Compounds, currently known as (i) SPK-9001-101 (which involves the dosing of patients with SPK-9001 and following such patients for a period of [**] after the enrollment and dosing of the last patient in the SPK-9001-101 study) and (ii) SPK-9001-LTFU-001 (which involves the continued following of patients dosed with SPK-9001 in the SPK-9001-101 study for a period of [**] after the enrollment of the last patient in the SPK-9001-LTFU-101 study).”

3.3 Non-Exclusive License Grants. Section 2.2 of the License Agreement is hereby amended by replacing Section 2.2 in its entirety with the following:

“2.2 Non-Exclusive License Grants.

2.2.1 Compounds and Licensed Products. Without limiting any other license granted under this Agreement, subject to the terms of this Agreement and, as applicable, the terms of the Existing Spark License Agreements and any Third Party Licenses entered into by Spark pursuant to Section 3.4.3(b) applicable to sublicensees thereunder, Spark hereby grants to Pfizer a non-exclusive license under all Patent Rights, Know-How and other Intellectual Property Rights Controlled (as of the Effective Date or at any time during the Term) by Spark or its Affiliates to use, have used, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized, and otherwise exploit Compounds and Licensed Products in the Field in the Territory during the Term.

2.2.2 Companion Diagnostic Assays. Without limiting any other license granted under this Agreement,

(a) subject to the terms of this Agreement and, as applicable, the terms of the Existing Spark License Agreements and any Third Party Licenses entered into by Spark pursuant to Section 3.4.3(b) applicable to sublicensees thereunder and (subject to Section 2.2.2(c) below) the terms of any agreement between Spark and a Third Party under which Spark Controls rights to any of the Spark Companion Diagnostic Technology (each, a “Spark Third Party Companion Diagnostic Technology Agreement”), Spark hereby grants to Pfizer a fully paid, royalty-free (subject to Section 2.2.2(d) below), irrevocable, perpetual, worldwide, non-exclusive license, with, subject to Section 2.3, the right to grant sublicenses (through multiple tiers), under all Spark Companion Diagnostic Technology and
Spark’s interest in the Joint Companion Diagnostic Technology to use, have used, Develop, have Developed, make, have made, sell, have sold, offer for sale, import, export, and otherwise exploit Companion Diagnostic Assays that are Developed for purposes of assessing whether a clinical trial subject or a patient is a candidate for treatment with a Licensed Product;

(b) subject to the terms of this Agreement and, as applicable (but subject to Section 2.2.2(c) below), the terms of any agreement between Pfizer and a Third Party under which Pfizer Controls rights to any of the Pfizer Companion Diagnostic Patent Rights (each a “Pfizer Third Party Companion Diagnostic Technology Agreement”), Pfizer hereby grants to Spark a fully paid, royalty-free (subject to Section 2.2.2(d) below), irrevocable, perpetual, worldwide, non-exclusive license, with, subject to Section 2.3, the right to grant sublicenses (through multiple tiers), under all Pfizer Companion Diagnostic Patent Rights and Pfizer’s interest in the Joint Companion Diagnostic Technology to use, have used, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized, and otherwise exploit Companion Diagnostic Assays;

(c) in the event either Party enters into an agreement with a Third Party under which such Party seeks to gain a license to intellectual property that is necessary or useful for the development, manufacture, use, sale or other exploitation of Companion Diagnostic Assays or Companion Diagnostic Assay Improvements, as applicable, such Party shall use its Commercially Reasonable Efforts to seek to have the ability to grant to the other Party the licenses described in Sections 2.2.2(a) or 2.2.2(b) above, as applicable. In addition, the Parties acknowledge that while, under Spark Third Party Companion Diagnostic Technology Agreements, Spark may not always obtain such rights and, under Pfizer Third Party Companion Diagnostic Technology Agreements, Pfizer may not always obtain such rights, and, if such rights are not obtained by Spark or Pfizer, as applicable, each Party (the “Contracting Party”) hereby represents and warrants that it has not and covenants that it will not agree in any such agreement between it or its Affiliates and any such Third Party to include (i) restrictions or limitations, including payments by such Third Party to such Contracting Party based on the grant to the other Party of such license, that would restrict or limit the other Party’s ability to obtain directly from the applicable Third Party a nonexclusive patent license to Develop, Manufacture, use, offer for sale, sell and import the Companion Diagnostic Assays, each to the extent owned or controlled by such Third Party or (ii) without
otherwise limiting such Third Party’s obligations with respect to the use of or maintaining the confidentiality of the Contracting Party’s confidential information, a prohibition against such Third Party using, in connection with the development of Companion Diagnostic Assays or Companion Diagnostic Assay Improvements by such Third Party on behalf of the other Party, residual knowledge (defined similarly to the definition of Residual Knowledge in Section 1.1.128 but as applicable to the confidentiality obligations undertaken in the agreement between such Third Party and the Contracting Party) that such Third Party may have as a result of its activities in developing a Companion Diagnostic Assay under the agreement between such Third Party and the Contracting Party; and

(d) the licenses granted in Sections 2.2.2(a) and 2.2.2(b) shall be subject to the grantee Party agreeing [**].

Notwithstanding any provision to the contrary in this Agreement, the licenses granted under this Section 2.2.2 shall survive expiration or any termination of this Agreement.”

3.4 Sublicenses. Section 2.3 of the License Agreement is hereby amended by replacing Section 2.3 in its entirety with the following:

“2.3 Sublicenses. Pfizer, subject to Section 4.11.1, and Spark each shall have the right to sublicense any of the rights granted to it pursuant to Section 2.1 and Section 2.2 in multiple tiers to Affiliates and Third Parties, provided that:

2.3.1 Pfizer shall include or otherwise substantively incorporate in each such sublicense granted by it all terms and conditions that sublicensees are required to be subject to under (i) this Agreement, (ii) the Existing Spark License Agreements, (iii) Third Party Licenses entered into by Spark pursuant to Section 3.4.3(b) after the Effective Date under which Pfizer has elected to receive a sublicense, and (iv) any Spark Third Party Companion Diagnostic Technology Agreement, each as applicable;

2.3.2 Spark shall include or otherwise substantively incorporate in each such sublicense granted by it all terms and conditions that sublicensees are required to be subject to under (i) this Agreement and (ii) any Pfizer Third Party Companion Diagnostic Technology Agreement, each as applicable;

2.3.3 Each of Pfizer and Spark shall remain responsible for its obligations hereunder and, to the extent necessary to satisfy such obligations, shall be responsible for its sublicensees’ performance under each sublicense agreement;

2.3.4 Should any sublicensee of Pfizer fail to comply with the terms and conditions that such sublicensee is required to be subject to under this
Agreement, the Existing Spark License Agreements, other Third Party license(s) entered into by Spark after the Effective Date under which Pfizer has elected to receive a sublicense or any Spark Third Party Companion Diagnostic Technology Agreement, each as applicable, Pfizer shall either promptly cause such sublicensee to comply with such terms and conditions or terminate the applicable sublicense;

2.3.5 Should any sublicensee of Spark fail to comply with the terms and conditions that such sublicensee is required to be subject to under this Agreement or any Pfizer Third Party Companion Diagnostic Agreement, as applicable, Spark shall either promptly cause such sublicensee to comply with such terms and conditions or terminate the applicable sublicense; and

2.3.6 Pfizer shall deliver to Spark a true and complete copy of each sublicense agreement between Pfizer and any Third Party sublicensee and Spark shall deliver to Pfizer a true and complete copy of each sublicense agreement between Spark and any Third Party sublicensee, each within [**] days after Pfizer or Spark, as applicable, enters into any such sublicense and, upon request by Spark or Pfizer, as applicable, from time to time, Pfizer or Spark, as applicable, shall promptly identify all Affiliates to which Pfizer or Spark, as applicable, has granted sublicenses. Notwithstanding the foregoing, the Party providing a copy of a sublicense Agreement it has entered into may redact from such copy (i) any information and provisions not relating to the rights sublicensed pursuant to this Section 2.3, (ii) all financial provisions of such sublicense agreement, (iii) confidential information of the Third Party, and (iv) other information that is competitively sensitive. Each such sublicense agreement provided by a Party to the other Party pursuant to this Section 2.3.5, is hereby deemed to be included as part of the providing Party’s Confidential Information.

Pfizer and Spark shall be equally responsible for compliance with the provisions of this Section 2.3 as to sub-sublicenses granted by its sublicensees, as if such sub-sublicenses were granted directly by Pfizer or Spark, as applicable.”

3.5 Development Costs. Section 3.2.1 of the License Agreement is hereby amended by replacing Section 3.2.1 in its entirety with the following:

“3.2.1 Product Development Costs.

(a) During the portion of the Collaboration Period prior to the later of (i) [**] or (ii) the completion of [**] (the later of (i) or (ii), the “Cost Responsibility Transition Date”), Pfizer shall reimburse Spark for [**] percent ([**]% of the Development Costs and [**] percent ([**]% of the Manufacturing Costs incurred under Product Development Plan, in accordance with the Budget. To the extent that the actual total Development Costs and Manufacturing Costs for expenses incurred under Product
Development Plan expended prior to the end of the Collaboration Period exceed a cumulative aggregate of $[*] U.S. dollars ($[*]) (the “Cap”), Pfizer will subject to Section 4.3.2(i) reimburse Spark for one hundred percent (100%) of the Development Costs and Manufacturing Costs in excess of the Cap; and thereafter if actual Development Costs and Manufacturing Costs exceed the Cap, Pfizer will, subject to the limitations set forth in Section 4.3.2(e), have final decision-making authority in the JSC with respect to any Disputed Matters. Following the Collaboration Period, Pfizer will pay all Development Costs and Manufacturing Costs.

(b) Beginning on the Cost Responsibility Transition Date and for the remainder of the Collaboration Period, Pfizer shall reimburse Spark for all Development Costs incurred under the Product Development Plan, in accordance with the Budget. Beginning on the Cost Responsibility Transition Date, Pfizer will, subject to the limitations set forth in Section 4.3.2(e), have final decision-making authority in the JSC with respect to any Disputed Matters.

(c) Following the Collaboration Period, Pfizer will be responsible for all Development Costs and Manufacturing Costs it incurs.”

3.6 Governance. Section 4.3.2(g) of the Agreement is hereby amended by replacing Section 4.3.2(g) in its entirety with the following:

“(g) Post-Collaboration Period Role. Following the Collaboration Period, the JSC shall cease to have the responsibilities set forth in Section 4.3.2(d) and the decision-making authority set forth in Section 4.3.2(e) and, thereafter will no longer function as a decision-making body, at which point in time such committee will be dissolved and reconstituted and renamed as the Information Sharing and Advisory Committee (“ISAC”) with the understanding that, as of the end of the Collaboration Period, all references in the License Agreement to “the JSC” in the License Agreement will be replaced by “the ISAC” to the extent such references are applicable to activities occurring after the end of the Collaboration Period. Beginning on the earliest of (i) the Cost Responsibility Transition Date, (ii) the date on which Pfizer, pursuant to Section 3.2.1(a) becomes responsible for one hundred percent (100%) of the Development and Manufacturing Costs or (iii) the end of the Collaboration Period, Pfizer shall have final decision-making authority for matters previously within the JSC’s authority, subject to Pfizer’s obligations and Spark’s rights, under this Agreement, including Section 4.9.”

3.7 End of Phase II Meetings; Regulatory Activities. The Parties agree that (a) the joint preparation requirements of Section 4.10.3 of the License Agreement shall apply only to the first EOP2 Meeting and (b) Spark shall have no further obligation under Section 4.10.3 of the License Agreement after the completion of the first EOP2 Meeting, provided, however, that thereafter Spark, at no cost to Pfizer, shall provide reasonable available additional
information, in the form Spark has such information, relating to the Phase I/II Clinical Trial, other pre-clinical studies conducted by Spark, Spark’s manufacture of any Compound or Licensed Product, or Spark’s development, validation or conduct of assays or analytical methods relating thereto, each as reasonably requested by Pfizer, to assist Pfizer in its preparation for subsequent EOP2 Meetings, its preparation of any filings with a Regulatory Authority relating to the Compound or Licensed Product and its preparation for or of any other meeting or communication with any Regulatory Authority relating to the Compound or Licensed Product.

3.8 Regulatory Communications. Section 4.10.6 of the License Agreement is hereby amended by replacing Section 4.10.6 in its entirety with the following:

“4.10.6 Regulatory Communications. With respect to each of the Major Market Countries, Canada and Japan, on a country by country basis, following the Collaboration Period and prior to the [**] of the first Licensed Product Developed by Spark pursuant to this Agreement (the “Regulatory Participation Period”), upon Spark’s reasonable request, Pfizer will reasonably consider and endeavor to accommodate Spark’s requests to attend, either in person or via teleconference (at Spark’s discretion), material meetings (including using reasonable efforts to request permission from the applicable Regulatory Authority to allow a reasonable number of employees of Spark to attend the portion of any material meeting with such Regulatory Authorities pertaining to the applicable Licensed Product developed by Spark under this Agreement (each a “Spark Developed Licensed Product”)) between Pfizer employees and Regulatory Authorities in such country when such meeting relates substantially to such Spark Developed Licensed Product, with any such attendance being at Spark’s sole cost and expense. Without limiting the generality of the foregoing, during the Regulatory Participation Period, Pfizer, to the extent practicable, shall notify Spark reasonably in advance of any such upcoming material meeting or material discussion that relates substantially to such Spark Developed Licensed Product(s), whether in-person, by teleconference or by video-conference, that Pfizer has scheduled with Regulatory Authorities in any of the Major Market Countries, Canada or Japan. During the Regulatory Participation Period, if requested by Spark with respect to any particular material meeting or material discussion attended in person or via teleconference by one or more Spark employees, Pfizer will provide Spark with copies of (i) the minutes (in a form where information not substantially related to the Spark Developed Licensed Product or Compound may be redacted by Pfizer) of any such material meeting or material discussion that relates substantially to such Spark Developed Licensed Product(s), whether in-person, by teleconference or by video-conference, that Pfizer has scheduled with Regulatory Authorities in any of the Major Market Countries, Canada or Japan. During the Regulatory Participation Period Pfizer will provide to the ISAC at its regularly scheduled meetings an update regarding Pfizer’s regulatory plans, material communications with Regulatory Authorities and outcomes of such material regulatory interactions, each to the extent substantially related to such Spark Developed Licensed Product. Additionally, if requested by Spark to aid its understanding of the updates Pfizer provides to the ISAC during the Regulatory Participation Period, Pfizer shall reasonably consider Spark’s requests for access to copies of relevant portions of material filings, material notices and
material correspondence with, to or from a Regulatory Authority in any of the Major Market Countries, Canada or Japan which are in Pfizer’s possession and substantially relate to the Licensed Product) specified by Spark, provided that Pfizer may redact any information that is not substantially related to a Spark Developed Licensed Product, that relates to any product other than the Spark Developed Licensed Product or that is otherwise proprietary to Pfizer. Any copies of documents provided by Pfizer to Spark under this Section 4.10.6 may be provided by Pfizer by posting copies of such documents to a secure electronic repository to which Spark employees having a need to know such information are provided access. All materials and information made available to Spark, whether directly or indirectly, by Pfizer, or through Spark’s attendance at any meeting or discussion with any Regulatory Authority as provided herein, shall be deemed to be Pfizer’s Confidential Information and shall be treated by Spark as such pursuant to Article 6 of this License Agreement.”

3.9 Commercial Participation and Information Sharing. Section 4.11 of the License Agreement is hereby amended by adding the following to the end thereof as new Sections 4.11.3 and 4.11.4:

“4.11.3 Advisory Boards. Following the Second Amendment Effective Date and prior to the earlier of (x) the [**] of a Spark Developed Licensed [**] or (y) the [**], Pfizer shall notify Spark reasonably in advance of any upcoming physician or patient advisory boards (all such advisory boards, “Ad Boards”) scheduled by Pfizer [**], which Ad Boards relate substantially to the Spark Developed Licensed Product. Upon Spark’s written request, Pfizer will invite Spark to have a reasonable number of employees of Spark to attend such Ad Boards, which attendance will be at Spark’s sole cost and expense. Pfizer shall have no obligation to invite any Spark employee and Spark shall have no right to have any of its employees attend [**], and it shall be Spark’s responsibility to ensure that its employees attending any such Ad Board are aware of such restrictions and take appropriate action to immediately discontinue their attendance at and participation in [**]. Pfizer may require each such Spark employee to sign a confidential disclosure agreement prior to permitting such Spark employee’s attendance at such Ad Board which confidential disclosure agreement may restrict such employee from using in any manner or disclosing to Spark or to any third party any information that [**] is obtained by such Spark employee in connection with his or her attendance at or participation in such Ad Board. All information made available, directly or indirectly, to Spark including, any discussions at any Ad Boards, under this Section 4.11.3 shall be deemed to be Pfizer’s Confidential Information and shall be treated by Spark as such pursuant to Article 6 of this License Agreement, provided, however, that the term of Spark’s obligations, as provided under Section 6.2 of the License Agreement, with respect thereto, shall expire [**] years after the expiration or earlier termination of the License Agreement. Notwithstanding the foregoing, in the event that a Spark employee receives any information [**] in connection with his or her attendance at
any Ad Board, Spark agrees that such information (i) also shall be deemed to be Pfizer’s Confidential Information, (ii) shall be treated as such by Spark pursuant to Article 6 of this License Agreement, provided, however, that the term of Spark’s obligations, as provided under Section 6.2 of the License Agreement, with respect to such Confidential Information, shall expire [**] years after the expiration or earlier termination of the License Agreement, and (iii) shall not be used by Spark for any purpose.”

“4.11.4 Information Sharing. Following the Second Amendment Effective Date, Pfizer shall provide Spark with copies of clinical Development plans prepared by or on behalf of Pfizer that relate to the Licensed Product in any Major Market Country, Canada or Japan, provided, however, that Pfizer shall have the right to redact portions of any such clinical Development plans that, in whole or in part, relates to or includes information regarding any gene therapy product (other than the Licensed Product) owned or controlled by Pfizer or its Affiliates or that Pfizer or its Affiliates is developing or plans to Commercialize. All information provided to Spark under this Section 4.11.4 shall be deemed to be Pfizer’s Confidential Information and shall be treated by Spark as such pursuant to Article 6 of this License Agreement.”

3.10 Certain Spark Obligations; Transfer of Technology and Materials.

3.10.1 The Parties hereby agree that as of the Second Amendment Effective Date, any obligation of Spark remaining to be performed under (a) the Manufacturing Technology Transfer Plan (as it existed prior to the Second Amendment Effective Date), (b) the Technology Transfer Plan (as it existed prior to the Second Amendment Effective Date) and (c) Sections 4.5.1, 4.8.1, 4.8.4, 4.8.5 and 4.15 of the License Agreement each shall be and hereby is deleted from the License Agreement and superseded in its entirety and such obligations collectively shall be replaced by the obligations set forth in Sections 3.1.2, 3.6, and 3.9.4 of this Second Amendment and the obligations set forth in Section 4.5.3 of the License Agreement, as amended below. The Parties further agree that the Amended and Restated Technology Transfer Plan (as defined below) attached to this Second Amendment as Exhibit D, supersedes and replaces the Technology Transfer Plan and the Manufacturing Technology Transfer Plan (as each such plan existed prior to the Second Amendment Effective Date). From and after the Second Amendment Effective Date, any references in the License Agreement to the Manufacturing Technology Transfer Plan shall be deemed to be references to the Amended and Restated Technology Transfer Plan.

3.10.2 The Parties hereby agree that following the Collaboration Period, any obligation of Spark remaining to be performed under the final sentence of Section 4.10.2 of the License Agreement shall be and hereby is superseded in its entirety and such obligation shall be replaced by the obligations set
forth in Section 4.5.3 of the License Agreement, as amended below, and the obligations set forth in Section 3.2, 3.6 and 3.9.4 of this Second Amendment.

3.10.3 Section 4.5.3 of the License Agreement is hereby deleted and replaced in its entirety with:

“4.5.3 Technology Transfer Plans. The Parties shall each use Commercially Reasonable Efforts to discharge in a timely manner the responsibilities set forth in the technology transfer plan set forth in Exhibit D to the Second Amendment (the “Amended and Restated Technology Transfer Plan”). In connection therewith, and, without limiting Spark’s obligations set forth in Section 4.5.2, Spark shall transfer or cause to be transferred to Pfizer, in a reasonably timely manner, the Manufacturing Process Technology and Spark Technology, as set forth in the Amended and Restated Technology Transfer Plan in order to enable (i) Pfizer and Spark to perform its respective activities set forth in the Roles and Responsibilities Plan and Amended and Restated Technology Transfer Plan and (ii) enable Pfizer to manufacture or have manufactured Compound and Licensed Products pursuant to Section 5.8 of the License Agreement and prepare the necessary Regulatory Approvals for the manufacture of Compounds and Licensed Products pursuant to Section 4.10 of the License Agreement. Each Party shall bear its own expenses in carrying out its responsibilities under the Amended and Restated Technology Transfer Plan. In addition, Spark agrees to perform such further acts and execute and deliver such further documents and materials as may be reasonably requested by Pfizer in order to more fully effect the transfer to Pfizer of Manufacturing Process Technology and Spark Technology, provided that Pfizer shall reimburse Spark for the reasonable out of pocket costs incurred by Spark in fulfilling such additional requests.”

3.10.4 Biological Samples.

(a) “Biological Samples” means biological materials (such as blood, urine, tissue, cells, cell cultures or saliva) collected from study subjects during the conduct of the Phase I/II Clinical Trial during such times as Spark was the sponsor of the IND(s) for the Phase I/II Clinical Trial.

(b) “Surplus Samples” means any Biological Samples that remain after completion of all protocol-required testing conducted as part of the Phase I/II Clinical Trial by or on behalf of Spark prior to the time that Spark transfers to Pfizer and Pfizer becomes the sponsor of the IND(s) for the Phase I/II Clinical Trial.

(c) “Applicable Requirements” means: (i) the terms of the Agreement, including, but not limited to, standard operating procedures (“SOPs”) and other documents referred to in the Agreement or otherwise used by Spark in the conduct of the Phase I/II Clinical Trial; (ii) the
protocol(s) for the Phase I/II Clinical Trial (the “Protocols”); (iii) the Investigator Brochure(s) for the Phase I/II Clinical Trial; (iv) the terms of the IRB/IEC approval(s) for the Phase I/II Clinical Trial; (v) all Applicable Laws; and (vi) all applicable GxP.

(d) To the extent (x) permissible or not prohibited under the Applicable Requirements and (y) permissible under informed consent documents signed by the applicable Study Subject, Spark, at or before the end of the Collaboration Period (or such later date as Pfizer may specify) shall transfer all Surplus Samples to Pfizer or to Pfizer’s designee. If Spark is unable to transfer any of the Surplus Samples to Pfizer, Spark shall cooperate with Pfizer and shall take such actions as may be necessary to allow for the continued use and testing of the Surplus Samples by or under the direction of Pfizer in connection with the development of any Licensed Product, including:

(i) using reasonable efforts to amend the informed consent document signed by the applicable Study Subject to allow for the transfer to and use by Pfizer or Pfizer’s designee of such Surplus Samples;

(ii) using reasonable efforts to obtain waivers or authorizations from the applicable IRB/IEC to allow for the transfer to and use by Pfizer or Pfizer’s designee of such Surplus Samples;

(iii) using reasonable efforts to enter into an agreement (which agreement shall be subject to prior written approval of Pfizer) and/or facilitating Pfizer’s entry into an agreement with a Third Party to hold such Surplus Samples and make use thereof under the direction of Pfizer or Pfizer’s designee; and/or

(iv) other actions as the Parties may mutually agree will achieve the goal of allowing Pfizer or Pfizer’s designee to hold and use such Surplus Samples.

Pfizer and, as applicable, Pfizer’s designee, shall comply with all Applicable Requirements regarding its handling and use of the Surplus Samples once received from Spark. Costs incurred by Spark in taking any of the foregoing actions shall be borne solely by Spark, provided, however, that to the extent any Surplus Samples are to be held by a Third Party after the end of the Collaboration Period in order to allow the continued use thereof the amounts payable to such Third Party for performing its obligations with respect to the Surplus Samples under such Agreement shall be borne by Pfizer.
3.11 **Materials Transfer.** The Parties agree that Spark’s transfer of any materials to Pfizer or its Affiliates or, if requested by Pfizer, directly to a Third Party designee, in each case, for use in the Development (whether directly by Pfizer or through one or more Affiliates or Third Party contractors) of the Companion Diagnostic Assay or any other assay to be used to assess the efficacy, potency or safety of any Licensed Product (such development, the “Assay Development” and such materials, excluding any materials addressed in Section 3.10.4, collectively, the “Spark Materials”) shall be subject to this Section 3.11. The Spark Materials constitute Confidential Information of Spark, and shall be used by Pfizer, its Affiliates or Third Party designees (i) only as set forth in Exhibit E hereto and (ii) solely for Assay Development. Any transfer by Spark directly to a Third Party designated by Pfizer shall be pursuant to an agreement between Pfizer (or one of its Affiliates) and such Third Party that contains terms governing the use and treatment of such Spark Materials which terms are no less restrictive than the material transfer terms set forth in Exhibit E hereto. Spark acknowledges that Pfizer will and has the right to transfer certain of the Spark Materials to [**] and/or one or more affiliates of [**] (collectively, “[**]”) in order for [**] to perform its Companion Diagnostic Assay Development obligations under a Companion Diagnostic Assay Development Initiation Agreement and potentially one or more related agreements to be entered into by and between Pfizer and [**] or one or more Affiliates of [**] (as such agreement(s) may be amended, supplemented or restated by such parties, the “[**] Agreement”). Pfizer agrees that it shall not transfer any Spark Materials to any other Third Party for Assay Development without a written agreement between Pfizer and such transferee containing material transfer terms consistent with this Section 3.11 and Exhibit E hereto (any such agreement, including the [**] Agreement, a “Transfer Agreement” and any such transferee of Spark Materials, a “Transferee”). For clarity, this Section 3.11 and the material transfer terms set forth in Exhibit E shall have no effect on Pfizer’s right to use materials provided by Spark or to transfer to a Third Party materials provided by Spark, in each case for the manufacture of Licensed Products.

3.12 **Payments.** In consideration for Spark performing its obligations under this Second Amendment, including, without limitation, the timely performance of Spark’s obligations under each of the Roles and Responsibilities Plan and the Amended and Restated Technology Transfer Plan, Pfizer hereby agrees to make the following payments to Spark:

3.12.1 a one-time payment to Spark in the amount of ten million dollars ($10,000,000), which payment shall be made within [**] days after the Second Amendment Effective Date;

3.12.2[**] dollars ($[**]) due as follows:

   (a)a one-time payment to Spark in the amount of [**] dollars ($[**]) due upon the [**]. Such payment shall be made within [**] days after Spark submits an invoice therefor to Pfizer, provided that such invoice shall not be submitted to Pfizer prior to the end of the [**]; and
(b) a one-time payment to Spark in the amount of [**] dollars ($[**]) upon completion, [**], a “Milestone 2 Activity” and, [**]. Such payment shall be made within [**] days after Spark submits an invoice therefor to Pfizer, provided that such invoice shall not be submitted to Pfizer prior to the end of the [**]. In the event that Pfizer, in good faith, disputes that Spark has, prior to the end of the [**], completed, in all material respects, one or more Milestone 2 Activities, Pfizer shall so notify Spark and the Parties shall use reasonable efforts to resolve such dispute, provided however, that (a) notwithstanding the existence of such dispute, Pfizer shall timely pay the portion of such invoice corresponding to any Milestone 2 Activity that Pfizer is not disputing has been completed in all material respects prior to the end of the [**], calculated at a rate of [**] dollars ($[**]) per Milestone 2 Activity and (b) the period for making payment with respect to any Milestone 2 Activity that is the subject of a good faith dispute by Pfizer shall be tolled pending the resolution of such dispute. Either Party may, at any point after Spark’s delivery of an invoice hereunder, escalate and submit a dispute under this Section 3.12.2(b) for resolution in accordance with Section 10.9 of the License Agreement, in which case the only consideration shall be whether Spark completed the disputed Milestone 2 Activity(s) in all material respects prior to the end of the [**]. If the resolution of such dispute is that Spark has completed one or more disputed Milestone 2 Activity(s) in all material respects prior to the end of the [**], then Pfizer shall pay the previously unpaid portion(s) of the invoiced amounts corresponding to the applicable disputed Milestone 2 Activity(s) on or before the later of (i) [**] days after Pfizer’s receipt of the applicable invoice submitted as described above in this Section 3.12.2(b) or (ii) [**] Business Days of such resolution (calculated as set forth above). If the resolution of such dispute is that Spark did not complete the disputed Milestone 2 Activity(s) in all material respects prior to the end of the [**], or if Spark concedes that it failed to complete a Milestone 2 Activity in all material respects prior to the end of the [**], then Spark shall forfeit the previously unpaid portion(s) of the invoiced amounts corresponding to such Milestone 2 Activity(s) (calculated as set forth above).

3.12.3 a one-time payment to Spark in the amount of [**] dollars ($[**]) due upon [**] as provided in the Roles and Responsibilities Plan, provided that such payment shall be made within [**] days after Spark submits an invoice therefor to Pfizer, which invoice shall not be submitted to Pfizer until [**]; and

3.12.4 a one-time payment to Spark in the amount of [**] dollars ($[**]) due upon [**], a “Milestone 4 Activity”, and, [**] on or before [**] (each, a “Target

16
Such payment shall be made within [**] days after Spark submits an invoice therefor to Pfizer, provided that such invoice shall not be submitted to Pfizer until Spark believes, in good faith, that it has completed the Milestone 4 Activities in all material respects and delivered to Pfizer each of the deliverables required to be delivered to Pfizer as part of the completion of each such activity. In the event that Pfizer, in good faith, disputes that Spark on or before the applicable Target Date(s), has completed, in all material respects, one or more Milestone 4 Activities, Pfizer shall so notify Spark and the Parties shall use reasonable efforts to resolve such dispute, provided however, that (a) notwithstanding the existence of such dispute, Pfizer shall timely pay the portion of such invoice corresponding to any Milestone 4 Activity that Pfizer is not disputing that Spark has performed such Milestone 4 Activity in all material respects by the applicable Target Date, calculated at a rate of $[**] and (b) the period for making payment with respect to any Milestone 4 Activity that is subject to a good faith dispute by Pfizer shall be tolled pending the resolution of such dispute. Either Party may, at any point after Spark’s delivery of an invoice hereunder, escalate and submit a dispute under this Section 3.12.4 for resolution in accordance with Section 10.9 of the License Agreement, in which case the only consideration shall be whether Spark completed the disputed Milestone 4 Activity(s), in all material respects, prior to the applicable Target Date(s). If the resolution of such dispute is that Spark completed the disputed Milestone 4 Activity(s), in all material respects, prior to the applicable Target Date(s), then Pfizer shall pay the previously unpaid portion(s) of the invoiced amounts corresponding to such disputed Milestone 4 Activity(s) on or before the later of (i) [**] days after Pfizer’s receipt of the applicable invoice submitted as described above in this Section 3.12.4 or (ii) [**] Business Days after such resolution (calculated as set forth above). If the resolution of such dispute is that Spark did not complete the disputed Milestone 4 Activity(s), in all material respects, prior to the applicable Target Date(s), or if Spark concedes that it failed to complete a Milestone 4 Activity, in all material respects, prior to the applicable Target Date, then Spark shall forfeit the previously unpaid portion(s) of the invoiced amounts corresponding to such Milestone 4 Activity(s) (calculated as set forth above).

In the event Spark fails to complete, in all material respects, any activity required of it under either the Roles and Responsibilities Plan or the Amended and Restated Technology Transfer Plan, as applicable, on or before the target completion date specified in the Roles and Responsibilities Plan or the Amended and Restated Technology Transfer Plan, as applicable, with respect to such activity, Spark shall remain obligated to complete such activity, in all material respects, regardless of whether any particular payment described above in this Section 3.12 becomes due and payable.

[Signature page follows]
IN WITNESS WHEREOF, authorized representatives of the Parties have duly executed this Second Amendment as of the Second Amendment Effective Date.

PFIZER INC.

By: /s/ Robert J. Smith
Name: Robert J. Smith
Title: Senior Vice President

SPARK THERAPEUTICS, INC.

By: /s/ Jeffrey D. Marrazzo
Name: Jeffrey D. Marrazzo
Title: Chief Executive Officer

Second Amendment – Signature Page
### EXHIBIT A

**SPARK COMPANION DIAGNOSTIC PATENT RIGHTS**

<table>
<thead>
<tr>
<th>Title</th>
<th>Country</th>
<th>Status</th>
<th>Application Number</th>
<th>Filing Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 4 pages were omitted. [**]

Exhibit A – Page 1
EXHIBIT B

CLINICAL COMPARABILITY CRITERIA

[**]

Exhibit B – Page 1
EXHIBIT C

ROLES AND RESPONSIBILITIES PLAN

Capitalized terms used and not otherwise defined in this Roles and Responsibilities Plan shall have the meaning assigned to such terms the License Agreement, as amended.

Clinical

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Pfizer’s Role</th>
<th>Spark’s Role</th>
<th>Timing of Spark Involvement</th>
<th>Milestone 2 Activity</th>
<th>Completion Required Prior to IND Transfer</th>
</tr>
</thead>
</table>

Medical

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Pfizer’s Role</th>
<th>Spark’s Role</th>
<th>Timing of Spark Involvement</th>
<th>Milestone #2 Activity</th>
<th>Completion Required Prior to IND Transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>
### Regulatory

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Pfizer’s Role</th>
<th>Spark’s Role</th>
<th>Timing of Spark Involvement</th>
<th>Milestone #2 Activity</th>
<th>Completion Required Prior to IND Transfer</th>
</tr>
</thead>
</table>

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 2 pages were omitted. [**]

### Assays

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Pfizer’s Role</th>
<th>Spark’s Role</th>
<th>Timing of Spark Involvement</th>
<th>Milestone #2 Activity</th>
<th>Completion Required Prior to IND Transfer</th>
</tr>
</thead>
</table>

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 7 pages were omitted. [**]
## Information Transfer

<table>
<thead>
<tr>
<th>Category</th>
<th>Detail</th>
<th>Timing</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>

Exhibit D – Page 1
### Materials Transfer

<table>
<thead>
<tr>
<th>Category</th>
<th>Detail</th>
<th>Timing</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>

---

Exhibit D – Page 2
### Testing/Consulting

<table>
<thead>
<tr>
<th>Category</th>
<th>Detail</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>

Exhibit D – Page 3
Attachment 1 to Amended and Restated Technology Transfer Plan:
DS & DP Methods for ICH Batches

[**]

[**]

Exhibit D – Page 4
Attachment 1 to Amended and Restated Technology Transfer Plan:
DS & DP Methods for ICH & PV/Commercial Batches

[**]

Exhibit D – Page 5
EXHIBIT E

MATERIAL TRANSFER TERMS

- Transferee shall use the Spark Material and any related information solely to conduct the Assay Development work, other testing, or product manufacturing activities, each as applicable and as described in the Transfer Agreement.
- Transferee shall maintain in confidence the Spark Material and any related information provided in connection with the Transfer Agreement.
- Transferee shall limit use and disclosure of the Spark Material and any related information to its representatives who are bound by the terms of the Transfer Agreement and any confidentiality agreement between Pfizer, and Transferee and who have an actual need to know. Transferee shall be liable for any breach of these terms by its representatives.
- Transferee shall take reasonable precautions to prevent loss or theft of the Spark Material.
- Transferee shall, upon completion of the work described in the Transfer Agreement, return any remaining used and/or unused Spark Material to Pfizer, and/or shall destroy any such remaining Spark Material at Pfizer's request.
- Except as required by applicable laws or regulations or as may be ordered by a governmental authority of competent jurisdiction, Transferee shall not disclose information related to the Spark Material or any related information to any third party.
- Transferee shall represent and warrant that any person or parties providing services in connection with the Spark Materials shall be bound by these provisions.
- Transferees shall neither analyze nor attempt to determine or reverse engineer the Spark Material, nor furnish the Spark Material to a third party for such analysis.
- Transferee shall not use the Spark Material in humans.
- Transferee shall hold Spark harmless for any claims for injury resulting from such party’s use of the Spark Material, and for any claims for injury resulting from use of the Spark Material by any third party who received the Spark Material from such party.
- No express or implied warranties with respect to the Spark Material are made by Spark, including, but not limited, to any express or implied warranties of merchantability or fitness for a particular purpose.
SUPPLY AGREEMENT

THIS SUPPLY AGREEMENT (the “Agreement”) is entered into as of this 24th day of January, 2018 (the “Effective Date”), by and between Spark Therapeutics, Inc., a Delaware corporation organized under the laws of the State of Delaware, having a principal place of business at 3737 Market Street, Suite 1300, Philadelphia, PA 19104, USA (“Spark”), and Novartis Pharma AG, a Swiss company, with offices at Lichtstrasse 35, CH-4056 Basel, Switzerland (“Novartis”). Spark and Novartis are sometimes referred to herein each as a “Party” and collectively as the “Parties”.

BACKGROUND:

WHEREAS, Spark is a biopharmaceutical company specializing in the development of gene therapies;

WHEREAS, Spark has experience and expertise in the Manufacture of the Drug Substance (as defined below);

WHEREAS, Novartis is a pharmaceutical company engaged in, among other things, the development, marketing and sale of certain pharmaceutical products;

WHEREAS, Spark and Novartis have entered into that Licensing and Commercialization Agreement, dated as of the Effective Date (as amended from time to time, the “License Agreement”);

WHEREAS, pursuant to Section 5.6 of the License Agreement, Spark and Novartis have agreed that Novartis shall purchase all of Novartis’ and its Affiliates’ and their respective Sublicensees’ and distributors’ technical, clinical and commercial requirements for the Products in the Novartis Territory (each capitalized term as defined below) from Spark, and Spark shall Manufacture and supply all of Novartis’ and its Affiliates’ and their respective Sublicensees’ and distributors’ technical, clinical and commercial requirements for the Products in the Novartis Territory; and

WHEREAS, the Parties wish to set forth the terms by which Spark shall Manufacture and/or supply Products to Novartis, and Novartis shall purchase the Products from Spark;

NOW, THEREFORE, in consideration of the promises, rights and obligations set out in this Agreement, the sufficiency of which is acknowledged, the Parties agree as follows:

1. DEFINITIONS. The following terms shall have the meanings ascribed to them below.
1.1 “Apparent Defect” means a Defect easily identifiable as a result of a visual inspection of a Product, such as quantity deviation with respect to the contents of a vial and damage in packaging or as a result of an inspection of accompanying Certificate of Analysis and shipment documentation.

1.2 “Approved Subcontractor(s)” means any subcontractor of Spark that is relevant to, and specified in, the Regulatory Approvals, as currently set forth on Exhibit D attached hereto. Such Exhibit D shall, at the time of full execution and delivery of the Quality Agreement by both Parties, be superseded and replaced by the Approved Subcontractor annex incorporated in such Quality Agreement, which annex may be updated and amended from time to time in accordance with Section 2.3 and the Quality Agreement.

1.3 “Batch of Diluent Product” means a batch of Diluent Product comprised of [**] vials of Diluent Product.

1.4 “Batch of Drug Substance” means a bulk batch of Drug Substance comprised of the purified output of [**] weekly sublots of drug substance intermediate (roughly estimated to be about [**] mL).

1.5 “Batch Record” means the final executed batch production and quality control records, prepared in accordance with cGMP, for each batch of Product, as applicable, Manufactured under this Agreement.

1.6 “Certificate of Analysis” means a document certifying that a batch of Product meets the applicable Specifications, as signed and dated by a duly authorized representative of Spark’s quality assurance department.

1.7 “cGMP” means the current Good Manufacturing Practices and standards as provided for (and as amended from time to time) in the United States of America and the European Union, Japan, China and Canada relating to the manufacture of Product, including, without limitation, European Commission Directive 2003/94/EC on the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and in the Current Good Manufacturing Practice Regulations of the United States Code of Federal Regulations (21 CFR §§ 210-211) in relation to the production of pharmaceutical intermediates and active pharmaceutical ingredients, as interpreted by ICH Harmonized Tripartite Guideline ICH Q7, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.

1.8 “CMC Documentation” means the Chemistry, Manufacturing and Controls section of a Regulatory Approval.

1.9 “Commence Manufacture” means the Calendar Year in which Spark commences the Manufacture of a Batch of Drug Substance, whether to be supplied as a Batch of Drug Substance or as Resulting Vials of Drug Product to Novartis, pursuant to a Purchase Order.
1.10 **Cost of Diluent Product** means the total amount payable by Spark to the Fill and Finish Subcontractor for each Batch of Diluent Product as calculated in accordance with Accounting Standards, including:

(a) the internal and external costs of Spark that directly relate to the Manufacture of a Batch of Diluent Product (including fees paid to the Fill and Finish Subcontractor);

(b) any fees charged by the Fill and Finish Subcontractor for [**];

(c) any pass-through costs together with any mark-up thereto for the purchase of Materials charged by the Fill and Finish Subcontractor;

(d) any fees charged by the Fill and Finish Subcontractor relating to [**];

(e) the applicable categories and components thereof identified in Column B of Exhibit A attached hereto (excluding all other columns), which categories and components shall serve as the general basis for calculating “Cost of Diluent Product” for any Calendar Year, subject to (i) the JSC’s discussion and input as to the specific units and allocation methodologies to be used to calculate the costs for each such category and components thereof for a particular Calendar Year, (ii) the provision of supporting details on cost allocations to the Cost of Diluent Product, and (iii) the Parties’ understanding that in some Calendar Years, it is possible that a category or any of its components thereof may include no costs; and

(f) any other items as mutually agreed by the Parties in writing from time to time.

1.1 **Cost of Drug Product** means the aggregate of:

(a) the Cost of Drug Substance; and

(b) the internal and external costs of Spark and its Affiliates to perform all fill, finish and packaging processes relating to the Batch of Drug Substance to produce the Resulting Vials of Drug Product (such fill, finish and packaging processes collectively, the “Drug Product Finishing Activities”), all as calculated in accordance with Accounting Standards and which are directly related to the performance of Drug Product Finishing Activities, including:

(i) all fees and costs directly relating to the purchase of Materials, [**];

(ii) the applicable categories and components thereof identified in Column B of Exhibit A attached hereto (excluding all other columns), which categories and components shall serve as the general basis for calculating “Cost of Drug Product” for any Calendar Year, subject to (A) the JSC’s discussion and input as to the specific units and allocation methodologies to be used to calculate the costs for each such category and components thereof for a particular Calendar Year, (B) the provision of supporting details on cost allocations to the Cost of Drug Product, and (C) the Parties’ understanding that in some Calendar Years, it is possible that a category or any of its components thereof may include no costs; and
any other items as mutually agreed between the Parties in writing from time to time.

For clarity, if Spark or any of its Affiliates performs all or any part of the Drug Product Finishing Activities, the “Cost of Drug Product” shall include the actual direct costs incurred by Spark or any of its Affiliates for conducting the Drug Product Finishing Activities. If an Approved Subcontractor performs all or any part of the Drug Product Finishing Activities, the “Cost of Drug Product” shall include the total amount payable by Spark to such Approved Subcontractor including:

(a) any pass-through costs charged by an Approved Subcontractor, together with any mark-up thereto for the purchase of Materials charged by an Approved Subcontractor;
(b) any fees charged by an Approved Subcontractor for [**];
(c) any fees charged by the Fill and Finish Subcontractor relating to [**];
(d) the applicable categories and components thereof identified in Column B of Exhibit A attached hereto (excluding all other columns), which categories and components shall serve as the general basis for calculating “Cost of Drug Product” for any Calendar Year, subject to (i) the JSC’s discussion and input as to the specific units and allocation methodologies to be used to calculate the costs for each such category and components thereof for a particular Calendar Year, (ii) the provision of supporting details on cost allocations to the Cost of Drug Product, and (ii) the Parties’ understanding that in some Calendar Years, it is possible that a category or any of its components thereof may include no costs; and
(e) any other items as mutually agreed between the Parties in writing from time to time.

1.2 “Cost of Drug Substance” means the aggregate of the internal and external costs of Spark that directly relate to the Manufacture of a Batch of Drug Substance (but, for clarity, without performing any Drug Product Finishing Activities), all as calculated in accordance with Accounting Standards, including:

(a) all fees and costs relating to the purchase of Materials, [**];
(b) the applicable categories and components thereof identified in Column B of Exhibit A attached hereto, which categories and components shall serve as the general basis (excluding all other columns) for calculating “Cost of Drug Substance” for any Calendar Year, subject to (i) the JSC’s discussion and input as to the specific units and allocation methodologies to be used to calculate the costs for each such category and components thereof for a particular Calendar Year, (ii) the provision of supporting details on cost allocations to the Cost of Drug Substance, and (ii) the Parties’ understanding that in some Calendar Years, it is possible that a category or any of its components thereof may include no costs; and
any other items as mutually agreed between the Parties in writing from time to time. For the avoidance of doubt, “Cost of Drug Substance” shall exclude costs of failed Batches of Drug Substance or any costs associated with the disposal of failed Drug Substance batches.

1.3 “Defective” means, with respect to a Product, Product that does not meet the Product Warranty, and “Defect” shall be construed accordingly.

1.4 “Diluent Product” means a vial of diluent as more specifically described in the Diluent Product Specifications, which vial shall be a naked vial unless otherwise set forth in Section 2.1(e).

1.1 “Diluent Product Specifications” means the written release specifications for the Diluent Product as set out in Exhibit B, which shall be superseded and replaced by specifications to be incorporated in the Quality Agreement, and which may be amended from time to time by the Parties in accordance with Section 5.4 and the Quality Agreement.

1.2 “Drug Product” means a [**] of Drug Substance more specifically described in the Drug Product Specifications, which vial shall be a naked vial unless otherwise set forth in Section 2.1(e).

1.3 “Drug Product Specifications” means the written release specifications for the Drug Product as set out in Exhibit B, which shall be superseded and replaced by specifications to be incorporated in the Quality Agreement, and which may be amended from time to time by the Parties in accordance with Section 5.4 and the Quality Agreement.

1.4 “Drug Substance” means voretigene neparvovec (AAV2-hRPE65v2), as more specifically described in the Drug Substance Specifications.

1.5 “Drug Substance Specifications” means the written release specifications for the Drug Substance as set out in Exhibit B, which shall be superseded and replaced by specifications to be incorporated in the Quality Agreement, and which may be amended from time to time by the Parties in accordance with Section 5.4 and the Quality Agreement.

1.6 “Escrow Materials” means the documents and materials specifically described on Exhibit C.

1.7 “Fill and Finish Subcontractor” means an Approved Subcontractor appointed by Spark to fill and finish the Drug Product and/or the Diluent Product, which as of the Effective Date is [**].

1.8 “Fill and Finish Subcontractor Facility” means the applicable facility of the Fill and Finish Subcontractor, which as of the Effective Date is [**] facility located at [**].

1.9 “First Rolling Forecast Date” means the first day of the first full quarter to occur after the Effective Date.
1.10  “Fixed Facility Fee” means for Batches of Drug Substance that Spark Commences Manufacturing in the Calendar Years [**], a fee not exceeding [**] US Dollars (US$[**]) per annum, and for Batches of Drug Substance that Spark Commences Manufacturing in each of the next [**] Calendar Years (the period from [**], the “Initial Fixed Facility Fee Period”), a fee equal to [**] percent ([**]% of the Fixed Manufacturing Cost (regardless of whether Novartis orders any Drug Substance or Resulting Vials of Drug Product in those [**] Calendar Years), provided that:

(a) if, during the Term, the Parties agree in writing to allocate additional Batches of Drug Substance to Novartis pursuant to Section 3.2(b), then:

   (i) if Novartis orders [**] Batches of Drug Substance, or the Resulting Vials of Drug Product corresponding to [**] Batches of Drug Substance, and the Calendar Year that Spark Commences Manufacturing of such Batches of Drug Substance is any of [**], the Fixed Facility Fee shall not exceed US$[**] for such Calendar Year; and

   (ii) if Novartis orders [**] Batches of Drug Substance, or the Resulting Vials of Drug Product corresponding to [**] Batches of Drug Substance, and is delivered the same in any of the next [**] Calendar Years, the Fixed Facility Fee shall be [**] percent ([**]% of Spark’s actual Fixed Manufacturing Cost for the Calendar Year in which Spark Commences Manufacturing of such Batches of Drug Substance; and

   (iii) if Novartis orders [**] Batches of Drug Substance, or the Resulting Vials of Drug Product corresponding to [**] Batches of Drug Substance, and is the Calendar Year that Spark Commences Manufacturing of such Batches of Drug Substance is any of [**], the Fixed Facility Fee shall not exceed US$[**]; and

   (iv) if Novartis orders [**] Batches of Drug Substance, or the Resulting Vials of Drug Product corresponding to [**] Batches of Drug Substance, and is delivered the same in any of the next [**] Calendar Years, the Fixed Facility Fee shall be [**] percent ([**]% of Spark’s actual Fixed Manufacturing Cost for the Calendar Year in which Spark Commences Manufacturing of such Batches of Drug Substance;

(b) if, during the Term, the capacity of the Spark Facility increases beyond [**] Batches of Drug Substance or the Resulting Vials of Drug Product corresponding to such number of Batches of Drug Substance per Calendar Year, Spark shall adjust the [**], unless the Parties agree otherwise in the Capacity Plan;

(c) if, during the Term, the Manufacture of the Drug Substance is transferred to Novartis or its designated Affiliate or a Third Party contract manufacturer, the Fixed Facility Fee shall be [**] from the date of the last delivery to Novartis;

(d) if in any [**] during the Term, Novartis fails to place at least [**] Purchase Orders requiring Manufacture of a Batch of Drug Substance in that [**], then the Fixed Facility Fee shall [**], provided that:
(i) without prejudice to any other rights or remedies Novartis may have under this Agreement, the Fixed Facility Fee for such [*] shall be reduced by [*] percent ([*]%) if Novartis orders [*] of Drug Substance and reduced by [*] percent ([*]%) if Novartis orders [*] of Drug Substance, where Novartis (acting reasonably) withholds one or more Purchase Orders or delays the proposed delivery date for such Purchase Order(s), as a result of (A) the occurrence of a Supply Failure event, or (B) the Parties (acting reasonably) agreeing that there is a reasonable likelihood that the Batches of Drug Substance or Resulting Vials of Drug Product will not conform with the Product Warranty (with any dispute as to the likelihood of conformity to be escalated to the JSC);

(ii) without prejudice to any other rights or remedies Novartis may have under this Agreement, the Fixed Facility Fee for a [*] shall be reduced by [*] percent ([*]%) if Novartis orders [*] of Drug Substance and reduced by [*] percent ([*]%) if Novartis orders [*] of Drug Substance, where Novartis (acting reasonably) withholds one or more Purchase Orders or delays the proposed delivery date for such Purchase Orders as a result of a failure or delay by Spark in obtaining EU Regulatory Approval, except that if Spark subsequently obtains EU Regulatory Approval and the Products Manufactured pursuant to Sections 3.1 and 3.3 comply with the Product Warranty, then the Fixed Facility Fee shall not be so reduced and Novartis shall pay to Spark the remaining portion of the Fixed Facility Fee that it is has not yet paid for such [*] to Spark; and

(iii) Spark shall reduce the Fixed Facility Fee by [*] percent ([*]%) if it uses [*] the vacant manufacturing slots for itself or Third Parties and by [*] percent ([*]%) if it uses [*] the vacant manufacturing slots for itself or Third Parties (with any such use to be agreed with Novartis in writing in advance).

(c) if in any [*] during the Term, Spark fails to deliver one or more Batches of Drug Substance or the Resulting Vials of Drug Product as a result of a breach of the terms of this Agreement, the Fixed Facility Fee for that [*] shall be reduced by [*] percent ([*]%) if Spark delivers [*] of Drug Substance or the Resulting Vials of Drug Product and reduced by [*] percent ([*]%) if Spark fails to deliver [*] of Drug Substance or the Resulting Vials of Drug Product, provided that if Spark delivers such Drug Substance or the Resulting Vials of Drug Product in a subsequent [*], then without prejudice to any other rights or remedies it may have under this Agreement, Novartis shall pay the Fixed Facility Fee for the original [*] in which Manufacture was to occur during the [*] in which such Drug Substance or the Resulting Vials of Drug Product is actually delivered by Spark in accordance with Section 3.5; and

(f) in [*], the Parties will discuss the best use of the available capacity in the Spark Facility in both Parties’ best interests and agree in good faith on the levels of capacity to be committed for Novartis. The Parties will agree in good faith to a new Fixed Facility Fee to apply after the expiration of the Initial Fixed Facility Fee Period (or such earlier time as the Parties may agree) and for each [*] thereafter during the period for which such fee should apply, based on the same principles that applied as of the Effective Date (namely a percentage of the Fixed Manufacturing Cost based on the percentage of capacity of the Spark Facility that is committed for Novartis).
1.11 “**Fixed Manufacturing Cost**” means those Manufacturing overhead costs incurred by Spark and its Affiliates relating exclusively to the Spark Facility and directly relate to the Manufacture of Drug Substance, which may include costs relating to utilities, insurance, audits and inspections, Manufacturing administrative and facilities costs, analytical testing and other testing, non-capitalized equipment purchase and maintenance, quality control, compliance, Spark Facility and equipment depreciation, process development costs, cleaning, personnel costs relating to the Spark Facility and compliance, all of the foregoing calculated in accordance with Accounting Standards, and any other items as mutually agreed between the Parties following discussion at the JSC from time to time. In the event that a portion of the Spark Facility is used to manufacture another product or program, then to the extent that any of the foregoing costs are attributable both to the Drug Substance and to one or more other products or programs of Spark or an Affiliate, such costs shall be included in the Fixed Manufacturing Cost and allocated between the Drug Substance and other products as mutually agreed between the Parties following discussion at the JSC. The applicable categories and components thereof identified in Column B of Exhibit A (excluding all other columns) attached hereto shall serve as the general basis for calculating “**Fixed Manufacturing Cost**” for any, subject to the JSC’s discussion and input as to the specific units and allocation methodologies to be used to calculate the costs for each such category and components thereof for a particular and the Parties’ understanding that in, it is possible that a category or any of its components thereof may include no costs.

1.12 “**Latent Defect**” means any Defect that is discovered by Novartis before the Product expires, which is not an Apparent Defect.

1.13 “**Material**” means any starting materials or components, raw materials, ingredients and other materials used in the Manufacture, filling, finishing or packaging of the Drug Substance, the Drug Product or the Diluent Product, as applicable.

1.14 “**Product**” means (a) the Resulting Vials of Drug Product, (b) the Batch of Diluent Product, and/or (c) subject to Section 2.1(c) the Batch of Drug Substance, as applicable.

1.15 “**Purchase Order**” means a written purchase order in the form mutually agreed by the Parties that sets forth an order for the applicable Product and quantity thereof to be Manufactured by or on behalf of Spark for Novartis; the delivery schedule therefore; and the shipment destination.

1.16 “**Purchase Price**” means the Drug Product Purchase Price, the Drug Substance Purchase Price or the Diluent Product Purchase Price, as applicable.

1.17 “**Residual Shelf Life**” means a remaining shelf life of:

(a) in respect of Drug Products, the longer of (i) [**], or (ii) the shelf life specified in the EU Regulatory Approval minus [**];

(b) in respect of Batches of Drug Substance, the longer of (i) [**], or (ii) the shelf life specified in the EU Regulatory Approval minus [**]; or
in respect of Diluent Products, the longer of (i) [**]% of the shelf life specified in the EU Regulatory Approval, or (ii) the shelf life specified in the EU Regulatory Approval minus [**].

1.18 “Resulting Vials of Drug Product” means the vials of Drug Product that are filled by the Fill and Finish Subcontractor out of the same single Batch of Drug Substance Manufactured by Spark, which shall be comprised of a minimum of [**] vials of Drug Product.

1.19 “Spark Facility” means Suite 1 of Spark’s Manufacturing facility for the Drug Substance located at 3737 Market Street, Suite 1300, Philadelphia PA 19104, Philadelphia, PA, or such other Manufacturing location as Novartis may consent to pursuant to Section 5.5(a).

1.20 “Specifications” means the Drug Substance Specifications, Drug Product Specifications or the Diluent Product Specifications, as applicable.

1.21 “Supply Failure” means Spark’s failure to deliver to Novartis within [**] of the delivery date set forth in the applicable Purchase Order, the Resulting Vials of Drug Product or Batch of Drug Substance (as the case may be) that meets the Product Warranty.

1.22 “Supply Transition Event” means:

(a) a Supply Failure occurs [**] or more times within any [**] period;

(b) Spark fails to deliver to Novartis the Resulting Vials of Drug Product or Batch of Drug Substance that meet the Product Warranty within [**] of the delivery date set forth in the applicable Purchase Order due to the occurrence of a Force Majeure Event which only affects Spark and not Novartis or any of its Affiliates;

(c) Novartis terminates this Agreement pursuant to Section 14.2 for any reason other than (i) a Supply Failure, or (ii) a material breach relating to supply of Diluent Product;

(d) Spark is subject to an Insolvency Event;

(e) if the JSC does not approve a corrective action plan issued by Spark pursuant to Section 2.5 or if Spark fails to comply with the terms of an approved corrective action plan, and Spark thereafter fails to meet the Minimum Yearly Capacity (i) in the [**] in which Novartis does not approve a corrective action plan or the start date of an approved corrective action plan occurs and (ii) by the [**] of the date on which the JSC approved or rejected the corrective action plan issued by Spark pursuant to Section 2.5; or

(a) if, after the expiration of the Base Royalty Term (as defined in the License Agreement and without regard to the extension of Regulatory Exclusivity within an individual country in such Royalty Region), the aggregate Net Sales in [**] fall below [**] Dollars ($[**]) per Calendar Year.

1.23 “Technology Transfer Plan” means one or more written plans setting out the responsibilities of each of the Parties with respect to the provision by Spark of the information,
materials and services described in Section 9.2. The Technology Transfer Plan shall also include the requirements for the successful completion of technology transfer.

As used in this Agreement, the following terms shall have the meanings ascribed thereto in the respective Sections of this Agreement set forth opposite each such term below. In addition, capitalized terms used but not defined herein shall have the meanings set forth in the License Agreement. In the event of a conflict between a term defined herein and the same term as defined in the License Agreement, the definition ascribed to such term in this Agreement will control.

<table>
<thead>
<tr>
<th>TERM</th>
<th>SECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974 Convention</td>
<td>Section 15.2</td>
</tr>
<tr>
<td>Accounting Standards</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Actual Costs</td>
<td>Section 4.1(e)</td>
</tr>
<tr>
<td>Affiliate</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Agreement</td>
<td>Preamble</td>
</tr>
<tr>
<td>Auditor</td>
<td>Section 4.3(a)</td>
</tr>
<tr>
<td>Base Royalty Term</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Breaching Party</td>
<td>Section 14.2</td>
</tr>
<tr>
<td>Business Day</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Calendar Year</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Capacity Plan</td>
<td>Section 2.4</td>
</tr>
<tr>
<td>CDA</td>
<td>Section 15.6</td>
</tr>
<tr>
<td>Confidential Information</td>
<td>License Agreement</td>
</tr>
<tr>
<td>covering</td>
<td>Section 4.4</td>
</tr>
<tr>
<td>Deficiency Notice</td>
<td>Section 3.8</td>
</tr>
<tr>
<td>Diluent Product Purchase Price</td>
<td>Section 4.1(c)</td>
</tr>
<tr>
<td>Discretionary Change</td>
<td>Section 5.4(b)</td>
</tr>
<tr>
<td>Drug Product Finishing Activities</td>
<td>Section 1.11</td>
</tr>
<tr>
<td>Drug Product Purchase Price</td>
<td>Section 4.1(a)</td>
</tr>
<tr>
<td>Drug Substance Purchase Price</td>
<td>Section 4.1(b)</td>
</tr>
<tr>
<td>Effective Date</td>
<td>Preamble</td>
</tr>
<tr>
<td>EMA</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Escrow Agent</td>
<td>Section 9.1</td>
</tr>
<tr>
<td>Estimated Costs</td>
<td>Section 4.1(d)</td>
</tr>
<tr>
<td>EU Regulatory Approval</td>
<td>License Agreement</td>
</tr>
<tr>
<td>FDA</td>
<td>Section 3.2(b)(i)</td>
</tr>
<tr>
<td>Firm Forecast</td>
<td>Section 3.1</td>
</tr>
<tr>
<td>Force Majeure Event</td>
<td>Section 15.10</td>
</tr>
<tr>
<td>Forecast</td>
<td>Section 3.1</td>
</tr>
<tr>
<td>Governmental Authority</td>
<td>License Agreement</td>
</tr>
<tr>
<td>HSE</td>
<td>Section 8</td>
</tr>
<tr>
<td>HSE Requirements</td>
<td>Section 8.1</td>
</tr>
<tr>
<td>Indemnified Party</td>
<td>Section 13.3</td>
</tr>
<tr>
<td>TERM</td>
<td>SECTION</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Indemnifying Party</td>
<td>Section 13.3</td>
</tr>
<tr>
<td>Initial Fixed Facility Fee Period</td>
<td>Section 1.24</td>
</tr>
<tr>
<td>Initial Period</td>
<td>Section 3.2(b)(i)</td>
</tr>
<tr>
<td>Insolvency Event</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Intellectual Property</td>
<td>License Agreement</td>
</tr>
<tr>
<td>JSC</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Law</td>
<td>License Agreement</td>
</tr>
<tr>
<td>License Agreement</td>
<td>Recitals</td>
</tr>
<tr>
<td>Losses</td>
<td>Section 13.1</td>
</tr>
<tr>
<td>Luxturna</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Manufacture</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Manufacturer Personnel</td>
<td>Section 12.3</td>
</tr>
<tr>
<td>Maximum Yearly Capacity</td>
<td>Section 3.2(b)(ii)</td>
</tr>
<tr>
<td>Minimum Yearly Capacity</td>
<td>Section 3.2(a)</td>
</tr>
<tr>
<td>Minimum Yield</td>
<td>Section 2.5</td>
</tr>
<tr>
<td>Non-Breaching Party</td>
<td>Section 14.2</td>
</tr>
<tr>
<td>Non-Conforming Product</td>
<td>Section 3.8</td>
</tr>
<tr>
<td>Notified Law</td>
<td>Section 5.1(b)</td>
</tr>
<tr>
<td>[**]</td>
<td>Section 1.21</td>
</tr>
<tr>
<td>Novartis</td>
<td>Preamble</td>
</tr>
<tr>
<td>Novartis Indemnitees</td>
<td>Section 13.2</td>
</tr>
<tr>
<td>Novartis Territory</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Party, Parties</td>
<td>Preamble</td>
</tr>
<tr>
<td>Person</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Pharmacovigilance Agreement</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Product Warranty</td>
<td>Section 3.7</td>
</tr>
<tr>
<td>Quality Agreement</td>
<td>Section 5.6</td>
</tr>
<tr>
<td>Regulatory Approval</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Regulatory Authority</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Regulatory Exclusivity</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Related Agreement</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Required Change</td>
<td>Section 5.4(a)</td>
</tr>
<tr>
<td>Response Notice</td>
<td>Section 3.9(a)</td>
</tr>
<tr>
<td>Royalty Regions</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Severed Clause</td>
<td>Section 15.5</td>
</tr>
<tr>
<td>Spark</td>
<td>Preamble</td>
</tr>
<tr>
<td>Spark Indemnitees</td>
<td>Section 13.1</td>
</tr>
<tr>
<td>Spark Territory</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Sublicensee</td>
<td>License Agreement</td>
</tr>
<tr>
<td>Taxes</td>
<td>Section 4.4</td>
</tr>
<tr>
<td>Taxing Jurisdiction</td>
<td>Section 4.4</td>
</tr>
<tr>
<td>Term</td>
<td>Section 14.1</td>
</tr>
</tbody>
</table>
2. MANUFACTURE AND SUPPLY

2.1 Supply.

(a) Subject to the terms and conditions of this Agreement, during the Term, Spark shall Manufacture and supply the Products exclusively (except for Spark’s and its Affiliates’, licensees’ and collaborators’ requirements in the Spark Territory) to Novartis and its Affiliates and their respective Sublicensees and distributors, and Novartis agrees to purchase from Spark, all of the requirements of Novartis and its Affiliates and their respective Sublicensees and distributors for the Products in the Novartis Territory.

(b) Notwithstanding anything to the contrary set forth herein, and subject to Section 2.1(c), the Parties acknowledge and agree that unless otherwise agreed Novartis shall forecast and order its and its Affiliates’ and their respective Sublicensees’ and distributors’ requirements for Drug Product and Diluent Product in terms of number of vials, and that Novartis shall pay for Drug Product and Diluent Product on a per vial basis, provided that in any given Purchase Order, Novartis shall not order more than [**] vials of Drug Product. The Parties acknowledge that the actual number of vials of Drug Product may vary among Batches of Drug Substance. Except for Supply Failures, any variance between the Drug Products ordered by Novartis and the Resulting Vials of Drug Product delivered to Novartis in compliance with the Product Warranty shall be subject to the yield mechanism in Section 2.5, and it shall not be a breach of this Agreement if the Resulting Vials of Drug Product is less than the number of vials ordered by Novartis.

(c) At any point during the Term Novartis may, in its discretion, notify Spark in writing that it shall forecast and order Batches of Drug Substance, and that Spark shall deliver to Novartis Batches of Drug Substance instead of Drug Product. Novartis shall pay for Batches of Drug Substance on a per batch basis instead of on a per vial basis. Any such notice shall be given at least [**] prior to the first required delivery date of any Batches of Drug Substance. Following such notice, the Parties will mutually agree on the applicable lead time for delivery, the appropriate delivery Incoterm, and the process for moving from placing Purchase Orders for Drug Products to placing Purchase Orders for Batches of Drug Substance and how to handle any open Purchase Orders for Drug Products. If it elects to order Batches of Drug Substance instead of Drug Product, Novartis may also, in its discretion, notify Spark in writing that it no longer wishes to purchase Diluent Product directly from Spark and/or that it no longer wishes the Fill and Finish Subcontractor to fill and finish the Drug Product, and Spark shall:

(i) provide (or procure the provision of) to Novartis or its designated Affiliate or Third Party manufacturer:
all technical documentation (including master Batch Records), specifications, procedures and
know-how in its possession or control that are reasonably required for the filling, finishing and release testing of Drug
Products or Diluent Products (as the case may be); and

(B) samples of materials relating to the Manufacture of Drug Products or Diluent Products (as the
case may be), including process descriptions, master Batch Records and other related materials,
in all cases, to the extent controlled by Spark at the date of the notice and to the extent necessary or reasonably useful
for the Manufacture of Drug Products or Diluent Products (as the case may be); and

(ii) make reasonably available to Novartis, relevant scientific and technical personnel to answer questions,
provide on-site support at one fill and finish facility, and to train personnel from such facilities, and/or provide instruction
relating to Manufacture of Drug Products or Diluent Products (as the case may be) during one site visit to each facility for a
period of no more than [**] each; and

(iii) cooperate with Novartis to transition any relevant analytical test methods for the Drug Product and/or
Diluent Product to Novartis or its Third Party manufacturer, which cooperation shall be limited to one visit per analytical
testing site for a period of no more than [**] each; and

(iv) [**].

(d) Notwithstanding anything to the contrary set forth in this Agreement or in the License Agreement, Novartis and
its Sublicensees and their respective distributors shall purchase Products only for purposes permitted under the License Agreement.
In addition, all Diluent Product purchased by Novartis shall be used only for purposes of administration of the Drug Substance to end
users in accordance with the relevant Regulatory Approval.

(e) By [**] (or such other date as the Parties may agree in writing), Novartis will determine in its sole discretion
whether the vials of Diluent Product and Drug Product shall be delivered labeled with a single universal label as specified by
Novartis or as naked vials for the Novartis Territory and provide written notice of its decision to Spark. Spark shall not be obligated
to supply any Diluent Product or Drug Product with a single universal label until Novartis has supplied to Spark a PDF file of the
applicable single universal label by such date as the Parties may mutually agree in writing following Novartis’ provision of written
notice of its decision to Spark.

2.2 Materials.

(a) Spark shall be responsible for procuring, paying for and ensuring timely delivery of all Materials necessary to
meet Spark’s supply obligations under this Agreement. Spark will promptly notify Novartis in writing of any difficulty in obtaining
any of the Materials that may result in a delay in delivery of Products to Novartis.
(b) Unless otherwise agreed in writing with Novartis, Spark shall only order sufficient quantities of Materials reasonably required to meet the volumes set out in each Firm Forecast. All purchases of Materials by Spark for the purpose of this Agreement shall be made on Spark’s own behalf and not as an agent for Novartis. Spark shall: (i) be responsible for the sampling, testing, analysis, release and approval of each delivery of Materials, in accordance with the Quality Agreement and otherwise, prior to their use in Manufacture; (ii) only use Materials in the Manufacture of the Products by Spark which comply with the requirements of the Quality Agreement, any relevant specifications (including the Specifications), cGMP and which are suitable for their intended purpose; and (iii) store and warehouse all Materials in premises that are cGMP.

(c) Spark shall ensure that all Materials are manufactured as required under this Agreement (including the Quality Agreement and the HSE Requirements as set forth in Section 8). Spark shall and shall cause its Approved Subcontractors, at its cost (subject to Section 4.1(d), to be passed through to Novartis under Sections 1.9, 1.10 or 1.11, as applicable), to purchase, qualify, test, inspect and approve all such Materials required in its Manufacturing, storage, shipping or receiving of the Products. In relation to its Approved Subcontractors Spark shall:

(i) provide Novartis with copies of written supply agreements with any and all Approved Subcontractors, subject to any and all confidentiality agreements as may be in place with such Approved Subcontractors and subject to redactions of any provisions in such supply agreements that do not relate to the Products;

(ii) proactively manage its Approved Subcontractors, including by regularly auditing and evaluating such Approved Subcontractors and by having effective performance management and supplier relationship management regimes; and

(ii) ensure that critical Materials are only supplied from Approved Subcontractors, as may be further detailed in the Quality Agreement.

2.3 Subcontractors. Spark shall [*] Novartis’ prior written consent to appoint subcontractors to perform its obligations under this Agreement [*] where the appointment of such a subcontractor would need to be specified in the Regulatory Approvals. Spark shall ensure that all subcontractors shall comply with the applicable terms and conditions of this Agreement. Any changes to the Approved Subcontractors, or to the premises from which those Approved Subcontractors will perform any subcontracted obligations, shall require Novartis’ prior written consent (such consent not to be unreasonably withheld) and shall be conducted in accordance with the change control procedure set out in the Quality Agreement, provided that the outgoing Approved Subcontractor will continue to perform Spark’s obligations under this Agreement until Novartis has made all necessary variations to the Regulatory Approvals in order to reflect the appointment of the new Approved Subcontractor or the performance of the subcontracted obligations at new premises. Spark shall remain responsible for the performance of all of its obligations under this Agreement notwithstanding its appointment of any subcontractor.

2.4 Capacity
(a) Within [**] after the Effective Date, the Parties shall negotiate in good faith a written plan regarding the securing and increase of Spark’s capacity to Manufacture Drug Products (the “Capacity Plan”), which Capacity Plan will address [**], and (v) such other topics as the Parties may agree. Once agreed, Spark shall perform the Capacity Plan and use commercially reasonable efforts to achieve the objectives of the Capacity Plan, but the Parties agree that Spark does not provide any guarantees that the objectives of the Capacity Plan will be achieved. The Parties shall review and update the Capacity Plan regularly and it shall be a standing topic at the JSC. All incremental costs incurred by each of the Parties to implement the Capacity Plan (to the extent not included in the Drug Product Purchase Price or the Drug Substance Purchase Price) shall be [**]. If the Parties mutually agree that the objectives of the Capacity Plan cannot be achieved or have not been achieved after the implementation of the Capacity Plan, Novartis shall have the right to request that Spark establish a secondary source supplier(s) for the Drug Substance (which exercise is not deemed to be a Supply Transition Event hereunder), and if it exercises such right:

(i) such secondary source supplier shall be deemed to be an “Approved Subcontractor” of Spark under this Agreement under the sole control of Spark, and Spark shall obtain Novartis’ prior written consent prior to appointing such secondary source as an “Approved Subcontractor” in accordance with Section 2.3;

(ii) Spark shall provide (or procure the provision) to such secondary source supplier:

(A) all technical documentation (including master Batch Records), specifications, procedures, relevant analytical test methods and know-how in its possession or control that are reasonably required for the Manufacture of Drug Substance (as the case may be); and

(B) samples of materials relating to the Manufacture of Drug Substance (as the case may be), including process descriptions, master Batch Records and other materials,

in all cases, to the extent controlled by Spark at the date of the notice and to the extent necessary or reasonably useful for the Manufacture of Drug Substance; and

(iii) make reasonably available to its secondary source supplier, relevant scientific and technical personnel to answer questions, provide on-site support at one Drug Substance manufacturing facility, and to train personnel from such facilities, and/or provide instruction relating to Manufacture of Drug Substance,

provided that the costs of compliance with paragraphs (ii) and (iii) shall be [**], and any pass through costs of such secondary source supplier shall be discussed at the JSC.

(b) Spark shall offer Novartis any first rights to any additional or unused capacity that becomes available at the Spark Facility during the Term.
2.5 Yield. Spark will (a) use commercially reasonable efforts to maximize the Resulting Vials of Drug Product from each Batch of Drug Substance and (b) shall always exceed a minimum of [**] Resulting Vials of Drug Product per Batch of Drug Substance (“Minimum Yield”), except that the Minimum Yield may be less for any Batches of Drug Substance above the Minimum Yearly Capacity. The Parties will review the numbers of Resulting Vials of Drug Product from each Batch of Drug Substance in the previous Calendar Year and it shall be a standing topic at the JSC. If in that Calendar Year the numbers of Resulting Vials of Drug Product fell below the Minimum Yield, Spark shall prepare and submit to the JSC for approval a corrective action plan addressing the issue, such approval not to be unreasonably withheld or delayed.

3. FORECASTS, ORDER AND DELIVERY

3.1 Rolling Forecasts. Commencing on the First Rolling Forecast Date, on or before [**] thereafter during the Term, Novartis shall provide Spark with a rolling [**] forecast of its and its Affiliates and their respective Sublicensees’ and distributors’ requirements for Products in the Novartis Territory for such period (or the period until the expiration of the Term, if shorter) (each, a “Forecast”). The first [**] of each Forecast shall be binding on both Parties (a “Firm Forecast”). Except with respect to the Purchase Orders accepted by Spark and the Firm Forecasts, a Forecast shall not be binding on either Party. For the avoidance of doubt, all Forecasts placed by Novartis shall be consistent with the applicable Maximum Yearly Capacity set forth in Section 3.2(b) below. Without limiting the foregoing, the initial Forecast shall include at least one Batch of Drug Substance to be Manufactured by Spark during [**], and if Novartis provides Spark with a Purchase Order for vials of Drug Product in accordance with Section 3.3 on or before [**], Spark shall deliver the corresponding Resulting Vials of Drug Product from Spark’s Manufacture of a Batch of Drug Substance for such Purchase Order on or before [**].

3.2 Yearly Capacity.

(a) Minimum Yearly Capacity. Commencing on [**], and for each Calendar Year thereafter during the Term, Spark shall reserve capacity for Novartis in the Spark Facility and ensure that sufficient resources are available to support Manufacture for Novartis of a minimum number of [**] Batches of Drug Substance per Calendar Year or the corresponding Resulting Vials of Drug Product (i.e., [**] vials of Drug Product) if ordered by Novartis (the “Minimum Yearly Capacity”).

(b) Maximum Yearly Capacity.

(i) Notwithstanding anything to the contrary set forth herein, during the period commencing with the first full quarter to occur after the Effective Date and continuing until [**] (the “Initial Period”), Novartis may place a Purchase Order for [**] vials of Drug Product and (at its option) [**] vials of Diluent Product for each quarter during the Initial Period. If Novartis fails to place a Purchase Order for a calendar quarter during the Initial Period or places a Purchase Order for less than [**] vials of Drug Product and/or [**] vials of Diluent Product during the Initial Period, the quantity not ordered by Novartis may be added to the quantity of vials of Drug Product and Diluent Product that Novartis may order during the next quarter to occur. Thereafter, any quantity of vials of Drug Product and
Diluent Product available to order by Novartis for a quarter which Novartis does not order shall be added to the quantity of vials of Drug Product and Diluent Product that Novartis may order for the next quarter. Such vials of Drug Product and Diluent Product will be supplied by Spark out of its existing inventory of finished Drug Product maintained by Spark and labeled in accordance with U.S. Food and Drug Administration (“FDA”) requirements for distribution in the United States at the cost of US$[**] per vial of Drug Product and at a price per vial of Diluent Product to be agreed by the Parties in good faith prior to the first Purchase Order. For the avoidance of doubt Novartis is under no obligation to purchase any of the vials of Drug Product and Diluent Product made available pursuant to this Section 3.2(b)(i) and where it does purchase any such vials, the amount specified in (or agreed pursuant to) the previous sentence shall constitute the full price of the Products and no other amounts (including the Fixed Facility Fee) shall be payable in respect of such Products.

(ii) Subject to Section 3.2(b)(i), commencing during the period [**] to [**], and for each Calendar Year thereafter during the Term, a maximum of [**] Batches of Drug Substance can be Manufactured by Spark for Novartis, except that in any given Calendar Year during the Term the Parties may agree in writing to allocate additional Batches of Drug Substance to Novartis up to a maximum of [**] Batches of Drug Substance (“Maximum Yearly Capacity”). The Maximum Yearly Capacity shall be increased in the event that the capacity at the Spark Facility is increased pursuant to the Capacity Plan.

3.3 Purchase Orders.

(a) **Drug Product**. During the Term, Novartis shall place each Purchase Order for vials of Drug Product in accordance with its current Forecast at least [**] prior to the required delivery date specified in such Purchase Order. Subject to Section 3.4(a), the vials of Drug Products ordered by Novartis as set forth in each Purchase Order will be firm and binding on both Parties. For the avoidance of doubt, all Purchase Orders placed by Novartis for vials of Drug Products shall be consistent with the Maximum Yearly Capacity.

(b) **Batch of Drug Substance**. Where Novartis has issued a notice to Spark pursuant to Section 2.1(c), Novartis shall place each Purchase Order for a Batch of Drug Substance in accordance with its current Forecast and the lead time agreed by the Parties. Subject to Section 3.4(a), the Batches of Drug Substance ordered by Novartis as set forth in each Purchase Order will be firm and binding on both Parties. For the avoidance of doubt, all Purchase Orders placed by Novartis for Batches of Drug Substance shall be consistent with the Maximum Yearly Capacity.

(c) **Diluent Product**. During the Term, Novartis shall place each Purchase Order for the Diluent Product in accordance with its current Forecast at least [**] prior to the required delivery date specified in such Purchase Order. All Purchase Orders placed for the Diluent Product shall be specified in Batches of Diluent Product (i.e., one (1) Batch of Diluent Product or multiples thereof) and shall specifically identify the quantity of the Diluent Product required, such that that no amounts less than one (1) Batch of Diluent Product may be ordered and amounts falling between batch increments shall be rounded up to the next batch increment (e.g., a quantity of [**] vials of the Diluent Product required shall be rounded up so that the order placed will be for [**] Batches
of Diluent Product). Subject to Section 3.4(a), the quantity of Diluent Product ordered by Novartis as set forth in each Purchase Order will be firm and binding on both Parties.

(d) Acceptance. Spark shall accept all Purchase Orders that meet the terms and conditions of this Agreement and that are consistent with the current Forecast by sending an acknowledgment to Novartis within [**] after its receipt of the Purchase Order confirming that Spark is able to deliver the requested quantities by the requested delivery date or agree with Novartis on alternative quantities and/or an alternative delivery date. If Spark fails to acknowledge receipt of such Purchase Order within such [**] period, the Purchase Order shall be deemed to be accepted by Spark. Upon receipt by Novartis of acknowledgement or deemed acceptance, each Purchase Order will be regarded by the Parties as a firm and binding [**] commitment by Novartis and/or its Affiliates to purchase from Spark, and for Spark to Manufacture and supply to Novartis and its Affiliates, the relevant quantity of Product according to the requirements set out in such Purchase Order. Notwithstanding anything to the contrary, Spark shall be obligated to confirm and deliver any Purchase Order which does not exceed the Firm Forecast.

(e) Supremacy. Other than the terms for quantities of the applicable Product ordered, delivery schedule and shipment destination set forth in a Purchase Order, the terms and conditions contained in or accompanying (whether in writing, electronic or in any other form) any Purchase Order submitted by Novartis shall have no force and effect and shall not be binding on Spark. In the event of any conflict between the terms and conditions set forth in or accompanying any Purchase Order, or any written acceptance or confirmation thereof, and the terms and conditions of this Agreement, the terms and conditions of this Agreement shall govern.

3.4 Changes to Purchase Orders.

(a) Spark shall reasonably consider and cooperate to accommodate any changes in delivery location or delivery phasing requested by Novartis in respect of Purchase Orders already placed by Novartis, provided that (i) all costs incurred by Spark to satisfy such Novartis request shall be borne by Novartis and (ii) Spark shall not be obligated to incur losses or expend resources to Spark’s detriment. All modifications to the delivery schedule (including any impact on the Residual Shelf Life) for the applicable Product set forth in the Purchase Order after acceptance by Spark shall be made in writing upon the mutual written agreement of Spark and Novartis.

(b) Notwithstanding anything to the contrary set forth herein, if Novartis cancels a Purchase Order that is accepted by Spark in accordance with Section 3.3(d) in whole or in part, Spark shall reasonably consider whether it is possible to re-allocate the Manufacturing slot (provided that the ultimate decision on re-allocation shall be at Spark’s discretion) for any such cancelled or postponed Purchase Orders for use by Spark and shall use reasonable efforts to mitigate its losses, and Novartis shall pay Spark for any losses that cannot be mitigated after having exercised such efforts. Spark shall not be obligated to incur costs or losses or expend resources to Spark’s detriment in order to re-allocate any Manufacturing slot.

3.5 Delivery.
(a) Spark shall deliver the Products set forth in a Purchase Order in accordance with the delivery schedule specified therein and shall invoice Novartis for the Purchase Price at the time of delivery.

(b) All Drug Product and Diluent Product shall be delivered to Novartis [**] (as defined in Incoterms 2010) [**] as defined in Section 1.21, or such Incoterm as the Parties may agree in the event a new Fill and Finish Subcontractor is appointed.

(c) All Batches of Drug Substance shall be delivered to Novartis or its designee in accordance with such Incoterm as the Parties may agree for deliveries of Batches of Drug Substance pursuant to Section 2.1(c).

(d) All deliveries of Drug Product or Diluent Product during the Initial Period shall be delivered to Novartis pursuant to Section 3.2(b)(i) on such Incoterm as the Parties may agree in writing.

(e) [**] will bear the risk of loss or damage to such Product in transit. Title to the applicable Product shall transfer to Novartis [**] of such Product in accordance with the above delivery terms.

(f) Novartis may reject any delivery of Resulting Vials of Drug Product for EU markets if at the time of delivery EU Regulatory Approval has been refused or delayed.

3.6 **Novartis Responsibility for Finished Product.** All finished packaging and labeling of the Drug Product and the Diluent Product for distribution to and use by consumers in the Novartis Territory shall be the sole responsibility of Novartis at Novartis’ sole cost and expense (excluding the single universal label to be applied to the Products, if any, which shall be the sole responsibility and cost of Spark).

3.7 **Product Warranty.** Spark hereby warrants that, at the time and place of delivery pursuant to Section 3.5, that each Product (the “**Product Warranty**”):

(a) has been Manufactured, prepared, handled and/or shipped in compliance with applicable cGMP, the Quality Agreement, applicable master Batch Records and/or any other procedures or documents agreed upon by the Parties in writing;

(b) conforms to the applicable Specifications and any other Product-related warranties and representations set out in this Agreement;

(c) has at least the Residual Shelf Life;

(d) is not adulterated within the meaning of the U.S. Food, Drug and Cosmetic Act or similar provisions under cGMP; and

(e) shall be transferred to Novartis free and clear of any security interests, liens or encumbrances.
3.8 **Inspection and Acceptance**. Promptly following delivery of an ordered Product, Novartis shall: (a) conduct a visual inspection of the delivered Product, and (b) conduct an inspection of the accompanying Certificate of Analysis to identify any Product that has an Apparent Defect. Novartis may reject any Product on a batch-by-batch basis in the event that such Product is Defective (a “Non-Conforming Product”) by providing written notice to Spark (a “Deficiency Notice”) within (i) [**] after the date of the delivery of the applicable Product, in the case of Apparent Defects, or (ii) within [**] following discovery of the Defect, in the case of Latent Defects. If Novartis does not reject such Product within the applicable [**] period by providing a Deficiency Notice to Spark, it shall be deemed to have accepted such Product.

3.9 **Replacement**.

(a) Upon receipt of a Deficiency Notice, Spark will have [**] to advise Novartis in writing that it disagrees in good faith with the contents of such Deficiency Notice (the “Response Notice”). If Spark does not respond within such [**] period, the Deficiency Notice will be deemed accepted by Spark. If the Parties fail to agree within [**] after Novartis’ receipt of a Response Notice from Spark, then the Parties will promptly select a mutually acceptable, independent, third party expert with expertise in the field of gene therapy manufacturing to evaluate the batch review and release records relating to the Product that is the subject of the Deficiency Notice and determine whether such Product is Non-Conforming Product. If Novartis has not yet paid the Purchase Price for the Product that is the subject of such Deficiency Notice, Novartis’ payment obligations with respect to such Product shall be stayed until the third-party expert determines that such Product is conforming Product.

(b) If a Deficiency Notice is accepted or deemed accepted by Spark, or the independent third party expert referred to in Section 3.9(a) determines that a Product is deemed to be a Non-Conforming Product:

(i) Spark shall promptly (x) (and in no event any later than within [**]) replace any Non-Conforming Product with conforming Product at no additional cost to Novartis, with such conforming Product to be invoiced on delivery in accordance with Section 3.5(a); (y) issue a credit note in respect of any unpaid invoices issued by Spark to Novartis under this Agreement in respect of such Non-Conforming Product; or (z) refund the Purchase Price paid for such Non-Conforming Product by Novartis; and

(ii) Spark shall bear any costs, expenses, fees associated with the transportation, testing and disposal (as applicable) of any Non-Conforming Product (including without limitation Novartis’ internal costs of conducting associated quality investigations) and the costs of shipping the replacement of the Non-Conforming Product to Novartis.

Further, and without prejudice to Novartis’ other rights hereunder and/or governing Law, Spark shall promptly instruct Novartis to either send back to Spark or dispose of any Non-Conforming Products, at Spark’s discretion. Any remedial action taken by Spark shall comply with the Quality Agreement. Spark shall not rework any rejected Non-Conforming Products, unless expressly authorized in writing to do so by Novartis. Any replacement Batches of Drug
Substance or corresponding Resulting Vials of Drug Product delivered in a Calendar Year subsequent to the Calendar Year of the original delivery date shall not count towards the Minimum Yearly Capacity or the Maximum Yearly Capacity in that subsequent Calendar Year and shall instead count towards the Minimum Yearly Capacity and the Maximum Yearly Capacity in the Calendar Year of the original delivery date. Any replacement Batches of Drug Substance or corresponding Resulting Vials of Drug Product that are delivered in the same Calendar Year shall count towards the Minimum Yearly Capacity and the Maximum Yearly Capacity for that Calendar Year.

3.10 If a Product is not deemed to be a Non-Conforming Product by the third-party expert, then Novartis will be deemed to have accepted delivery of such Product.

3.11 **Exclusion of Other Warranties**. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, SPARK DOES NOT MAKE ANY WARRANTY IN RESPECT OF THE PRODUCT, WHETHER EXPRESS OR IMPLIED BY STATUTE, CUSTOM OF THE TRADE OR OTHERWISE, INCLUDING ANY WARRANTY RELATING TO THE DESCRIPTION OR QUALITY OF ANY BATCH OF DRUG SUBSTANCE OR ANY PRODUCT, ITS MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR USE UNDER ANY CONDITIONS, AND ANY SUCH WARRANTY IS HEREBY EXPRESSLY EXCLUDED.

4. **PAYMENT**

4.1 **Purchase Price**.

(a) The total purchase price for the Resulting Vials of Drug Product from a Batch of Drug Substance shall be equal to the sum of (a) the Cost of Drug Product plus [**] percent ([**]%) of the Cost of Drug Product and (b) the Fixed Facility Fee (a) and (b) together, the "**Drug Product Purchase Price**"). The cost per vial of Resulting Vials of Drug Product from any Batch of Drug Substance shall be calculated by dividing the Drug Product Purchase Price by the number of Resulting Vials of Drug Product delivered in respect of that Batch of Drug Substance.

(b) The total purchase price for a Batch of Drug Substance shall be equal to the sum of (a) the Cost of Drug Substance plus [**] percent ([**]%) of the Cost of Drug Substance, and (b) the Fixed Facility Fee ((a) and (b) together, the "**Drug Substance Purchase Price**").

(c) The total purchase price for a Batch of Diluent Product shall be the Cost of Diluent Product plus [**] percent ([**]%) of the Cost of Diluent Product (the “**Diluent Product Purchase Price**”). The cost per vial of Diluent Product delivered to Novartis is the Diluent Product Purchase Price divided by the number of Diluent Vials delivered.

(d) Prior to [**] of each Calendar Year, Spark shall provide to Novartis in writing a good faith estimate of (i) the Drug Product Purchase Price; (ii) the Drug Substance Purchase Price (if applicable); (iii) the Diluent Product Purchase Price; (iv) the planned number of vials of Resulting Vials of Drug Product; (v) the planned number of vials of Diluent Product; (vi) the cost per vial of the Resulting Vials of Drug Product; and (vii) the cost per vial of Diluent Product, for the following Calendar Year (the “**Estimated Costs**”). The Estimated Costs shall be used to invoice Novartis during the following Calendar Year. The Parties shall mutually agree to the timing for the provision
of any Estimated Costs for the Purchase Orders to be placed pursuant to the final sentence of Section 3.1.

(e) **Actual Costs** are the actual Cost of Drug Product, the actual Cost of Diluent Product and the actual cost of Drug Substance in any Calendar Year. On or before [**] of each Calendar Year, Spark shall send Novartis a preliminary report of the Actual Costs in a format to be agreed by the Parties through discussion at the JSC, which shall be a standing topic at the JSC. In addition to the Estimated Costs, the Actual Costs report will include the Maximum Yearly Capacity for the Calendar Year in which Manufacturing of Drug Substance (or the Batches of Drug Substance used to Manufacture the Resulting Vials of Drug Product) occurred. The report shall provide the Actual Costs for [**] through [**] of such Calendar Year together with a forecast of the Actual Costs for [**] and [**] of such Calendar Year. As soon as reasonably possible but no later than [**] of each Calendar Year, Spark shall send a report in a format to be agreed by the Parties through discussion at the JSC comparing the total amount of Actual Costs incurred in the immediately preceding Calendar Year and the total amount invoiced to Novartis in such immediately preceding Calendar Year based on the Estimated Cost. Such report shall be reviewed and approved by the JSC. Any payment required to compensate for the difference between the Actual Costs incurred and the Estimated Cost invoiced shall be made by the respective Party according to the payment terms set out in this Agreement.

(f) Spark shall use commercially reasonable efforts to minimize the Cost of Drug Product, Cost of Drug Substance and Cost of Diluent Product. If on receipt of Spark’s Estimated Costs, the estimated Cost of Drug Product, Cost of Drug Substance, the Cost of Diluent Product or the Fixed Facility Fee for the forthcoming Calendar Year has increased by more than [**] percent ([**]%) compared to the previous Calendar Year, Spark shall notify Novartis in writing and representatives of the Parties shall meet to review and discuss the same and whether there may be any ways to work together to mitigate the proposed increase.

(g) For the avoidance of doubt, any cost charged to Novartis under Actual Costs shall not be invoiced separately to Novartis under any other term of this Agreement, and shall only be charged once regardless of the Calendar Year the cost is incurred by Spark.

4.2 **Payment.**

(a) Novartis agrees to pay all undisputed invoices hereunder in U.S. Dollars within [**] after the invoice date.

(b) All payments shall be made to the account set forth below (or such other account as requested by Spark via written notice to Novartis):

Bank Routing and Transit Number: [**]
SWIFT Code: [**]
General Bank Reference Address: [**]
Spark Therapeutics, Inc. – Account Number: [**]

4.3 **Financial Audit.**
For a period of [**] following the close of each Calendar Year, Novartis will have the right, [**], to have an independent, internationally-recognized, certified public accounting firm (the “Auditor”), selected by Novartis and reasonably acceptable to Spark, upon the written request of Novartis, not more than [**] and not more frequently than [**] with respect to records covering any specific period of time, review such of the records of Spark, in the location(s) where such records are customarily maintained upon reasonable notice and during regular business hours, for the sole purpose of verifying the basis and accuracy of the Cost of Drug Substance, the Cost of Drug Product and the Cost of Diluent Product within the prior [**] period.

Before beginning its audit, the Auditor shall execute an undertaking reasonably acceptable to Spark by which the Auditor agrees to keep confidential all information reviewed during the audit. The Auditor shall have the right to disclose to the Parties only its conclusions regarding any payments owed under this Agreement. In addition, Novartis shall only be entitled to audit the books and records of Spark from the [**] in which the audit request is made. Novartis agrees to hold in confidence all information received and all information learned in the course of any audit or inspection, except to the extent necessary to enforce its rights under this Agreement or to the extent required to comply with any applicable Law.

The Auditor shall provide its audit report and basis for any determination to Spark at the time such report is provided to Novartis before it is considered final. If the review of such records reveals that the Spark has failed to accurately report information pursuant to this Agreement, then Spark shall promptly pay to Novartis any resulting amounts due under this Agreement together with interest calculated in the manner provided in Section 6.9 of the License Agreement. In the event amounts paid by Novartis in any Calendar Year exceeded the actual amount due under this Agreement, then Spark will pay the overpayment to Novartis and, if such overpayment was greater than [**] percent ([**]%)) of the applicable Cost of Drug Substance, Cost of Drug Product or Cost of Diluent Product then Spark shall pay the reasonable costs of Novartis performing such audit. In the event the amounts paid by Novartis in any Calendar Year are less than the actual amount due under this Agreement, then Novartis will pay the same to Spark in accordance with the payment terms in Section 4.2(a).

4.4 Taxes and Other Charges. All amounts invoiced by Spark to Novartis under this Agreement shall be [**] of any taxes, tariffs, or other charges that may be imposed on the Manufacture, sale, transportation, delivery, production, storage, export, or import of (collectively, for purposes of this Section 4.4, “covering”) the Product or that may otherwise apply to or arise in connection with the transactions contemplated by this Agreement, except for taxes imposed on Spark’s net income by a national, state or local taxing jurisdiction (each a “Taxing Jurisdiction”) in which Spark is resident or conducts business other than solely by reason of this Agreement (collectively and with that exception, “Taxes”). Novartis shall pay Taxes imposed under the authority of any Taxing Jurisdiction and shall not reduce any amounts owed to Spark hereunder on account of any such Taxes. Novartis shall timely furnish Spark with a valid tax exemption certificate issued by each Taxing Jurisdiction or entity where such certificate is required as a condition to the lawful avoidance of Taxes covering any Product to be sold under this Agreement, and shall otherwise cooperate with reasonable requests by Spark to lawfully reduce or avoid any such Taxes. In any case in which Spark has the legal obligation to pay or collect any Taxes, Spark shall submit an
invoice to Novartis for such Taxes (or, at Spark’s option, separately state the amount of such Taxes on the corresponding Product invoice), and Novartis shall pay such invoice (or such amount, together and simultaneously with the remaining balance shown on such Product invoice) as provided in Section 4.2.

5. QUALITY CONTROL

5.1 General.

(a) Spark shall Manufacture and supply Products in accordance with (a) the applicable Specifications; (b) the Quality Agreement; (c) cGMP; (d) applicable U.S. and EU Laws; and (e) subject to Section 5.1(b), any Notified Law.

(b) In the event that Novartis requests Spark to comply with an applicable Law in the Novartis Territory that is not required in the United States or the European Union or by cGMP, Novartis shall provide notice of such applicable Law to Spark (a “Notified Law”), together with all available information regarding such Notified Law, so that Spark may understand the nature, scope and requirements of such Notified Law. Novartis shall use reasonable efforts to consult with Spark and/or include Spark in such discussions, to fully consider Spark’s input regarding the steps necessary to achieve compliance with the requirements of such Notified Law and to identify means for addressing compliance with such Notified Law that are mutually agreeable to Spark and Novartis, and Spark shall participate in such discussions and provide such supporting documentation and information as Novartis may reasonably request. Novartis and Spark shall discuss and work together in good faith and Spark will use commercially reasonable efforts to come into compliance with such Notified Law as quickly as possible. The Parties shall share equally in the costs of complying with such Notified Law if such Notified Law is required in any of [...]. Novartis shall bear the costs of complying with such Notified Law is such Notified Law is required in any other jurisdiction in the Novartis Territory.

5.2 Certificate of Analysis. Spark shall provide Novartis with a Certificate of Analysis for each batch of Product released for shipment to Novartis hereunder. Such Certificate of Analysis shall include (without limitation) the Manufacturing location(s), the date(s) of Manufacture and the expiry date for the applicable Product. For the avoidance of doubt, Spark shall provide a Certificate of Analysis for both Drug Product and Drug Substance for Resulting Vials of Drug Product released for shipment to Novartis hereunder.

5.3 Quality Control. Spark shall perform such quality control tests for each Product as are required per its standard operating procedures and the applicable Specifications. Spark shall make the results of its quality control tests available to Novartis on or before the date of delivery of the corresponding Batch of Diluent Product or Resulting Vials of Drug Product, as applicable, delivered to Novartis. No Batch of Diluent Product or Resulting Vials of Drug Product shall be released for shipment by Spark unless Spark’s quality control tests confirm that such Batch of Diluent Product or Resulting Vials of Drug Product meets the standards set forth in the applicable Specifications. Should any Product fail to meet the standards set forth in the applicable Specification, Novartis may, at its option, investigate the cause of such failure or request that Spark do so and
provide Novartis with a written report summarizing the results of Spark’s investigation in accordance with the Quality Agreement.

5.4 **Product Specification Manufacturing and Facility Changes**.

(a) **Required Changes.** “**Required Change**” means any change required by a Governmental Authority.

(i) Subject to Spark’s obligations pursuant to Section 4.4.1(a) of the License Agreement, Novartis shall promptly notify Spark of any Required Change in the Novartis Territory that specifically relates to any Product, any Specifications or to the Manufacture of any of the Products by Spark, provided that, throughout any discussions between Novartis and such Governmental Authority relating to such Required Change, Novartis shall use reasonable efforts to consult with Spark and/or include Spark in such discussions, to fully consider Spark’s input regarding any such proposed requirement and to advocate to the applicable Governmental Authority means for addressing the issue underlying the proposed requirement that are mutually agreeable to Spark and Novartis. Spark shall use commercially reasonable efforts to implement such Required Change as promptly as possible within the timeframe requested by such Governmental Authority at Novartis’ sole cost and expense.

(ii) Spark shall use commercially reasonable efforts to implement any Required Change (whether in the Spark Territory or the Novartis Territory) that do not relate specifically to any Product, any Specifications or to the Manufacture of any of the Products, provided that:

(A) throughout any discussions between Spark and such Governmental Authority relating to such Required Change, Spark shall use reasonable efforts to consult with Novartis and/or include Novartis in such discussions to the extent the Required Change may impact the Products or their Manufacture, to fully consider Novartis’s input regarding any such proposed requirement and to advocate to the applicable Governmental Authority means for addressing the issue underlying the proposed requirement that are mutually agreeable to Spark and Novartis;

(B) if such Required Change results from a change in applicable Laws or cGMP in [**], Spark shall pay the costs and expenses of implementing such Required Change;

(C) if such Required Change results from a change in applicable Law or cGMP in [**], the Parties shall share the costs and expenses of implementing such Required Change equally; and

(D) if such Required Change results from a change in applicable Laws or cGMP outside [**], Novartis shall notify Spark of such Required Change and Spark shall provide Novartis with an estimate of the timeframe and cost required
to implement the change, and subject to Novartis’ prior written agreement Novartis shall pay the costs and expenses of implementing such Required Change.

(iii) Spark shall pay the costs and expenses of implementing any Required Change in the Spark Territory, provided that if a Governmental Authority in the Spark Territory requires a change that may reasonably impact the Specifications or the Manufacture of the Products, Spark shall promptly notify the JSC of such proposed change, Novartis shall provide Spark with an estimate of the timeframe and cost required for Novartis to implement the change in the Novartis Territory and the JSC shall agree to an implementation plan that will set forth the timeframe and costs and expenses for Novartis to implement such Required Change. If Spark determines in its discretion to implement such Required Change, it shall bear Novartis’ costs and expenses of implementing such Required Change, to the extent such costs and expenses are set forth in the implementation plan.

(b) **Discretionary Change**. Each Party shall be entitled to request a change to the Specifications or the Manufacture of the Products that is not a Required Change (a “**Discretionary Change**”). The requesting Party shall submit a written request to the other Party for any such Discretionary Change. If the Parties agree to make a Discretionary Change requested by Novartis, Spark shall then determine (i) one-time and/or ongoing costs that would be incurred resulting from such Discretionary Change, (ii) any resulting planned changes in timing for the delivery of the Products and (iii) the estimated time of implementing such Discretionary Change. Spark shall provide such information to Novartis and set forth the costs and other terms on which Spark would be willing to make the Discretionary Change. Upon written approval by the Parties to such terms, the Parties shall cooperate in good faith in implementing such Discretionary Change in accordance with the Quality Agreement. All costs and expenses incurred by Spark to implement Discretionary Changes:

(i) requested by Spark shall be at the sole cost and expense of Spark, and

(ii) requested by Novartis shall be at the sole cost and expense of Novartis, which Spark shall invoice Novartis for as incurred,

provided that where the Discretionary Change leads to cost savings or other benefits for both Parties, the Parties shall agree an appropriate allocation of costs in proportion to the benefit received.

5.5 **Manufacturing Facilities** .

(a) Spark shall Manufacture all Drug Substance at the Spark Facility. Spark shall not relocate the Manufacture of the Drug Substance without Novartis’ consent, such consent not to be unreasonably withheld or delayed.

(b) Spark agrees to operate and maintain the Spark Facility and all equipment used, directly or indirectly, to Manufacture the Products in accordance with cGMP and all applicable U.S. and EU Laws. Spark shall be responsible for validating the equipment (including without limitation conducting installation, operational and performance qualification), production, cleaning,
packaging, process and any other appropriate steps performed at the Spark Facility in accordance with its standard operating procedures. Spark shall ensure that any Approved Subcontractors comply with the requirements of this Section 5.5(b) in respect of any facilities and equipment used, directly or indirectly, to Manufacture the Products.

5.6 **Quality Agreement.** Each Party shall perform its obligations under the quality agreement to be negotiated in good faith and entered into by and among the Parties within [**] after the Effective Date (but in any case prior to the first delivery of any Product to Novartis) (the “Quality Agreement”). In the event of any conflict between this Agreement and the Quality Agreement, with respect to any quality-related terms and conditions, the Quality Agreement shall control. In the event of a conflict of any other term or conditions, this Agreement shall control, unless otherwise agreed to by the Parties in writing.

6. **REGULATORY MATTERS; COMPLIANCE.**

6.1 **Licenses and Permits.** Spark shall be responsible for promptly obtaining and maintaining any establishment licenses or permits for the Spark Facility required by the FDA or by applicable U.S. and EU Laws or cGMP, and shall ensure that all Approved Subcontractors obtain and maintain any manufacturing authorizations or permits for their respective facilities in accordance with applicable Laws and applicable cGMP. Spark hereby grants to Novartis (or shall procure the grant of) the right to reference such establishment files, licenses, permits and authorizations for the purpose of obtaining and maintaining any Regulatory Approvals for the Products in the Novartis Territory.

6.2 **Environmental Compliance.** The generation, collection, storage, handling, transportation, movement and release of hazardous materials and waste generated by or on behalf of Spark in connection with the Manufacture of Drug Substance at the Spark Facility, and any Approved Subcontractor facility will be the responsibility of Spark and the Approved Subcontractor as applicable (such reasonable cost and expense to be included in Cost of Drug Product, Cost of Drug Substance or the Cost of Diluent Product, as applicable). Without limiting other legally applicable requirements, Spark will prepare, execute, and maintain as the generator of waste, all licenses, registrations, approvals, authorizations, notices, shipping documents and waste manifests required under applicable U.S. and EU Laws for the Spark Facility.

6.3 **Audit by Novartis.** Upon the reasonable prior written notice from Novartis, Novartis shall have the right to inspect and audit the Spark Facility, the Fill and Finish Subcontractor Facility, and the facilities of all Approved Subcontractors during reasonable business hours for the purpose of assuring Spark and its Approved Subcontractors’ compliance with its obligations under this Agreement including Spark’s, the Fill and Finish Subcontractor’s and the Approved Subcontractors’ compliance with applicable cGMP, (which audit may have up to [**] individuals from Novartis for a period of up to [**] attend such audits) [**], or more frequently in any instance of existing or imminent violation of the applicable Laws, or reasonable suspicion thereof, each as demonstrated by reasonably detailed documentation, and subject to confidentiality obligations agreed by the Parties. For the avoidance of doubt at least [**] shall be conducted prior to commercial launch of the Products in the EU. In addition, Spark will support the Product Approval Inspection (PAI) of
the FDA or the EMA at no cost to Novartis or equivalent regulatory inspection for other jurisdictions (where applicable) at Novartis’s cost and provide a copy of the resulting report to Novartis.

6.4 **Regulatory Authority Inspections**. Spark will be responsible for inspections of the Spark Facility by Regulatory Authorities, and will, within [**] of receipt of notice from a Regulatory Authority in the Novartis Territory, notify Novartis if such inspections are directly related to the Manufacture of Products or if the results of a non-related inspection could materially impair the ability of Spark or any Approved Subcontractor to perform in accordance with this Agreement. With respect to inspections by Regulatory Authorities in the Novartis Territory directly related to the Manufacture of Products, Spark will (a) provide Novartis with copies of all documents, reports or communications received from or given to any Regulatory Authority in the Novartis Territory associated therewith; (b) subject to confidentiality obligations as requested by Spark, permit Novartis’ representatives to be present on site and participate, as appropriate, based on questions or requests specific to Novartis or the Products, and as permitted by Regulatory Authorities in the Novartis Territory, in such inspections; and (c) allow Novartis the opportunity (at least [**] where reasonably possible) to review and provide comments to Spark with respect to matters related to the Manufacture of the Products, and Spark will draft any such correspondence to Regulatory Authorities in the Novartis Territory taking into account Novartis’ comments where Spark determines it is reasonable to do so.

6.5 **Interactions with Regulatory Authorities**.

(a) Novartis will be responsible at its sole cost and expense for the preparation and filing of any Regulatory Approval (excluding the EU Regulatory Approval) relating to the Products in the Novartis Territory, if any, and for all contacts and communications with any Regulatory Authorities in the Novartis Territory with respect to matters specifically relating to the Products and the EU Regulatory Approval once transferred to Novartis pursuant to the License Agreement. Spark will use commercially reasonable efforts to assist Novartis upon Novartis’ request with any interactions with such Regulatory Authorities in the Novartis Territory regarding the Manufacturing of the Drug Substance, including the preparation and provision of access to any CMC Documentation, at Spark’s cost and expense.

(b) Spark shall notify Novartis immediately (and in no event later than [**]) after Spark receives any contact or communication from any Regulatory Authority (or is notified of the same by an Approved Subcontractor) in the Novartis Territory related in any way to the Manufacturing of the Products or which could be reasonably expected to have an adverse effect on the Manufacturing of the Products. Spark will provide Novartis with copies of any such correspondence or other communication within [**] of receipt of such communication by Spark. Spark will consult with Novartis regarding the response to any inquiry or observation from any Regulatory Authority in the Novartis Territory relating to the Manufacturing of the Products and will allow Novartis (or use commercially reasonable efforts to procure a right for Novartis) to participate in or control any further contacts or communications relating solely to the Manufacturing of the Products.

6.6 **Safety Issues**.
(a) Spark will provide to Novartis prompt notice of any information it receives relating to the safety of a Product, including any confirmed or unconfirmed information on adverse, serious, or unexpected events associated with their use.

(b) The Parties will share information relating to safety issues with respect a Product in accordance with the Pharmacovigilance Agreement.

6.7 Recalls. If the Product should be recalled in the Novartis Territory, Spark and Novartis will take all reasonably appropriate corrective actions. Spark will be responsible for all recall costs to the extent it can be demonstrated that the recall resulted directly from a breach of the Product Warranty. In all other cases, Novartis shall be responsible for all recall costs. Spark and Novartis will fully cooperate and provide all reasonable assistance to each other in good faith in conducting any recall.

(a) If any Regulatory Authority issues or requests a recall or takes a similar action in connection with a Product in the Novartis Territory, or if either Party determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal in the Novartis Territory, the Party notified of such recall or similar action, or the Party that desires such recall or similar action, shall, within [**], advise the other Party thereof by telephone or high-priority email. Novartis, in consultation with Spark, shall decide whether to conduct a recall in the Novartis Territory and the manner in which any such recall shall be conducted, and shall notify Spark as soon as possible of any such decision. For the avoidance of doubt, Novartis shall have sole discretion as to whether to conduct a recall in the Novartis Territory and in the manner so conducted. Spark will make available to Novartis, upon request, all of Spark’s pertinent records that Novartis may reasonably request to assist Novartis in effecting any recall. Novartis shall bear the expense of any such recall, except to the extent such recall is directly caused by or due to the fault of Spark, its Affiliates, Sublicensees or vendors, in which case Spark shall bear the expense of any such recall.

(b) If any Regulatory Authority issues or requests a recall or takes a similar action in connection with a Product in the Spark Territory, or if either Party determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal in the Spark Territory, the Party notified of such recall or similar action, or the Party that desires such recall or similar action, shall, within [**], advise the other Party thereof by telephone or high-priority email. Spark shall decide, in consultation with Novartis, whether to conduct a recall in the Spark Territory and the manner in which any such recall shall be conducted and shall notify Novartis as soon as possible of any such decision. Novartis will make available to Spark, upon request, all of Novartis’ pertinent records that Spark may reasonably request to assist Spark in effecting any recall. Spark shall bear the expense of any such recall in the Spark Territory.

(c) If either Party becomes aware of information relating to a Product that indicates that a vial or batch of Product may not conform to the Product Warranty, or that potential adulteration, misbranding, or other issues have arisen that relate to the safety or efficacy of a Product, it shall promptly so notify the other Party. To the extent practicable, the Parties shall immediately discuss the circumstances of any potential product recall, field correction, or withdrawal of such Product and possible appropriate courses of action resulting from such notification. As to any recall,
field correction, or withdrawal of Product in the Novartis Territory, Novartis shall be the sole decision maker, provided that Novartis shall consider in good faith the views of Spark as to whether any recall, field correction, or withdrawal is necessary or appropriate and shall bear the costs of such recall in accordance with Section 6.7(a). As to any recall, field correction, or withdrawal of Product in the Spark Territory, Spark shall be the sole decision maker, provided that Spark shall consider in good faith the views of Novartis as to whether any recall, field correction, or withdrawal is necessary or appropriate and shall bear the costs of such recall in accordance with Section 6.7(b). Each Party shall maintain complete and accurate records of any recall, field correction, or withdrawal in its respective territory for such periods as may be required by applicable Laws.

7. RESPONSIBLE PROCUREMENT

7.1 Novartis promotes the societal and environmental values of the United Nations Global Compact to its external suppliers and uses its influence where possible to encourage their adoption. Spark shall use reasonable efforts to:

(a) comply with the Novartis Supplier Code (and any published updates that Novartis has provided written notice of Spark) which can be viewed and downloaded from https://www.novartis.com/about-us/corporate-responsibility/resources-news/codes-policies-guidelines (Spark may request a copy free of charge from Novartis);

(b) with regard to Section 9.6 of the Novartis Supplier Code, provide information and documentation upon the reasonable written request of Novartis’ Alliance Manager (as defined therein) to Spark, after consultation with the JSC, to allow Novartis to verify compliance with the Novartis Supplier Code in the form requested, provided that Novartis and its Alliance Manager may request this information and documentation [**], and such information and documentation disclosed is subject to confidentiality obligations agreed by the Parties;

(c) rectify identified non-compliances with the Novartis Supplier Code (where capable of remedy) and report remediation progress to Novartis on request;

(d) require that Spark’s Affiliates and Approved Subcontractors are also bound to comply with the above requirements relating to the Novartis Supplier Code;

7.2 Notwithstanding anything to the contrary set forth herein and in the Novartis Supplier Code, Novartis and Spark expressly agree that Sections 9.4 (Third Party Relationships) and 9.5 (Audit Rights) of the Novartis Supplier Code are superseded by the terms of this Agreement.

8. HEALTH, SAFETY, ENVIRONMENTAL (“HSE”) AND RISK MANAGEMENT

8.1 HSE Requirements . Spark will comply and shall use reasonable efforts to cause its cause its Approved Subcontractors to comply with the HSE requirements set forth in this Agreement including without limitation (i) any applicable Law in the United States relating to HSE protection; and (ii) any terms of the Quality Agreement relating to HSE (collectively, the “HSE Requirements”).
8.2 **HSE Audits**. Spark shall permit Novartis, its Affiliates or its designated representatives to audit the Spark Facility in order to verify compliance with the HSE Requirements under this Agreement, which audit may have up to [**] individuals from Novartis for a period of up to [**] attend such audits and may occur [**], or more frequently in any instance of existing or imminent violation of the applicable Laws in the United States, or reasonable suspicion thereof, each as demonstrated by reasonably detailed documentation, and subject to confidentiality obligations agreed by the Parties.

8.3 **Risk Management**. In order to ensure continuity of supply and in connection with diligent Risk Management practices, Spark will develop, implement and keep current a Risk Management program consistent with the principles outlined in ICH Q9 (Quality Risk Management) including a risk register and associated mitigation plans that shall detail strategies for responses to and recovery from a range of potential risks. Spark will promptly make such guidance document, policy or SOP governing its quality risk management program available to Novartis, its Affiliates or their designated representatives for review. Such quality risk management plan does not relieve Spark from any liability under this Agreement.

9. **TECHNOLOGY TRANSFER**

9.1 **Escrow Arrangements**. Within time period(s) and via methods and procedures to be established by the Parties by [**], Spark will make preparations for and ensure that the Escrow Materials are stored at the facilities of one or more independent Third Party(s) of Spark’s choosing but reasonably acceptable to Novartis and on terms reasonably acceptable to both Spark and Novartis (the “Escrow Agent”). Spark shall also notify Novartis as to the location of the Escrow Agent’s facilities and contact Persons at Spark and the Escrow Agent having access to such facilities. Novartis shall bear all reasonable and documented costs associated with the preparation of the Escrow Materials and the transport to and storage of the Escrow Materials at such Escrow Agent’s facilities. The agreement among Spark, Novartis and the Escrow Agent shall provide for, among other things, the release of the Escrow Materials to Novartis upon the occurrence of a Supply Transition Event or if Spark is subject to an actual or threatened Insolvency Event.

9.2 **Technology Transfer**

(a) Without prejudice to its other rights or remedies under this Agreement, Novartis may issue a written notice to Spark at any time requesting a transfer of all or part of the Manufacture of the Products to Novartis or its designated Affiliate or a Third Party contract manufacturer (a “Transfer Notice”) if a Supply Transition Event occurs or if Spark is subject to a threatened Insolvency Event.

(b) Within [**] after receipt of a Transfer Notice, the Parties shall agree on a Technology Transfer Plan, pursuant to which Spark shall provide (or procure the provision) to Novartis or its designated Affiliate or Third Party manufacturer:

(i) all technical documentation (including master Batch Records), specifications, procedures, know-how, process descriptions and other written materials in its possession or control that are reasonably required for the Manufacture of Products; and
(ii) samples of materials as set out in the Technology Transfer Plan relating to the Manufacture of Products, in all cases, to the extent controlled by Spark at the date of the Transfer Notice and to the extent necessary or reasonably useful for the Manufacture of Products (or the part of the Manufacturing process that is being transferred); and (ii) make reasonably available to Novartis, relevant scientific and technical personnel to answer questions, provide on-site support at one Drug Substance Manufacturing site, one Diluent Product Manufacturing site, and one fill and finish facility (or such subset of the above as reasonably necessary in the case of a transfer of part of the Manufacturing process), and to train personnel from such facilities, and/or provide instruction relating to Manufacture of Products during one site visit to each facility for a period of no more than [**] each. This includes support of performance of comparability studies and analytical methods and support in the resolution of technical and regulatory issues related to the technology transfer.

(c) In the case of a Supply Transition Event elected by Novartis pursuant to clauses (a), (c), (d) or (e) of the definition of Supply Transition Event, such transfer shall take place as soon as reasonably practicable following the date of transfer requested by Novartis and all reasonable costs shall be borne by Spark.

(d) In the case of a Supply Transition Event elected by Novartis or Spark pursuant to clause (b) of the definition of Supply Transition Event, unless otherwise agreed by the Parties such transfer shall take place as soon as reasonably practicable following the date of transfer requested by Novartis and all costs associated therewith shall be apportioned between the Parties as mutually agreed in the Technology Transfer Plan.

(e) In the case of a Supply Transition Event pursuant to clause (f) of the definition of Supply Transition Event, unless otherwise agreed by the Parties pursuant to Section 10.7.5 of the License Agreement, such transfer shall take place as soon as reasonably practicable following the date of transfer requested by Novartis and all costs associated therewith shall be borne by Novartis.

(f) In the case where no Supply Transition Event has occurred, but the Parties have agreed to a Technology Transfer Plan because Spark is subject to a threatened Insolvency Event, no transfer shall actually take place or be made by Spark until a Supply Transition Event has actually occurred, and the costs associated therewith shall be determined in accordance with clauses (c)-(e) above.

(g) The Technology Transfer Plan may also provide for a transfer by Spark to Novartis of agreed quantities of Products at a purchase price to be set forth in the Technology Transfer Plan.

9.3 Step-In Rights. Upon receipt of a Transfer Notice, if requested by Novartis Spark shall use commercially reasonable efforts to allow Novartis, its Affiliate or Third Party contract manufacturing organization to obtain the benefit (whether through assignment, step in rights, subcontracting or otherwise) of Spark’s agreements with Approved Subcontractors and suppliers of Materials.
10. CONFIDENTIAL INFORMATION

10.1 Article 8 of the License Agreement shall govern the confidentiality obligations and use restrictions of the Parties with respect to Confidential Information disclosed under this Agreement and the Quality Agreement.

11. INTELLECTUAL PROPERTY

11.1 Article 7 of the License Agreement shall govern the ownership of any Intellectual Property arising under this Agreement.

12. REPRESENTATIONS AND WARRANTIES

12.1 Corporate Action. Each Party represents to the other Party that (a) it is a corporation duly organized and validly existing under the Laws of its jurisdiction of organization; (b) the execution and delivery of this Agreement has been authorized by all requisite corporate action, and (c) this Agreement is and will remain a valid and binding obligation of such Party, enforceable in accordance with its terms.

12.2 Absence of Other Contractual Restrictions. Each Party represents and warrants that it is under no contractual or other obligation or restriction that is inconsistent with its execution or performance of this Agreement or the rights granted to such Party under this Agreement. Neither will it enter into any agreement, either written or oral, that would conflict with its obligations under this Agreement.

12.3 Qualifications of Manufacturer Personnel. Spark has, and will engage, employees and permitted subcontractors and/or consultants (“Manufacturer Personnel”) with the proper skill, training and experience to provide Manufacturing services. Spark will be solely responsible for paying Manufacturer Personnel and providing any employee benefits that they are owed.

12.4 No Debarment. Spark represents and covenants that it has not been debarred, and has not been threatened with debarment, under Section 306(a) or (b) of the U.S. Generic Drug Enforcement Act of 1992, as amended, in the Spark Territory and Spark will not knowingly use in any capacity under this Agreement any debarred person or entity in the Spark Territory.

12.5 Intellectual Property. To Spark’s knowledge, (i) the Manufacture and/or supply of Drug Substance, Drug Product, Resulting Vials of Drug Product and Batches of Diluent Product as provided herein does not infringe or misappropriate the Intellectual Property of any Third Party, and (ii) Spark has not received any written notice alleging such infringement or misappropriation.

13. INDEMNIFICATION; INSURANCE; LIMITATION OF LIABILITY

13.1 Indemnification of Spark. Novartis shall indemnify Spark, its Affiliates and its and their respective directors, officers, employees, subcontractors, agents and representatives (the “Spark Indemnites”), and defend and save each of them harmless, from and against any and all losses, damages, liabilities, costs and expenses (including reasonable attorneys’ fees and expenses) (collectively, “Losses”) in connection with any and all suits, investigations, claims or demands of
Third Parties (collectively, “Third Party Claims”) arising from or occurring as a result of: (a) any breach of covenant, representation or warranty set forth in this Agreement or the Quality Agreement by Novartis, (b) the Development, Manufacturing, use or Commercialization of the Drug Product, the Diluent Product or any product containing or comprised of foregoing in the Novartis Territory (save where such activities are performed by Spark), or (c) the gross negligence or willful misconduct of Novartis or its Affiliates or any of their respective Sublicensees, in each case, (a) - (c) except for those Losses for which Spark has an obligation to indemnify Novartis or any Novartis Indemnitee pursuant to Section 13.2.

13.2 Indemnification of Novartis. Spark shall indemnify Novartis, its Affiliates, and its and their respective directors, officers, employees, subcontractors, agents and representatives (the “Novartis Indemnitees”), and defend and save each of them harmless, from and against any and all Losses in connection with any and all Third Party Claims arising from or occurring as a result of (a) any breach of covenant, representation or warranty set forth this Agreement or the Quality Agreement by Spark, (b) Spark’s Manufacturing or supply of the Products, or (c) the gross negligence or willful misconduct of Spark, in each case (a) – (c) except for those Losses for which Novartis has an obligation to indemnify Spark or any Spark Indemnitee pursuant to Section 13.1.

13.3 Indemnification Procedures. Upon notice of any Third Party Claim, the indemnified Party (“Indemnified Party”) will promptly notify the indemnifying Party (“Indemnifying Party”) in writing. Failure to notify the Indemnifying Party will not relieve that Party of its indemnification obligations except to the extent the failure or delay is prejudicial. The Indemnifying Party will have control over the defense and any settlement of such claim; provided however that (a) the Indemnified Party will be entitled to participate in the defense of such claim and to employ counsel at its own expense to assist in the handling of such claim; and (b) the Indemnifying Party will obtain the prior written approval (not to be unreasonably withheld) from the Indemnified Party before entering into any settlement of such claim. The Parties will cooperate in furnishing such information and attending such conferences and hearings as reasonably requested in connection with the defense or prosecution of any Third Party Claim. If the Indemnifying Party fails to act within a reasonable time after receiving notice, the Indemnified Party will have the right to employ its own counsel at the expense of the Indemnifying Party.

13.4 Direct Claims for Breach. If a Party believes it has been damaged directly (i.e., not arising from a Third Party Claim), such Party shall provide a Notice of Dispute to the other pursuant to Section 12.3 of the License Agreement. All such disputes shall be governed by ARTICLE 11 of the License Agreement. For clarity, this Section 13.4 is not intended to limit any other right or remedy of a Party with respect to this Agreement.

13.5 Integration of this Agreement and License Agreement. Spark and Novartis each acknowledge that the License Agreement and this Supply Agreement were entered into as part of one integrated transaction. As such, in the case of a claim for damages or indemnification, neither Spark nor Novartis shall assert that the performance and/or payment under one agreement was separate and apart from payment and/or performance under the other agreement.

13.6 Measure of Damages. Neither Party shall have liability to the other under this Agreement, whether pursuant to this ARTICLE 13, ARTICLE 11 of the License Agreement, or
otherwise, in contract, tort or otherwise, for indirect, incidental, punitive, remote or speculative damages or other damages that are not probable and reasonably foreseeable; provided that

(a) the foregoing limitation shall not apply to any such damages paid or payable to Third Parties in connection with an indemnifiable Third Party Claim pursuant to this ARTICLE 13 or in the case of gross negligence or fraud; and

(b) without prejudice to Spark’s rights under ARTICLE 9 and Section 13.7, Spark’s total, aggregate liability in respect of Non-Conforming Products in any Calendar Year shall not exceed [**] percent (\[**\]% of the [**] under this Agreement [**]).

13.7 No Exclusion. Neither Party excludes any liability for death or personal injury caused by its negligence or that of its employees, agents or subcontractors to the extent such exclusion is prohibited by applicable Law.

14. TERMINATION

14.1 Term. This Agreement will become effective as of the Effective Date and shall continue until the expiration or early termination of the License Agreement, unless earlier terminated pursuant to Section 14.2 (the “Term”).

14.2 Termination for Material Breach. Upon any material breach of this Agreement by a Party (the “Breaching Party”), the other Party (the “Non-Breaching Party”) may give written notice to the Breaching Party specifying the claimed particulars of such breach. The Breaching Party shall have a period of [**] after such notice if such material breach is a breach of a payment obligation or [**] after such notice in the case of any other material breach in which to cure such breach; provided that, if such breach other than a payment breach is capable of being cured and cannot be cured within such [**] period, and the Breaching Party notifies the Non-Breaching Party within such period that it has initiated actions to cure such breach and thereafter diligently pursues such actions, the Breaching Party shall have such additional period as is reasonable in the circumstances, but in no event longer than [**] after the end of the original cure period, to cure such breach. Any termination by any Party under this Section 14.2 and the effects of termination provided in this ARTICLE 14 shall be without prejudice to any damages or other legal or equitable remedies to which it may be entitled from the other Party. If the Breaching Party fails to cure the breach within the time period set forth above, the Non-Breaching Party shall have the right thereafter to terminate this Agreement effective immediately by giving written notice to the Breaching Party to such effect; provided that the Non-Breaching Party may, by notice to the Breaching Party, designate a later date for such termination in order to facilitate an orderly transition of activities or elect not to terminate this Agreement.

14.3 Termination for Insolvency. Each Party shall have the right to terminate this Agreement upon written notice to the other Party if an Insolvency Event occurs with respect to such other Party. In any event when a Party first becomes aware of the likely occurrence of any Insolvency Event in regard to that Party, it shall promptly so notify the other Party in sufficient time to give the other Party sufficient notice to protect its interests under this Agreement.
14.4 **Termination of License Agreement.** This Agreement shall terminate automatically and without action of the Parties in the event of termination of the License Agreement for any reason whatsoever.

14.5 **Consequences of Termination.**

(a) Upon expiry of this Agreement or upon termination of this Agreement (in whole) by Novartis for Spark’s material breach in accordance with Section 14.2, for a Spark Insolvency Event pursuant to Section 14.3 or as a consequence of Novartis’s termination of the License Agreement for Spark’s material breach thereof, the following shall apply:

(i) at Novartis’s option, all undelivered Purchase Orders shall be cancelled;

(ii) on demand from Novartis, Spark shall notify Novartis in writing of the quantity and description of finished Product, semi-finished Product and Materials held by Spark as at the date of termination;

(iii) Novartis may, at its option, place an order with Spark:

(A) to purchase any finished Product (which meets the Specifications and otherwise complies with this Agreement) at the Purchase Price current at the termination date;

(B) to purchase any semi-finished Product at such pro-rata amount of the Purchase Price applicable to such semi-finished Product;

(C) to complete the Manufacture of any semi-finished Product in accordance with this Agreement and deliver the same to Novartis at the Purchase Price current at the termination date; and/or

(D) to purchase any Materials at cost price;

(iv) the terms and conditions of this Agreement shall apply to any order placed by Novartis in accordance with Section 14.5(a)(iii); and

(v) at Novartis’s request and subject always to applicable U.S. and EU Laws and cGMP, Spark shall, at its cost, destroy any finished Product and semi-finished Product that is not purchased by Novartis in accordance with Section 14.5(a)(iii) or that cannot be used by Spark in respect of supplies for the Spark Territory.

(b) Without prejudice to Section 14.5(a), upon termination of this Agreement for any other reason, the following shall apply:

(i) unless the Parties otherwise agree in writing, all undelivered Purchase Orders shall be deemed to be cancelled and Novartis shall purchase all finished Product,
semi-finished Product and Materials in Spark’s inventory as set forth in Sections 14.5(b)(ii) and (iii) below;

(ii) Spark shall notify Novartis in writing of the quantity and description of finished Product, semi-finished Product and Materials held by Spark and intended for use in the Novartis Territory as at the date of termination or expiration;

(iii) Novartis shall place an order with Spark to purchase:

(A) any finished Product (which meets the Specifications and otherwise complies with this Agreement) at the Purchase Price current at the termination date;

(B) any semi-finished Product at such pro-rata amount of the Purchase Price applicable to such semi-finished Product; and/or

(C) any Materials at cost price,

in each case provided that they were intended for use in the Novartis Territory and Novartis shall not be obliged to purchase any such finished or part finished Product or Materials in excess of the lesser of: (1) the amount required to meet the Purchase Orders current at the date of termination or expiration; or (2) the amount held by Spark on the date when notice of termination or expiration was served (excluding any amounts held by Spark in respect of supplies for the Spark Territory);

(iv) the terms and conditions of this Agreement shall apply to any order placed by Novartis in accordance with Section 14.5(b)(iii);

(v) Novartis shall pay the Fixed Facility Fee in its entirety (regardless of whether any Products are ordered by Novartis) in accordance with Section 10.7.2(b) of the License Agreement; and

(vi) Novartis shall pay all non-cancellable costs that Novartis is required to pay under the Capacity Plan.

14.6 **Accrued Obligations**. Neither the termination nor expiration of this Agreement shall release either of the Parties from any liability which at the time of such termination or expiration has already accrued to the other Party, nor affect in any way the survival of any other right, duty or obligation of either of the Parties which is expressly stated elsewhere in this Agreement to survive such termination or such non-renewal.

14.7 **Survival**. The following provisions shall continue in force in accordance with their respective terms notwithstanding the expiration or the termination of this Agreement for any reason: Sections 3.7 to 3.10, 4.3, 4.4, 6.6(b), 6.7, 9.2 and 14.5 to 14.7, and ARTICLES 10, 11, 13 and 15.

15. **MISCELLANEOUS**
15.1 **Dispute Resolution**. Subject to Section 3.9(a) and the decision-making authority of the JSC pursuant to Section 2.1.3(y) of the License Agreement in relation to issues arising under this Agreement (including, without limitation, disagreements regarding supply price increases (including the Fixed Facility Fee), capacity restrictions leading to supply shortages and, for a period of [**] following the Effective Date, review of the Capacity Plan), if any dispute or disagreement arises between Novartis and Spark in respect of this Agreement or any Related Agreement, ARTICLE 11 of the License Agreement shall apply.

15.2 **Choice of Law**. This Agreement shall be governed by and interpreted under, the Laws of the State of Delaware, United States, excluding: (a) any provision thereof that would apply the Law of any other jurisdiction; (b) the United Nations Conventions on Contracts for the International Sale of Goods; (c) the 1974 Convention on the Limitation Period in the International Sale of Goods (the “**1974 Convention**”); and (d) the Protocol amending the 1974 Convention, done at Vienna April 11, 1980.

15.3 **Jurisdiction and Venue**. Each Party irrevocably submits to the exclusive jurisdiction of the United States District Court for the District of Delaware for the purposes of any suit, action or other proceeding arising out of this Agreement. Each Party agrees to commence any such action, suit or proceeding in the United States District Court for the District of Delaware or if such suit, action or other proceeding may not be brought in such court for jurisdictional reasons, in the Superior Court of the State of Delaware, Wilmington. Each Party irrevocably and unconditionally waives any objection to the laying of venue of any such action, suit or proceeding arising out of this Agreement in the United States District Court for the District of Delaware (or the Superior Court of the State of Delaware, Wilmington, as applicable), and hereby and thereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum. For the avoidance of doubt, both Parties hereby irrevocably waive any right they may have to a trial by jury arising from any dispute under this Agreement.

15.4 **Notices**. All notices, instructions and other communications hereunder or in connection herewith shall be in writing, shall be sent to the address specified in this Section 15.4 and shall be: (a) delivered personally; (b) transmitted by facsimile; or (c) sent via a reputable international overnight delivery service. Any such notice, instruction or communication shall be deemed to have been delivered (i) upon receipt if delivered by hand or when transmitted with electronic confirmation of receipt, if transmitted by facsimile (if such transmission is on a Business Day; otherwise, on the next Business Day following such transmission), **provided that** an original document is sent via an internationally recognized overnight delivery service (receipt requested), or (ii) one (1) Business Day after it is sent via a reputable international overnight delivery service.
If to Spark:
Spark Therapeutics, Inc.
3737 Market Street, Suite 1300
Philadelphia, PA 19104, USA
Attention: General Counsel
Facsimile: [**]

With copy to:
WilmerHale LLP
60 State Street
Boston, MA 02109, USA
Attention: Steven D. Barrett, Esq.
Facsimile No.: (617) 526 5000

If to Novartis:
Novartis Pharma AG
Lichtstrasse 35
CH 4002 Basel
Switzerland
Attn: Head of Pharma BD&L
Fax: [**]

Novartis Pharma AG
Lichtstrasse 35
CH-4002 Basel
Switzerland
Attn: General Counsel
Fax [**]

With a copy to:
Arnold & Porter Kaye Scholer LLP
250 West 55th Street
New York, NY 10019-9710
Attention: Derek M. Stoldt, Esq.
Facsimile No.: [**]

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith.

15.5 Severability. If, under applicable Law, any provision of this Agreement is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision of this Agreement (such invalid or unenforceable provision, a “Severed Clause”), this Agreement shall endure except for the Severed Clause. The Parties shall consult one another and use reasonable, good faith efforts to agree upon a valid and enforceable provision that is a reasonable substitute for the Severed Clause in view of the intent of the Severed Clause and this Agreement.

15.6 Integration. This Agreement constitutes the entire agreement between the Parties hereto with respect to the subject matter of this Agreement and supersedes all previous agreements, whether written or oral including, without limitation, that certain Mutual Non-Disclosure Agreement by and between Novartis and Spark, dated September 27, 2017 (the “CDA”), which obligations between Novartis and Spark are hereby terminated as of the Effective Date, provided that the rights and obligations of the Parties in Section 8 of the CDA shall survive as set forth therein. The Parties acknowledge and agree that, as of the Effective Date, all Confidential Information (as defined in the CDA) disclosed by a Party pursuant to the CDA shall be considered Confidential Information of such Party and subject to the terms set forth in this Agreement. This Agreement may be amended.
only in writing signed by properly authorized representatives of each of Spark and Novartis. In the event of any conflict between a substantive provision of this Agreement and any Exhibit hereto or the License Agreement, the substantive provision of the License Agreement shall prevail.

15.7 Independent Contractors; No Agency. Neither Party shall have any responsibility for the hiring, firing or compensation of the other Party’s employees or for any employee benefits. No employee or representative of a Party shall have any authority to bind or obligate the other Party to this Agreement for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on the other Party without said Party’s written approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, each Party’s legal relationship under this Agreement to the other Party shall be that of independent contractor. Nothing contained in this Agreement shall be deemed to constitute a partnership, joint venture, or legal entity of any type between Spark and Novartis, or to constitute one as the agent of the other. Moreover, each Party agrees not to construe this Agreement, or any of the transactions contemplated hereby, as a partnership for any tax purposes.

15.8 Performance by Other Persons. Novartis may exercise its rights and perform its obligations under this Agreement itself or through any of its Affiliates or Sublicensees, as it deems appropriate without Spark’s consent. Novartis shall be responsible for the performance and compliance with this Agreement of its Affiliates, Sublicensees, authorized agents and subcontractors.

15.9 Assignment; Successors. Neither Party will assign, transfer or novate this Agreement without the prior written consent of the other Party, except assignment or transfer will be permitted by notice in writing, and without the prior written consent of the other Party, to: (a) any of the assigning Party’s Affiliates; or (b) a purchaser of a substantial part of a Party’s assets or business relating to the subject matter of this Agreement. This Agreement shall be binding upon, and shall inure to the benefit of, all successors and permitted assigns. Any permitted assignee will assume all obligations of its assignor under this Agreement. Any assignment, transfer or novation made in violation of this Section 15.9 shall be wholly void and invalid, the assignee, transferee or successor shall acquire no rights whatsoever, and the non-assigning Party shall not recognize, nor shall it be required to recognize, the assignment, transfer or novation.

15.10 Force Majeure. No Party shall be liable for failure of or delay in performing obligations set forth in this Agreement, and no Party shall be deemed in breach of its obligations, if such failure or delay is due to any natural disaster, explosion, fire, flood, act of nature (including tornadoes, thunderstorms, earthquakes, typhoons, hurricanes, and tsunamis), war, hostilities between nations, civil commotions, terrorism, riots, embargo, losses or shortages of power, [**], sabotage, or any other cause reasonably beyond the control of such Party (a “Force Majeure Event”). The Party affected by such force majeure shall provide the other Party with full particulars thereof as soon as it becomes aware of the same (including its good faith estimate of the likely extent and duration of the interference with its activities), and will use commercially reasonable efforts in good faith to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable. If the performance of any such obligation under this Agreement is delayed owing to such a force majeure for any continuous period of more than [**], the Parties
will consult with respect to an equitable solution, including the possibility of the mutual termination of this Agreement.

15.11 **No Third Party Beneficiaries.** Except for the Spark Indemnitees and the Novartis Indemnitees as set forth in Article 13, this Agreement shall not be construed as conferring any rights or remedies upon any Person other than the Parties and their respective successors and permitted assigns.

15.12 **Execution in Counterparts; Facsimile Signatures.** This Agreement may be executed in counterparts, each of which counterparts, when so executed and delivered, shall be deemed to be an original, and all of which counterparts, taken together, shall constitute one and the same instrument even if both Parties have not executed the same counterpart. Signatures provided electronically by PDF or facsimile transmission shall be deemed to be original signatures.

15.13 **English Language.** This Agreement is written and executed in the English language. Any translation into any other language shall not be an official version of this Agreement and in the event of any conflict in interpretation between the English version and such translation, the English version shall prevail.

15.14 **Expenses.** Except as otherwise expressly provided in this Agreement, each Party shall pay the fees and expenses of its respective lawyers and other experts and all other expenses and costs incurred by such Party incidental to the negotiation, preparation, execution and delivery of this Agreement:

15.15 **Cumulative Remedies.** No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under Law.

15.16 **Interpretation.** Unless the context of this Agreement otherwise requires: (a) words of one gender include the other gender; (b) words using the singular or plural number also include the plural or singular number, respectively; (c) the terms “hereof,” “herein,” “hereby,” and other similar words refer to this entire Agreement; (d) the words “include”, “includes”, and “including” when used in this Agreement shall be deemed to be followed by the words “without limitation”, unless otherwise specified; (e) the terms “Article” and “Section” refer to the specified Article and Section of this Agreement, unless otherwise specified; (f) “U.S.” or “United States” means the United States of America and its territories and possessions; and (g) all references to months, quarters or years are references to calendar months, calendar quarters, or Calendar Years, respectively, unless otherwise specified. All references to “$” amounts hereunder shall be deemed to be U.S. Dollars, and all payments due hereunder shall be made in U.S. Dollars.

*(signature page follows)*
IN WITNESS WHEREOF, the Parties have executed this Agreement as of the date first set forth above.

SPARK THERAPEUTICS, INC.

By: /s/ Jeffrey D. Marrazzo
Name: Jeffrey D. Marrazzo
Title: CEO

NOVARTIS PHARMA AG

By: /s/ Marc Ceulemans
Name: Marc Ceulemans
Title: Head Strategic Venture Capital Fund & Pharma Equities

By: /s/ Bartosz Dzikowski
Name: Bartosz Dzikowski
Title: Authorized Signatory
Exhibit A

Cost Definitions

[**]
Confidential Materials omitted and filed separately with the SEC. A total of 4 pages were omitted. [**]
Exhibit C

Escrow Materials

[**]
### Exhibit D

**Approved Subcontractors**

<table>
<thead>
<tr>
<th>Establishment Name, Address and Unique Facility Identifier</th>
<th>Specific Manufacturing Operations Being Conducted</th>
</tr>
</thead>
<tbody>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>
LICENSING AND COMMERCIALIZATION AGREEMENT

BY AND BETWEEN

SPARK THERAPEUTICS, INC.

AND

NOVARTIS PHARMA AG

January 24, 2018
# TABLE OF CONTENTS

## DEFINITIONS; INTERPRETATION 1

- Definitions 11

## GOVERNANCE 13

- Joint Steering Committee 13

## LICENSES; OPTIONS; OTHER RIGHTS 15

- Grants by Spark 15
- Grants by Novartis 17
- Section 365(n) of the U.S. Bankruptcy Code 19

## DEVELOPMENT, TECHNICAL DEVELOPMENT AND REGULATORY ACTIVITIES 20

- General 20
- Development Plan 20
- Development Studies 21
- Regulatory Activities 23
- Adverse Event and Product Complaint Reporting Procedures; Pharmacovigilance 25
- Terminate or Suspend a Study Based on Safety Concerns 25

## COMMERCIALIZATION 26

- Promotional Materials 26
- Reimbursement 26
- Responsibilities 27
- Supply 27

## FINANCIAL PROVISIONS 27

- Upfront Payments 27
- Milestones 27
- Royalties 28
- Reports; Invoices;
Payments

6.5 Records; Audits
12.9 Force Majeure
12.10 No Third Party Beneficiaries
12.11 Execution in Counterparts; Facsimile Signatures
EXHIBITS

Exhibit 1.1.21  Existing Spark Agreements

Exhibit 3.1.6  Relevant Sections of NIH Agreement

Exhibit 8.5.1  Press Releases
LICENSING AND COMMERCIALIZATION AGREEMENT

This Licensing and Commercialization Agreement (“Agreement”) is entered into as of January 24, 2018 (the “Effective Date”) by and between Spark Therapeutics, Inc., a Delaware corporation, with offices at 3737 Market Street, Suite 1300, Philadelphia, PA 19104, USA (“Spark”) and Novartis Pharma AG, a Swiss company, with offices at Lichtstrasse 35, CH-4056 Basel, Switzerland (“Novartis”).

INTRODUCTION

1. Spark is currently developing Luxturna (as defined below) and Commercializing Luxturna in the United States, for use in the treatment of inherited retinal disease;

2. Novartis is in the business of developing, manufacturing, marketing, promoting and selling pharmaceutical products throughout the world;

3. Spark desires to enter into an arrangement with respect to the development, manufacturing, marketing, promotion and sale of Luxturna outside of the United States; and

4. Spark and Novartis believe that an agreement between the Parties regarding Luxturna would be desirable.

NOW, THEREFORE, for and in consideration of the mutual covenants contained herein, Spark and Novartis hereby agree as follows:
ARTICLE 1  
DEFINITIONS; INTERPRETATION

1.1 Definitions. As used in this Agreement, the following terms shall have the meanings set forth below:

1.1.1 “Accounting Standards” mean, with respect to Spark, U.S. GAAP (United States Generally Accepted Accounting Principles) and, with respect to Novartis, IFRS (International Financial Reporting Standards), in each case, as generally and consistently applied for accounting and financial reporting purposes throughout the Party’s organization. Each Party may change the accounting standards that it uses throughout such Party’s organization, in which case such Party shall promptly notify the other Party in writing of such change and “Accounting Standards” shall be modified as to such Party accordingly, it being understood that each Party may only use internationally recognized accounting principles (e.g., IFRS, U.S. GAAP, or successor standards thereto).

1.1.2 “Affiliate” means with respect to a Party, any Person that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, “control” or “controlled” means direct or indirect ownership of fifty percent (50%) or more of the shares of stock entitled to vote for the election of directors in the case of a corporation or fifty percent (50%) or more of the equity interest in the case of any other type of legal entity; status as a general partner in any partnership; or any other arrangement whereby the Person controls or has the right to control the board of directors or equivalent governing body of a corporation or other entity or the ability to cause the direction of the management or policies of a corporation or other entity. The Parties acknowledge that in the case of entities organized under the laws of certain countries where the maximum percentage ownership permitted by law for a foreign investor is less than fifty percent (50%), such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management and policies of such entity. Notwithstanding the foregoing, The Children’s Hospital of Philadelphia shall be deemed to not be an Affiliate of Spark.

1.1.3 “Base Royalty Term” means, with respect to a Royalty Region, the period beginning on the Effective Date and continuing until twelve (12) years after the date of the First Commercial Sale of Luxturna in such Royalty Region, provided that if, on a country-by-country basis, the Base Royalty Term would otherwise expire before the expiration of Regulatory Exclusivity in such country, then the Base Royalty Term shall be extended until the expiration of Regulatory Exclusivity in such country (but not in the remainder of the applicable Region).

1.1.4 “Business Day” means a day other than (a) a Saturday or a Sunday, (b) a bank or other public holiday in New York, New York, Fort Worth, Texas, East Hanover, New Jersey, or Basel, Switzerland, or (c) the nine (9) consecutive days beginning on December 24th and continuing through January 1st to the extent not already covered in (a) or (b).

1.1.5 “Calendar Quarter” means each of the three (3) calendar month periods ending on March 31, June 30, September 30 and December 31 of any Calendar Year; provided that the first Calendar Quarter shall commence on the Effective Date and end on March...
31, 2018 and, unless otherwise agreed between the Parties, the last Calendar Quarter shall end on the effective date of expiration or termination of the Term.

1.1.6 “Calendar Year” means each successive period of twelve (12) months commencing on January 1 and ending on December 31; provided that the first year of the Term shall begin on the Effective Date and end on December 31, 2018 and the last year of the Term shall begin on the first day of such year and end on the last day of the Term.

1.1.7 “Claims” means all Third Party demands, claims, actions, proceedings and liability (whether criminal or civil, in contract, tort or otherwise) for losses, damages, reasonable legal costs and other reasonable expenses of any nature whatsoever.

1.1.8 “Combination Product” means a commercial product comprising Luxturna plus another Gene Therapeutic or other therapeutically active ingredient, whether coformulated or copackaged.

1.1.9 “Commercialization” or “Commercialize” means activities directed to obtaining pricing and reimbursement approvals, marketing, promoting, distributing, importing, exporting, offering to sell or selling a product, including pre-launch activities undertaken in preparation for a product launch and post-launch activities. Commercialization does not include Development or Manufacturing.

1.1.10 “Continued Royalty Term” means, with respect to a Royalty Region (or any country thereof for which the Base Royalty Term was extended due to Regulatory Exclusivity in such country), the period beginning upon the expiration of the Base Royalty Term applicable to such Region (or country) and ending (a) on December 31 of the Calendar Year in which a Royalty Termination Event described in Section 1.1.51(a) occurs, or (b) on the date a Royalty Termination Event described in Section 1.1.51(b) occurs, in each case ((a) and (b)) with respect to such Royalty Region (or country).

1.1.11 “Control” or “Controlled” means, with respect to any Intellectual Property right, Trademark or other intangible property, the possession by a Party (whether by license from an Affiliate or a Third Party, ownership, or control over an Affiliate having such possession by license or ownership) of the ability to grant to the other Party access or a license or sublicense as provided herein without violating the terms of any agreement with any Third Party.

(a) Subject to Section 3.1.6, Intellectual Property licensed by Spark from Third Parties under the Existing Spark Agreements that Spark is permitted to sublicense to Novartis as provided herein without violating the terms of such Existing Spark Agreements shall be deemed to be Controlled by Spark.

(b) Notwithstanding the foregoing, Spark shall not be considered to Control any Intellectual Property that it licenses from a Third Party under a license agreement other than an Existing Spark Agreement if (i) Spark would be required to make any payment in connection with the grant of, or Novartis’ exercise of rights under, a sublicense to such Intellectual Property hereunder, and (ii) Novartis does not agree, subject to Novartis’ right to offset a portion of such
payments against the royalties payable to Spark hereunder pursuant to Section 3.2.4, in writing to make any such payment to Spark or its designee.

(c) Notwithstanding the foregoing, Novartis shall not be considered to Control any Intellectual Property that it licenses from a Third Party if (i) Novartis would be required to make any payment in connection with the grant of, or Spark’s exercise of rights under, a sublicense to such Intellectual Property hereunder, and (ii) Spark does not agree in writing to make any such payment to Novartis or its designee.

1.1.12 “Cover”, “Covering” or “Covered” means, as to any subject matter and Patent Right, that, in the absence of a license granted under, or ownership of, such Patent Right, the making, using, selling, offering for sale, importation or other practice of such subject matter would infringe such Patent Right or, as to a pending claim included in such Patent Right, the making, using, selling, offering for sale, importation or other practice of such subject matter would infringe such Patent Right if such pending claim were to issue in an issued patent without modification, in each case, without regard to the validity or enforceability of such Patent Right.

1.1.13 “Development” or “Develop” means non-clinical and clinical research and drug development activities, including discovery activities, toxicology, pharmacology and other research and pre-clinical efforts, statistical analysis, clinical studies, regulatory affairs, and the preparation, filing and prosecution of Regulatory Approval and clinical study regulatory activities (but excluding all Manufacturing activities directed to the production of commercial supply other than any activities to be conducted by Spark pursuant to Section 4.1.2). Development does not include Technical Development.

1.1.14 “Development Plan” means the high-level plan, as updated on [**] basis and as amended from time to time in accordance with the terms of this Agreement, for (i) Development efforts with respect to Luxturna Development in the Novartis Territory proposed by Novartis pursuant to Section 4.2, including clinical, regulatory activities and milestones and Post-Approval Commitments, (ii) Technical Development as proposed by Spark pursuant to Section 4.2.1, and (iii) Technical Development as proposed by both Parties for life cycle management pursuant to Section 4.2.1.

1.1.15 “Diligent Efforts” means, with respect to the efforts to be expended by Novartis with respect to Development and Commercialization of Luxturna, such efforts shall be substantially equivalent to the efforts and resources commonly used by Novartis for products [**] owned by it or to which it has rights, which product is of similar market and economic potential as Luxturna, and at a similar stage in its Development or product life as Luxturna, taking into account the efficacy, safety, approved labeling, present and future market potential, and market exclusivity and other proprietary position of Luxturna as well as competitiveness thereof, the likelihood of Regulatory Approval of Luxturna given the regulatory structure involved and any jurisdictional-specific regulatory or clinical development requirements, the profitability to Novartis of Luxturna, and the costs, liabilities and external and internal resources required to achieve the relevant objective. For the avoidance of doubt, where Novartis has an obligation to use Diligent Efforts, the efforts of Novartis and its Affiliates and Sublicensees shall be considered in determining whether Novartis has satisfied such obligation.
1.1.16 "Distributor" means any Third Party appointed by Novartis or any of its Affiliates or its or their Sublicensees to distribute, market and sell Luxturna, with or without packaging rights, in one or more countries in the Novartis Territory, in circumstances where (a) the Third Party purchases Luxturna from Novartis or its Affiliates or its or their Sublicensees but does not otherwise make any upfront, royalty or other payment (separate from a payment for supply of Luxturna) to Novartis or its Affiliates or its or their Sublicensees with respect to Luxturna and (b) the Third Party does not engage in any material promotional activity with respect to Luxturna. If a Third Party has been appointed by Novartis or any of its Affiliates or its or their Sublicensees to distribute, market and sell Luxturna, with or without packaging rights, in one or more countries in the Novartis Territory, in circumstances where (a) the Third Party purchases Luxturna from Novartis or its Affiliates or its or their Sublicensees and otherwise makes an upfront, royalty or other payment (separate from a payment for supply of Luxturna) to Novartis or its Affiliates or its or their Sublicensees with respect to Luxturna or (b) the Third Party engages in material promotional activity with respect to Luxturna, such Third Party, each, a "Deemed Sublicensee Distributor," shall be deemed a Sublicensee for purpose of Net Sales and corresponding royalty calculations.

1.1.17 "EMA" means the European Medicines Agency or any successor agency thereto.

1.1.18 "EU Regulatory Approval" means, if a conditional Regulatory Approval has been issued by EMA, the Regulatory Approval granted following satisfaction of all conditions in the conditional Regulatory Approval that are required to be satisfied to permit Novartis to Commercialize Luxturna within the EU and, if a conditional Regulatory Approval has not been issued, the Regulatory Approval of Luxturna by EMA.

1.1.19 "European Union" or "EU" means (a) the economic, scientific and political organization of member states of Europe as constituted as of the Effective Date, namely Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom of Great Britain and Northern Ireland, (b) any member country of the European Economic Area that is not otherwise a member of the European Union, (c) any country not otherwise included in clauses (a) or (b) that participates in the unified filing system under the auspices of the EMA and (d) Switzerland. For clarity, the European Union will at all times be deemed to include each of France, Germany, Italy, Spain and the United Kingdom, whether or not the United Kingdom remains a member state of the European Union, except as expressly noted within this Agreement.

1.1.20 "Executive Officers" means the Chief Executive Officer of Spark and the Chief Executive Officer of Novartis Pharma or, in either case, the designee of such officer.

1.1.21 "Existing Spark Agreements" means the license agreements set forth on Exhibit 1.1.21, as well as any future amendments thereto, which shall automatically be incorporated into and become a part of Exhibit 1.1.21.

1.1.22 "Field" means the treatment, prevention, cure or control of RPE65-mediated retinal disease in humans, [**].
1.1.23 "First Commercial Sale" means, with respect to Luxturna in a given Royalty Region, the first bona fide arm’s length sale by or on behalf of Novartis or its Sublicensees to a Third Party for use or consumption of Luxturna in the first country in such Royalty Region, after all necessary Regulatory Approvals for Luxturna have been obtained in such country.

1.1.24 "Gene Therapeutic" means any product incorporating a gene-based approach utilizing a gene therapy, [**].

1.1.25 "Good Clinical Practice" means the current good clinical practice under applicable Law, to the extent such standards are not less stringent than the U.S. current good clinical practice.

1.1.26 "Good Laboratory Practice" means the current good laboratory practice under applicable Law, to the extent such standards are not less stringent than the U.S. current good laboratory practice, including 21 C.F.R. Part 58.

1.1.27 "Governmental Authority" means any federal, state, national, regional, provincial or local government, or political subdivision thereof, or any multinational organization or authority or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof), or any governmental arbitrator or arbitral body.

1.1.28 "Handle" or "Handling" means, with respect to a Patent Right, to prepare, file, prosecute, maintain or defend such Patent Right. For clarity, Handling does not include initiating any claim or action to enforce Patent Rights against actual or alleged infringers.

1.1.29 "HHMI" means the Howard Hughes Medical Institute, a not-for-profit institution located at 4000 Jones Bridge Road, Chevy Chase, MD 20815-6789, United States, a Third Party identified as a third party beneficiary of the CHOP Agreement.

1.1.30 "Insolvency Event" means, in relation to either Party, any one of the following: (a) that Party becomes insolvent; (b) that Party is the subject of voluntary or involuntary bankruptcy proceedings instituted on behalf of or against such Party (except for involuntary bankruptcy proceedings which are dismissed within sixty (60) days); (c) an administrative receiver, receiver and manager, interim receiver, custodian, sequestrator or similar officer is appointed in respect of that Party; (d) a notice shall have been issued to convene a meeting for the purpose of passing a resolution to wind up that Party, or such a resolution shall have been passed other than a resolution for the solvent reconstruction or reorganization of that Party; (e) a resolution shall have been passed by that Party or that Party’s directors to make an application for an administration order or to appoint an administrator; or (f) that Party proposes or makes any general assignment, composition or arrangement with or for the benefit of all or some of that Party’s creditors or makes or suspends or threatens to suspend making payments to all or some of that Party’s creditors.

1.1.31 "Intellectual Property" means Patent Rights, utility models, registered designs, unregistered design rights, registered and unregistered copyrights, Know-How,
Confidential Information, database rights, any rights in clinical study results, applications for and the right to apply for any such rights, and any similar or analogous rights anywhere worldwide. Intellectual Property does not include Trademarks.

1.1.32 **Know-How** means all clinical data, technical information, know-how, data and materials, including inventions (whether patentable or not), discoveries, trade secrets, specifications, instructions, processes, formulae, materials, cell banks and other cellular materials, expertise and other technology applicable to compounds, molecules, cell lines, formulations, compositions, products or to their manufacture, development, registration, use or commercialization or methods of assaying or testing them or processes for their manufacture, formulations containing them, compositions incorporating or comprising them and including all biological, chemical, pharmacological, biochemical, toxicological, pharmaceutical, physical and analytical, safety, quality control, manufacturing, preclinical and clinical data, and regulatory data rights, and instructions, processes, formulae, expertise and information, regulatory filings and copies thereof, relevant to the development, manufacture, use or commercialization of and/or which may be useful in studying, testing, development, production or formulation of products, or intermediates for the synthesis thereof.

1.1.33 **Law** means all laws, statutes, rules, regulations, orders, judgments, injunctions or ordinances of any Governmental Authority.

1.1.34 **Luxturna** means Spark’s proprietary Gene Therapeutic, *voretigene neparvovec*, which is known in the U.S. by the trade name *Luxturna™*.

1.1.35 **Manufacturing** or **Manufacture** means activities directed to producing, manufacturing, processing, sourcing of materials, filling, finishing, packaging, labeling, quality assurance testing and release, shipping, storage, quality control testing (including in-process, release and stability testing), supplying, shipping and release thereof.

1.1.36 **Net Sales** means the gross sales amounts invoiced by Novartis or any of its Affiliates or Sublicensees for Luxturna sold to Third Parties (including to Distributors, but excluding to Deemed Sublicensee Distributors) in *bona fide*, arms-length transactions, as determined in accordance with Novartis’ Accounting Standards as consistently applied, less a deduction of [**] percent ([***%]) for direct expenses related to the sale of Luxturna for distribution and warehousing expenses and for uncollectible amounts on previously-sold products and the following deductions booked on an accrual basis by Novartis and its Affiliates under the applicable Accounting Standards:

(a) normal and customary trade and cash discounts, actually allowed and properly taken, directly with respect to sales of Luxturna;

(b) amounts repaid or credited by reasons of defects, rejections, recalls or returns;

(c) rebates and chargebacks to customers and Third Parties (including, without limitation, Medicare, Medicaid, Managed Healthcare and similar types of rebates);
(d) amounts provided or credited to customers through coupons and other discount programs;

(e) delayed ship order credits, discounts or payments related to the impact of price increases between purchase and shipping dates or retroactive price reductions;

(f) customary fee for service payments paid to Distributors for maintaining agreed inventory levels and providing information; and

(g) other reductions or specifically identifiable amounts deducted for reasons substantially similar to those listed above in accordance with Novartis’ Accounting Standards.

In the case of any sale or other disposal of Luxturna between or among Novartis and its Affiliates or Sublicensees, for resale, Net Sales shall be calculated only on the value charged or invoiced on the first arm’s-length sale thereafter to a Third Party.

In the case of any sale which is not invoiced or is delivered before invoice, Net Sales shall be calculated at the time all the revenue recognition criteria required by Novartis’s Accounting Standards are met.

In the case of any sale or other disposal for value, such as barter or counter-trade, of Luxturna, or part thereof, other than in an arm’s length transaction exclusively for money, Net Sales shall be calculated on the value of the non-cash consideration received or the fair market price (if higher) of Luxturna in the country of sale or disposal.

For the avoidance of doubt, sales between Novartis, its Affiliates and Sublicensees shall not be considered Net Sales (unless such Person is the end user of Luxturna), but subsequent sales by Novartis, its Affiliates and Sublicensees to Third Party customers shall be included in the calculation of Net Sales.

In the event Luxturna is sold as a Combination Product, the calculation of Net Sales for Luxturna will be agreed by the Parties based on the [**].

1.1.37 “Novartis IP” means Intellectual Property in any country of the world that is: (i) Controlled by Novartis as of the Effective Date or thereafter during the Term; and (ii) conceived, reduced to practice, authored, created, developed or in-licensed by Novartis in the performance of its obligations under this Agreement or used by Novartis in exercise of Novartis’ rights under this Agreement in the Novartis Territory; and (iii) reasonably necessary or useful for the Development or Commercialization of Luxturna in the Field. The term Novartis IP shall not include Novartis’ rights in the Joint IP.

1.1.38 “Novartis Territory” means the entire world, excluding the Spark Territory.

1.1.39 “Parties” means Spark and Novartis.
1.1.40 “Party” means either Spark or Novartis.

1.1.41 “Patent Rights” means patents and patent applications, including all substitutions, divisions, continuations, continuations-in-part, reissues, reexaminations, additions, renewals, registrations, utility models, design patents and extensions (including supplemental protection certificates) thereof, and all counterparts thereof in any country.

1.1.42 “Person” means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government, or any agency or political subdivisions thereof.

1.1.43 “Post-Approval Commitments” means, with respect to a country, clinical studies, other clinical activities or other activities that either Party is required by the applicable Regulatory Authority or otherwise commits to perform after obtaining Regulatory Approval for Luxturna in such country.

1.1.44 “Product Trademark” means (a) the “Luxturna” Trademark and (b) any other Trademark that is approved by Novartis, after consultation with but not approval by the JSC, for use in connection with the Commercialization of Luxturna in the Novartis Territory. The term Product Trademark shall not include the corporate names or logos of either Party.

1.1.45 “Regulatory Approval” means the approval of the applicable Regulatory Authority necessary for the marketing and sale of a pharmaceutical product in a country (including, without limitation, the grant of manufacturing authorizations approval of all sites at which Luxturna will be Manufactured by or for Spark) by the relevant Regulatory Authority, excluding separate pricing or reimbursement approvals that may be required, as it may be amended or updated from time to time.

1.1.46 “Regulatory Authority” means any federal, national, multinational, state, provincial or local regulatory agency, department, bureau or other governmental entity with authority over the marketing and sale of a pharmaceutical product in a country.

1.1.47 “Regulatory Exclusivity” means, with respect to any country in the Novartis Territory, an additional market protection, other than patent protection, granted by a Regulatory Authority in such country which confers an exclusive Commercialization period during which Novartis, its Affiliates or sublicensees have the exclusive right to market and sell Luxturna in such country or other jurisdiction through a regulatory exclusivity right (e.g., new biologic entity exclusivity, new use or indication exclusivity, new formulation exclusivity, orphan drug exclusivity, pediatric exclusivity, or any applicable data exclusivity).

1.1.48 “Related Agreements” means any additional agreements that the Parties enter into relating to this Agreement, including the Supply Agreement, the Quality Agreement, the Pharmacovigilance Agreement and any agreements related thereto.

1.1.49 “Royalty Region” means each of the following [**] geographical regions, without duplication: [**].
1.1.50 "Royalty Term" means, with respect to a Royalty Region, the Base Royalty Term plus the Continued Royalty Term.

1.1.51 "Royalty Termination Event" means, with respect to a Royalty Region, and after expiration of the Base Royalty Term in such Royalty Region (without regard to the extension of Regulatory Exclusivity within an individual country in such Royalty Region), (a) the first occurrence of aggregate Net Sales in such Royalty Region falling below $[*] per Calendar Year or (b) a Supply Transition Event (as defined in the Supply Agreement), and a subsequent transition of Manufacturing rights to Novartis pursuant to Article 9 of the Supply Agreement as a consequence of such Supply Transition Event, occurs. For clarity, following a Royalty Termination Event, any Continued Royalty Term terminated thereby with respect to an applicable Royalty Region shall be fully exhausted and shall not be subject to reinstatement.

1.1.52 "Spark Change in Control" means any transaction or series of related transactions in which a Third Party (or group of Third Parties acting in concert) (a) acquires or becomes the beneficial owner of more than fifty percent (50%) of the outstanding voting securities of Spark, (b) becomes the surviving entity in any merger, consolidation, reorganization, tender offer or similar transaction to which Spark is a party, or as a result of which more than fifty percent (50%) of the total voting power of the stock outstanding of the surviving entity normally entitled to vote in elections of directors is not held by the Persons holding at least fifty percent (50%) of the outstanding shares of Spark preceding such transaction, or (c) acquires or otherwise receives the benefit of all or substantially all of the assets of Spark, including the rights to Luxturna for the Spark Territory.

1.1.53 "Spark IP" means the Intellectual Property that is Controlled by Spark as of the Effective Date or during the Term and reasonably necessary or useful for the Development or Commercialization of Luxturna in the Field in the Novartis Territory. The term Spark IP shall not include any Spark Manufacturing IP.

1.1.54 "Spark Manufacturing IP" means the Intellectual Property that is Controlled by Spark and reasonably necessary or useful for the Manufacture of Luxturna.

1.1.55 "Spark Territory" means the United States.

1.1.56 "Sublicensee" means any Person, other than an Affiliate or a distributor, to which a Party grants a sublicense of any right granted to such Party hereunder.

1.1.57 "Supply Agreement" means an agreement between the Parties entered into as of the Effective Date pursuant to which Spark shall Manufacture Luxturna and related products (e.g., diluent) for Commercialization by Novartis.

1.1.58 "Technical Development" means technical and CMC-related activities, including, without limitation, test method development and stability testing, assay development, process development (including life cycle management activities), formulation development, quality assurance and quality control development, validation and other testing,
packaging development, as well as record-keeping, data and database development, management, storage and retention activities relating to any of the foregoing.

1.1.59 "Third Party" means any Person other than a Party or any of its Affiliates.

1.1.60 "Third Party IP" means Intellectual Property owned or controlled by any Third Party relating to the subject matter of this Agreement as of the Effective Date or thereafter during the Term.

1.1.61 "Trademark" means any and all trademarks of every kind and nature, however designated, whether arising by operation of law, contract, license or otherwise, whether or not registered or unregistered, including product names, trade names, service marks, logos, program names, taglines, slogans, trade dress, and any other indicia of origin, including all related rights thereto, such as copyrights and design rights (including design patents rights) in pictures, logos, icons, drawings and the like, and any similar or analogous rights anywhere worldwide.

1.1.62 "United States" or "U.S." means the United States of America and its territories and possessions.

1.2 Additional Definitions. The definition of each of the following terms is set forth in the Section of this Agreement or the Supply Agreement as indicated below:

<table>
<thead>
<tr>
<th>Term</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974 Convention</td>
<td>12.1</td>
</tr>
<tr>
<td>Agreement</td>
<td>Preamble</td>
</tr>
<tr>
<td>Alliance Manager</td>
<td>2.2</td>
</tr>
<tr>
<td>Auditor</td>
<td>6.5</td>
</tr>
<tr>
<td>Breaching Party</td>
<td>10.2</td>
</tr>
<tr>
<td>Capacity Plan</td>
<td>Supply Agreement</td>
</tr>
<tr>
<td>CDA</td>
<td>12.5</td>
</tr>
<tr>
<td>CHOP Agreement</td>
<td>Exhibit 1.1.21</td>
</tr>
<tr>
<td>Code</td>
<td>3.3</td>
</tr>
<tr>
<td>Confidential Information</td>
<td>8.1</td>
</tr>
<tr>
<td>Created</td>
<td>7.1.2(a)</td>
</tr>
<tr>
<td>Deemed Sublicensee Distributor</td>
<td>1.1.16</td>
</tr>
<tr>
<td>Effective Date</td>
<td>Preamble</td>
</tr>
<tr>
<td>Existing Luxturna Clinical Program</td>
<td>4.3.1</td>
</tr>
<tr>
<td>Indemnification Claim Notice</td>
<td>9.11.3(a)</td>
</tr>
<tr>
<td>Indemnified Party</td>
<td>9.11.3(a)</td>
</tr>
<tr>
<td>Indemnifying Party</td>
<td>9.11.3(a)</td>
</tr>
<tr>
<td>Independent Patent Counsel</td>
<td>7.4</td>
</tr>
<tr>
<td>Invalidity Claim</td>
<td>7.3.7</td>
</tr>
<tr>
<td>Joint IP</td>
<td>7.1.2(b)</td>
</tr>
<tr>
<td>Term</td>
<td>Section</td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Joint Patent Rights</td>
<td>7.2.3</td>
</tr>
<tr>
<td>JSC</td>
<td>2.1.1</td>
</tr>
<tr>
<td>NIH Agreement</td>
<td>Exhibit 1.1.21</td>
</tr>
<tr>
<td>Non-Breaching Party</td>
<td>10.2</td>
</tr>
<tr>
<td>Notice of Dispute</td>
<td>11.1.1</td>
</tr>
<tr>
<td>Novartis</td>
<td>Preamble</td>
</tr>
<tr>
<td>Novartis Indemnified Parties</td>
<td>9.11.1</td>
</tr>
<tr>
<td>Novartis Patent Rights</td>
<td>7.2.1</td>
</tr>
<tr>
<td>Novartis Territory</td>
<td>5.1</td>
</tr>
<tr>
<td>Pharmacovigilance Agreement</td>
<td>4.5.1</td>
</tr>
<tr>
<td>Product(s)</td>
<td>Supply Agreement</td>
</tr>
<tr>
<td>Promotional Materials</td>
<td>5.3</td>
</tr>
<tr>
<td>Quality Agreement</td>
<td>5.6</td>
</tr>
<tr>
<td>Severed Clause</td>
<td>12.4</td>
</tr>
<tr>
<td>Spark</td>
<td>Preamble</td>
</tr>
<tr>
<td>Spark Indemnified Parties</td>
<td>9.11.2</td>
</tr>
<tr>
<td>Spark Patent Rights</td>
<td>7.2.2</td>
</tr>
<tr>
<td>Status Report</td>
<td>2.1.5</td>
</tr>
<tr>
<td>Supply Agreement</td>
<td>5.6</td>
</tr>
<tr>
<td>Supply Transition Event</td>
<td>Supply Agreement</td>
</tr>
<tr>
<td>Term</td>
<td>10.1</td>
</tr>
<tr>
<td>Terminated Country</td>
<td>4.1.1</td>
</tr>
<tr>
<td>UPenn Agreement</td>
<td>Exhibit 1.1.21</td>
</tr>
</tbody>
</table>

1.3 **Interpretation.** The definitions of the terms herein shall apply equally to the singular and plural forms of the terms defined. Whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms. The words “include”, “includes” and “including” shall be deemed to be followed by the phrase “without limitation”. The word “will” shall be construed to have the same meaning and effect as the word “shall.” The headings contained in this Agreement or any Exhibit and in the table of contents to this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Agreement. All dollar ($) amounts specified in this Agreement are United States dollar amounts. Unless the context requires otherwise, (a) any definition of or reference to any agreement, instrument or other document herein shall be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth therein); (b) the words “herein”, “hereof” and “hereunder”, and words of similar import, shall be construed to refer to this Agreement in its entirety and not to any particular provision hereof; (c) the word “extent” in the phrase “to the extent” means the degree to which a subject or other thing extends and such phrase does not mean simply “if”; (d) the word “or” shall be inclusive and not exclusive (i.e., “and/or”); (e) any reference to any Law refers to such Law as from time to time enacted, repealed or amended; (f) the word “notice” shall mean notice in writing (whether or not specifically stated) and shall include notices, consents,
approvals and other written communications contemplated under this Agreement; (g) provisions that require that a Party or the Parties hereunder “agree,” “consent” or “approve” or the like shall require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter, approved minutes or otherwise; (h) words using the singular or plural number also include the plural or singular number, respectively; and (i) all references herein to ARTICLES, Sections or Exhibits shall be construed to refer to ARTICLES, Sections and Exhibits of this Agreement. All Exhibits attached hereto or referred to herein are hereby incorporated in and made a part of this Agreement as if set forth in full herein. Any capitalized terms used in the Exhibits attached hereto but not otherwise defined therein shall have the meaning as defined in this Agreement. In the event of an ambiguity or a question of intent or interpretation, this Agreement shall be construed as if drafted jointly by the Parties and no presumption or burden of proof shall arise favoring or disfavoring either Party by virtue of the authorship of any provision of this Agreement.

ARTICLE 2
GOVERNANCE

2.1 Joint Steering Committee.

2.1.1 Formation; Purposes and Principles. Within [**] after the Effective Date, Spark and Novartis shall establish a joint steering committee (the “JSC”), which shall serve as a forum for the Parties to coordinate their respective activities and exchange appropriate information regarding their respective regulatory, Development, Commercialization and Manufacturing activities with respect to Luxturna. For clarity, the role of the JSC will be limited to coordination and exchange of information, and it shall have no decision-making power or authority except as expressly provided in Section 2.1.3. The JSC may, in its discretion, form sub-teams or subcommittees to address any of the issues within its purview.

2.1.2 Membership. The JSC shall be composed of three (3) representatives and an Alliance Manager appointed by each of Spark and Novartis who are [**] sufficient authority, relevant knowledge and expertise in the Development, Commercialization and Manufacturing activities of Luxturna. The initial members of the JSC from each Party shall be selected and identified to the other Party within [**] after the Effective Date or such later date as the Parties may agree. Each Party may replace any of its JSC representatives at any time upon written notice (e.g., by e-mail) to the other Party.

2.1.3 Consultative Purview of the JSC. The Parties agree that the JSC is not intended to and does not have any approval right and/or power over a Party’s activities or decisions related to the territory of such Party except as expressly detailed below. It is intended to be a consultative forum for coordination and exchange of certain information. The JSC shall discuss and coordinate on the following topics:

(a) the general strategy for seeking and obtaining Regulatory Approval in the Novartis Territory;
(b) the general strategy for pricing and reimbursement approval and the general strategy for discounting of Luxturna in the Parties’ respective territories;

(c) each Party’s free goods and compassionate use policy with respect to Luxturna for its respective territory, and such Party’s implementation of such policy;

(d) the Luxturna positioning and branding strategy for each Party’s Territory, including such Party’s strategies with respect to regional or local publications and Product Trademarks;

(e) the Development Plan and substantive updates or amendments thereof, including Technical Development conducted by the Parties pursuant to Section 4.1.2;

(f) pharmacovigilance matters pursuant to the Pharmacovigilance Agreement;

(g) each Party’s plans and strategies with respect to such Party’s presence at international congresses and conventions and other medical education activities; and

(h) joint activities, or activities of one Party to support activities of the other Party, under the Development Plan.

Without limiting the foregoing, the Parties acknowledge and agree that certain issues may have an impact on both the Novartis Territory and the Spark Territory. The following three items (x), (y) and (z) may be discussed at meetings of the JSC, but, in the event that the JSC is unable to resolve any such issue to the satisfaction of the Parties within [**], such issue shall be treated as a dispute and either Party may evoke the dispute resolution procedures set forth in ARTICLE 11.

(x) Issues arising with respect to obtaining the EU Regulatory Approval and the Parties’ obligations pursuant to Section 4.4.1(a).

(y) Issues arising under the Supply Agreement, including, without limitation, disagreements regarding supply price increases (including the Fixed Facility Fee), the annual review of numbers of Resulting Vials of Drug Product from each Batch of Drug Substance (as such capitalized terms are defined in the Supply Agreement) for the previous calendar year, as required by Section 2.5 of the Supply Agreement, capacity restrictions leading to supply shortages and, for a period of [**] following the Effective Date, review of the Capacity Plan.

(z) Bona fide scientific or safety concerns of a Party [**].

Notwithstanding the foregoing, neither Party shall have final decision-making authority with respect to the interpretation of, or either Party’s rights or obligations under, this Agreement or the Supply Agreement.

2.1.4 Meetings of the JSC. The JSC shall hold meetings at such times as the Parties shall mutually determine, but in no event shall such meetings of the JSC be held less
frequently than [**] during the Term. Other representatives of each Party or of Third Parties involved in the Development or Commercialization of Luxturna may attend meetings of the JSC as observers with the consent of each Party. Meetings of the JSC may be held in person, or by audio or video teleconference, as may be agreed by the Parties. Each Party shall be responsible for all of its own expenses of participating in the JSC.

2.1.5 **Status Reports.** At least [**] prior to each semiannual JSC meeting, each Party shall submit to the JSC a status report summarizing its contemplated and completed Development and Commercialization activities with respect to Luxturna in the applicable territory in the period following the previously-held JSC (each, a “**Status Report**”). Such Status Report shall include, at a minimum, information reasonably necessary to enable the JSC to discuss the matters set forth in Section 2.1.3. The JSC shall review and discuss, and may provide comments on, each Status Report, and the preparing Party shall reasonably consider all such comments.

2.1.6 **Dissolution.** Notwithstanding anything herein to the contrary, at any time following [**]. In the event that [**], the Parties will [**]. In any event, [**].

2.2 **Alliance Managers.** Each Party shall designate a single alliance manager for all of the activities contemplated under this Agreement (each, an “**Alliance Manager**”) who shall have sufficient seniority, experience and knowledge appropriate for managers with such project management responsibilities. Such Alliance Managers will be responsible for the day-to-day worldwide coordination of the collaboration contemplated by this Agreement and will serve to facilitate communication between the Parties. In addition, the Alliance Managers shall be responsible for calling JSC meetings, preparing and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting. Each Party may change its designated Alliance Manager from time to time upon notice (e.g., by e-mail) to the other Party.

**ARTICLE 3**

**LICENSES; OPTIONS; OTHER RIGHTS**

3.1 **Grants by Spark.**

3.1.1 **Development and Commercialization License.** Subject to the terms and conditions of this Agreement, Spark hereby grants to Novartis (i) an exclusive (even as to Spark and its Affiliates) right and license, with the right to grant sublicenses as set forth in Section 3.1.5 and 3.1.6, under the Spark IP and Spark’s interest in the Joint IP, to Develop, have Developed, Commercialize and have Commercialized Luxturna in the Field for the Novartis Territory, and (ii) a non-exclusive right and license under the Spark Manufacturing IP and Spark’s interest in the Joint IP to perform Technical Development activities with respect to life cycle management pursuant to Section 4.1.2(a)(iii) for the Development and Commercialization of Luxturna in the Field for the Novartis Territory. For the avoidance of doubt, except (a) following a Supply Transition Event and a subsequent transition of Manufacturing rights to Novartis pursuant to Article 9 of the Supply Agreement as a consequence of such Supply Transition Event or (b) with respect to Novartis’ packaging rights and responsibilities set forth in the Supply Agreement, the license granted to Novartis hereunder does not include any Manufacturing rights directed towards Manufacturing Drug Substance (as defined under the Supply Agreement); however, following a Supply Transition
Event and a subsequent transition of Manufacturing rights to Novartis pursuant to Article 9 of the Supply Agreement as a consequence of such Supply Transition Event, such license automatically shall be expanded, without further action of the Parties, to include the right and license (such license to be commensurate in scope with the license grant set forth in the first sentence of this section), under the Spark Manufacturing IP, to Manufacture Luxturna for sale in the Novartis Territory.

3.1.2 **Study Data License**. Subject to the terms and conditions of this Agreement, Spark hereby grants to Novartis an exclusive (even as to Spark and its Affiliates) right and license, with the right to grant sublicenses as set forth in Section 3.1.5, under Spark’s rights in study data Controlled by Spark from any clinical trials of Luxturna, solely to use such study data to Develop and Commercialize Luxturna in the Field for the Novartis Territory (including the right to cross reference or include such study data in regulatory filings made with Regulatory Authorities for the Novartis Territory). In addition, Novartis shall have the right to use any information concerning any adverse events, and any product quality and product complaints involving adverse events, related to Luxturna, to enable Novartis (or its applicable Affiliate or Sublicensee) to comply with its legal and regulatory obligations.

3.1.3 **Post-Royalty Term License**. Each license granted in Section 3.1.1 and 3.1.2 shall automatically convert, on a Royalty Region-by-Royalty Region basis, to a fully paid-up, non-royalty bearing, perpetual, non-exclusive license upon the expiration of the Royalty Term applicable to such Royalty Region (but not upon an earlier termination of this Agreement). For the avoidance of doubt, as to any country for which the Base Royalty Term is extended because of Regulatory Exclusivity in such country, the license granted in this Section 3.1.3 shall not take effect prior to the expiration of the Base Royalty Term in such country.

3.1.4 **Trademark License**. Subject to the terms and conditions of this Agreement, Spark hereby grants to Novartis an exclusive right and license, with the right to grant sublicenses as set forth in Section 3.1.5, to use any Product Trademark Controlled by Spark in connection with Developing and Commercializing Luxturna in the Field for the Novartis Territory.

3.1.5 **Sublicenses**. Novartis may, subject to Section 3.1.6, sublicense the rights granted to it by Spark under this Agreement at any time at its sole discretion. In any sublicense granted by Novartis, Novartis will include provisions that require the Sublicensee to satisfy the obligations under the Existing Spark Agreements specified in Section 3.1.6 and all applicable obligations under future Spark in-license agreements under which Novartis elects to receive sublicenses pursuant to Section 3.2.4. Novartis shall notify Spark in writing of the identity of each Sublicensee within [**] following the grant of any sublicense hereunder, and shall notify Spark in writing of the termination of any sublicense agreement within [**] following such termination. In addition, as provided in more detail in Section 12.8, Novartis may subcontract to Third Parties the performance of Novartis’ tasks and obligations with respect to the Development and Commercialization of Luxturna (and, subject to the applicable terms of the Supply Agreement, the Manufacture of Luxturna following a Supply Transition Event) as Novartis deems appropriate.

3.1.6 **Third Party Licenses**. The licenses granted by Spark hereunder may include sublicenses under the Existing Spark Agreements. Spark has, prior to the Effective Date, provided Novartis with copies of the Existing Spark Agreements. Novartis acknowledges that its
rights with respect to such Spark IP are subject to the terms and conditions of the applicable Existing Spark Agreements, including rights reserved to Third Parties set forth therein. However, the Parties agree that no such in-licensed Spark IP or Spark Manufacturing IP shall be licensed to Novartis, and the provisions of this Section 3.1.6 shall not apply to Novartis with respect thereto, until such time as Spark provides to Novartis a written description of the Spark IP and Spark Manufacturing IP, as applicable, in-licensed pursuant to each Existing License Agreement and Novartis accepts in writing that it desires to receive a sublicense to such Spark IP and Spark Manufacturing IP, as applicable.

(a) Novartis acknowledges that the licenses granted to Spark under the NIH Agreement are non-exclusive. Novartis shall comply with, and shall require its Sublicensees to comply with, the terms and conditions of such Existing Spark Agreements that are applicable to Novartis and its Sublicensees thereunder, including: (a) Sections 1.3, 1.4, 1.5, 4.3, 4.4, 6.5, 6.6 and 10 of the UPenn Agreement and (b) Sections 4.2, 4.4, 5.1-5.2, 8.1, 10.1, 10.2, 12.5, and 13.7-13.9 of the NIH Agreement, the text of which Sections are set forth on Exhibit 3.1.6 in compliance with Section 4.3 of the NIH Agreement.

(b) In addition, in the event that the licenses granted by Spark hereunder expand to include the Spark Manufacturing IP, the following provisions of this Section 3.1.6(b) shall apply solely to the extent that Novartis is exercising a sublicense to the applicable Patent Rights licensed to Spark pursuant to the applicable Existing Spark Agreement: (x) Novartis shall comply with, and shall require its Sublicensees to comply with, Sections 4.2, 4.4, 5.1-5.2, 7.1, 8.1, 10.1, 10.2, 10.3, 11.3-11.5, 12.5, 12.6 and 14.13 of the CHOP Agreement, (y) Novartis shall report to Spark the date of the First Commercial Sale in each country in the Novartis Territory occurring after such license expansion within [**] of such occurrence and (z) HHMI shall become an intended Third Party beneficiary of this Agreement for the purpose of enforcing HHMI’s rights, including indemnification and insurance provisions, under the CHOP Agreement. Notwithstanding anything to the contrary in this Agreement, Novartis shall have no obligation for any milestone, royalty and other payment obligations payable under the Existing Spark Agreements.

3.1.7 Rights Retained by Spark. Novartis shall receive only those rights of Spark expressly granted by Spark under the provisions of this Agreement, and any right of Spark not expressly granted to Novartis under the provisions of this Agreement shall be retained by Spark, including the sole right to Manufacture Luxturna for the Spark Territory and the Novartis Territory (except as expressly provided in Section 3.1.1).

3.2 Grants by Novartis.

3.2.1 Development and Commercialization Licenses. Subject to the terms and conditions of this Agreement, Novartis hereby grants to Spark:

(a) a non-exclusive, royalty-free, fully paid-up right and license, with the right to grant sublicenses, under the Novartis IP and Novartis’ interest in the Joint IP, to perform Spark’s obligations under this Agreement;

-17-
(b) a non-exclusive, royalty-free, fully paid-up right and license, with the right to grant sublicenses, under the Novartis IP and Novartis’ interest in the Joint IP to Develop and Commercialize Luxturna in the Field in the Spark Territory; and

c) a non-exclusive, worldwide, royalty-free, fully paid-up right and license, with the right to grant sublicenses under any Novartis IP or Novartis’ interest in any Joint IP developed as a result of Technical Development activities for which Spark pays [**] percent ([**]%) of the costs pursuant to Section 4.1.2(c) to Develop, Commercialize, Manufacture or otherwise exploit any product in any field.

3.2.2 Study Data License. Subject to the terms and conditions of this Agreement, Novartis hereby grants to Spark, an exclusive (even as to Novartis and its Affiliates), royalty-free, fully paid-up right and license, with the right to grant sublicenses, under Novartis’ rights in study data controlled by Novartis from any clinical trials of Luxturna conducted pursuant to this Agreement, solely to use such study data to Develop and Commercialize Luxturna in the Field for the Spark Territory (including the right to cross reference or include such study data in filings made with Regulatory Authorities for the Spark Territory). In addition, Spark shall have the right to use any information concerning any adverse events, and any product quality and product complaints involving adverse events, related to Luxturna, sufficient to enable Spark (or its applicable Affiliate or Sublicensee) to comply with its legal and regulatory obligations.

3.2.3 Rights Retained by Novartis. Spark shall receive only those rights of Novartis expressly granted by Novartis under the provisions of this Agreement, and any right of Novartis not expressly granted to Spark under the provisions of this Agreement shall be retained by Novartis.

3.2.4 Future In-License Agreements.

(a) [**].

(i) [**], the Parties shall [**].

(ii) [**] the Parties [**], a Party [**].

(b) Other Patent Rights.

(i) If [**] desires to enter any Third Party agreement for any Third Party Patent Right determined by [**] to be desirable (but not necessary) for the Development or Commercialization of Luxturna for the Novartis Territory, it shall provide written notice of such desire to the [**]. If the [**] agrees, in its reasonable discretion, that such Third Party Patent Rights are desirable for the Development or Commercialization of Luxturna for the Novartis Territory, then the [**] shall have the first right to enter into such a license. If the [**] determines to enter into such a license, then prior to doing so it shall provide the [**] with a reasonable opportunity to review and comment on the proposed terms of such license that are applicable to the [**] shall use reasonable efforts to negotiate the terms of such license accordingly. If neither the [**] nor any of its Affiliates enters into a Third Party agreement for such Third Party Patent Rights within [**] or,
if the [**] is using Commercially Reasonable Efforts to negotiate such Third Party Agreement, [**], or if the [**] provides written notice to the [**] that it does not intend to enter a license agreement for such Third Party Patent Rights, then the [**] may enter an agreement to obtain such a license.

(ii) If Spark enters into an agreement pursuant to Section 3.2.4(a) or 3.2.4(b)(i), and the agreement provides for a license under such Third Party Patent Rights in the Novartis Territory, then Spark shall inform Novartis and shall provide Novartis with a copy of such license. If Novartis notifies Spark in writing that it wishes to obtain a sublicense of such rights in the Novartis Territory, Spark shall grant such a sublicense to Novartis, and Novartis will be bound by the rights and obligations of such license as they apply to Novartis as a sublicensee, including all payment obligations that would be due under such agreement as a result of the sublicense thereof granted to Novartis and Novartis’ exercise of such sublicensed rights, which amounts Novartis shall pay within [**] after receipt of invoice from Spark in respect thereof (or such shorter period as may be necessary to enable Spark to timely pay the applicable upstream licensor).

(iii) If Novartis enters into an agreement pursuant to Section 3.2.4(a) or 3.2.4(b)(i), then Novartis [**]. If the agreement provides for a license under such Third Party Patent Rights in the Spark Territory, then Novartis shall inform Spark and shall provide Spark with a copy of such license. If Spark notifies Novartis in writing that it wishes to obtain a sublicense of such rights in the Spark Territory, Novartis shall grant such a sublicense to Spark, and Spark will be bound by the rights and obligations of such license as they apply to Spark as a sublicensee, including all payment obligations that would be due under such agreement as a result of the sublicense thereof granted to Spark and Spark’s exercise of such sublicensed rights.

(iv) Novartis shall have the right to deduct from royalty payments due under Section 6.3 [**] percent ([**]% of the amounts paid (including upfront license fees, milestone payments and royalties) by Novartis in respect of Third Party Patent Rights licensed or sublicensed to Novartis for the Novartis Territory in accordance with Section 3.2.4(a) or this 3.2.4(b); [**].

3.3 **Section 365(n) of the U.S. Bankruptcy Code.** For purposes of Section 365(n) of the U.S. Bankruptcy Code (the “Code”) and any similar laws in any other country, all rights and licenses granted under or pursuant to any Section of this Agreement are rights to “intellectual property” (as defined in Section 101(35A) of the Code). The Parties agree that the licensee of such rights under this Agreement will retain and may fully exercise all of its protections, rights and elections under the Code and any similar laws in any other country. Each Party hereby acknowledges that (a) copies of research data, (b) laboratory samples, (c) product samples, (d) formulas, (e) laboratory notes and notebooks, (f) data and results related to clinical trials, (g) regulatory filings and approvals, (h) rights of reference in respect of regulatory filings and approvals, (i) pre-clinical research data and results, and (j) marketing, advertising and promotional materials, in each case, that relate to such intellectual property, constitute “embodiments” of such intellectual property pursuant to Section 365(n) of the Code, and that the licensee will be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and the same, if not already in its possession, will be promptly delivered to it (i) upon any such commencement of a bankruptcy proceeding upon its written request therefor,
unless the licensor elects to continue to perform all of its obligations under this Agreement, or (ii) if not delivered under (i) above, upon written request therefor by the licensee following the rejection of this Agreement by or on behalf of the licensor. The provisions of this Section 3.3 are without prejudice to any rights the non-subject Party may have arising under the Code, Laws of other jurisdictions governing insolvency and bankruptcy, or other applicable Law. The Parties agree that they intend the following rights to extend to the maximum extent permitted by law, including for purposes of the Code and any similar laws in any other country: (x) the right of access to any intellectual property (including all embodiments thereof) of the licensor, or any Third Party with whom the licensor contracts to perform an obligation of such licensor under this Agreement which is necessary for the Development or Commercialization of Luxturna; (y) the right to contract directly with any Third Party described in (x) to complete the contracted work, and (z) the right to cure any breach of or default under any such agreement with a Third Party and set off the costs thereof against amounts payable to such licensor under this Agreement.

ARTICLE 4
DEVELOPMENT, TECHNICAL DEVELOPMENT, AND REGULATORY ACTIVITIES

4.1 General.

4.1.1 Development Activities. Novartis shall use Diligent Efforts to Develop and seek Regulatory Approval for Luxturna in the Novartis Territory. Novartis shall conduct such Development in accordance with the Development Plan (including any timelines specified therein), and shall conduct all such Development activities in accordance with applicable Laws and, as applicable, Good Laboratory Practice and Good Clinical Practice. Subject to Section 3.1.7, Novartis shall be free to perform any Development activities for Luxturna for the Novartis Territory. Without limiting the foregoing, in the event that (a) [**], or (b) [**] (a “Terminated Country”), (i) [**]; (iii) such Terminated Country shall be excluded from the scope of the licenses granted to Novartis in Section 3.1.1 and 3.1.2, and thereafter the “Novartis Territory” shall be deemed to exclude such Terminated Country(ies) and the “Spark Territory” shall be deemed to include such Terminated Country(ies); and (iv) the consequences set forth in Section 10.7.3 shall apply with respect to such Terminated Country(ies).

4.1.2 Technical Development Activities.

(a) In each case to the extent set forth in the Development Plan (as discussed by the JSC):

(i) Spark shall undertake Technical Development activities related to obtaining or maintaining Regulatory Approvals;

(ii) Spark shall undertake Technical Development activities related to [**]; and

(iii) the Parties shall undertake Technical Development activities in respect of [**]. Acknowledging that Spark Controls the Spark Manufacturing IP (and that Novartis does not have access to or rights to exercise the Spark Manufacturing IP except as specifically
provided in Section 3.1.1), Spark shall provide reasonable assistance and support to Novartis with respect to Novartis’ Technical Development activities.

(b) Each Party shall use commercially reasonable efforts to perform its obligations pursuant to this Section 4.1.2, and shall conduct all such Technical Development activities in accordance with applicable Laws.

(c) Novartis shall bear the costs of all Technical Development activities (except as otherwise expressly stated in Section 4.4.2), provided, however, that if Spark decides to use any developments or improvements resulting from such Technical Development within the Spark Territory, it shall [**]. For clarity, nothing in this Section 4.1.2(c) shall prejudice or otherwise override any cost sharing provisions of the Supply Agreement [**].

(d) For clarity, Spark shall not have an obligation to perform Technical Development included in any Development Plan or amendment to any Development Plan unless and until Spark has agreed to undertake such obligation.

4.2 Development Plan.

4.2.1 Both Parties may propose Development and Technical Development activities under the Development Plan. Novartis shall provide to Spark a preliminary Development Plan for [**] within [**] of the Effective Date, and shall update the Development Plan to reflect intended Development activities with respect to [**] within [**] of the Effective Date. In addition, subject to Section 4.4.2, if Novartis is required to conduct further Development of the Product for the EU following EU Regulatory Approval, including to satisfy Post-Approval Commitments to Regulatory Authorities, to seek label expansions or otherwise for product life cycle management purposes, Novartis shall provide to Spark a Development Plan for such activities. Either Party may propose a plan for Technical Development.

4.2.2 Updates to the Development Plan will be prepared by Novartis and discussed by the JSC on at least [**] basis. Subject to Section 4.1.2(d), the Parties shall use commercially reasonable efforts to perform activities allocated to such Party in the Development Plan.

4.2.3 The Parties expressly acknowledge and agree that there is no guarantee of a successful Development and that any Development program contains inherent risks. Novartis shall not be liable for failures to meet specified timeframes in the Development Plan due to technical impossibility or causes outside its reasonable control or caused by the other Party.

4.2.4 For the avoidance of doubt, nothing in this Section 4.2 grants the JSC an approval right or requires Novartis to Develop, seek Regulatory Approval and/or Commercialize Luxturna in a specific country(ies) or region(s).
4.3 Development Studies.

4.3.1 Spark Territory. Prior to the Effective Date, Spark has independently initiated ongoing clinical studies in the United States of Luxturna to support Spark’s efforts to obtain EU Regulatory Approval and Regulatory Approval in the Spark Territory (collectively, the “Existing Luxturna Clinical Program”). Novartis acknowledges and agrees that Spark will lead, control and be responsible for the continued execution of such clinical studies and any other studies that Spark determines are necessary or desirable for Regulatory Approval or Commercialization in the Spark Territory. Without limiting Section 4.4.1(a), Spark shall consider in good faith Novartis’ comments relating to the Existing Luxturna Clinical Program and such other studies to the extent the Existing Luxturna Clinical Program data and data from such other studies will be used by Novartis for the Development and Commercialization of Luxturna in the Novartis Territory under this Agreement.

4.3.2 Novartis Territory. Novartis will lead, control and be responsible for all studies, other than the Existing Luxturna Clinical Program, that Novartis determines are necessary or desirable for Development or Commercialization in the Novartis Territory. Any such studies will be included in the Development Plan, and Novartis may conduct such studies anywhere (in Novartis’ discretion) in the Novartis Territory.

4.3.3 Study Data. As between the Parties, all study data shall be owned by the Party that is the licensor of such data pursuant to Section 3.1.2 or 3.2.2, as applicable, and the other Party shall receive no interest in such study data except as provided pursuant to Section 3.1.2, 3.2.2 or 10.7, as applicable. If a Party so requests, then such study data shall be provided by the licensing Party to the other Party and its Affiliates for the permitted regulatory, Development, Commercialization purposes at no additional cost.

4.3.4 Records. Each Party shall keep, and shall cause its applicable Affiliates and Sublicensees to keep, complete, true and accurate records of all study data Controlled by such Party from any clinical trials of Luxturna sponsored by such Party and its Affiliates and Sublicensees. Each Party and its applicable Affiliates and Sublicensees shall keep such books and records for such period as required under applicable Law. The other Party will have the right, at its own expense and upon its written request, to review such of the records of the sponsoring Party, Affiliates and Sublicensees in support of such other Party’s rights and obligations hereunder. Each Party agrees to hold in confidence all information received and all information learned in the course of any audit or inspection, except to the extent necessary to enforce its rights under this Agreement or to the extent required to comply with any applicable Law.

4.4 Regulatory Activities.

4.4.1 Responsibilities.

(a) EU Regulatory Approval.

(i) General Obligation. Subject to Section 2.1.3, Spark shall use commercially reasonable efforts to obtain EU Regulatory Approval.
(ii) **Conditional Regulatory Approvals.**

(1) If EMA issues a conditional Regulatory Approval that permits Novartis to Commercialize Luxturna within the EU, then (a) Spark shall perform all necessary Technical Development activities in accordance with Section 4.1.2(a)(i) that are conditions of such Regulatory Approval, and (b) Novartis shall be responsible for performing all other Development activities required by EMA to satisfy the conditions in the conditional Regulatory Approval. As soon as reasonably practicable after issuance of the conditional Regulatory Approval, Spark shall assign or transfer such conditional Regulatory Approval, the orphan designation, and all other regulatory designations and/or exclusivities for Luxturna to Novartis.

(2) If EMA issues a conditional Regulatory Approval, or the European Commission issues a Regulatory Approval with conditions, in each case that does not permit Novartis to Commercialize Luxturna within the EU, then Spark shall be responsible for performing all Technical Development activities and Development activities required by EMA to obtain a Regulatory Approval that permits Novartis to Commercialize Luxturna within the EU (excluding conditions of the conditional Regulatory Approval that are not necessary to permit Novartis to Commercialize Luxturna within the EU once Spark performs the foregoing Technical Development activities and Development activities required by EMA for such Commercialization). As soon as reasonably practicable after EU Regulatory Approval, Spark shall assign or transfer such EU Regulatory Approval, the orphan designation, and all other regulatory designations and/or exclusivities for Luxturna to Novartis. For clarity, this Section 4.4.1(a)(ii)(2) shall not be construed to limit Spark’s obligations pursuant to Section 4.1.2.

(iii) **BREXIT.** In the event that prior to Spark obtaining EU Regulatory Approval, a separate Regulatory Approval becomes necessary for the Commercialization of Luxturna in the United Kingdom, Spark shall use commercially reasonable efforts to seek Regulatory Approval and to comply with the provisions of this subsection (a) with respect to the United Kingdom *mutatis mutandis*, provided that if additional clinical Development activities are required, the JSC shall meet and confer to discuss the role of the Parties with respect to such activities in accordance with the provisions of Section 2.1.3(x).

(iv) **Supremacy.** To the extent any other provision of this Section 4.4.1 contradicts any provision of this Section 4.4.1(a), the provision of this Section 4.4.1(a) shall govern.

(b) **Assistance.** Spark, at [**] cost and expense, shall provide reasonable available additional information, in the form Spark has such information, including without limitation information relating to clinical studies conducted by Spark as reasonably requested by Novartis, to assist Novartis in its activities to obtain and maintain Regulatory Approval, including preparation of any filings with a Regulatory Authority relating to Luxturna for the Novartis Territory and its preparation for or of any other meeting or communication with any Regulatory Authority relating to Luxturna for the Novartis Territory. Subject to the provisions of 4.4.1(a), Novartis shall be the holder of Regulatory Approvals for Luxturna in the Field for the Novartis Territory.

-23-
(c) **Participation.** The Party not responsible for interfacing, corresponding and meeting with the applicable Regulatory Authorities in a country with respect to Luxturna for the Novartis Territory shall have the right, but not the obligation, to have a senior, experienced employee reasonably acceptable to the responsible Party participate as an observer in material or scheduled face-to-face meetings, video conferences and any teleconferences, involving participation of personnel beyond regulatory experts, with the Regulatory Authorities in [**], and shall be provided with advance access to the responsible Party’s material documentation prepared for such meetings. Prior to submission of material correspondence to the applicable Regulatory Authority, the responsible Party shall, sufficiently in advance for the other Party to review and comment, provide the other Party any material correspondence with the applicable Regulatory Authority related to such meetings. The responsible Party shall also provide the other Party with copies of any material correspondence with the applicable Regulatory Authority relating to Development of, or the process of obtaining Regulatory Approval for, Luxturna in the Novartis Territory, and respond within a reasonable time frame to all reasonable inquiries by the other Party with respect thereto.

(d) **Post-Approval Commitments; Maintenance.** Subject to the specific provisions of Section 4.4.1(a), upon grant of Regulatory Approval (including any conditional Regulatory Approvals) for Luxturna for the Novartis Territory, Novartis shall perform all Post-Approval Commitments (other than activities for which Spark is responsible pursuant to Section 4.1.2) and comply with all requirements imposed by applicable Laws as the marketing authorization holder for Luxturna. Novartis shall be fully responsible for maintaining the Regulatory Approval for Luxturna for the Novartis Territory and Novartis, Spark and their respective Affiliates and Sublicensees shall not take any steps that might undermine such Regulatory Approval.

(e) **Transfers.** Except as required by a Regulatory Authority or applicable Laws or to a permitted assignee under Section 12.7, Novartis shall in no circumstances transfer any Regulatory Approval granted for Luxturna for the Novartis Territory to any Third Party without the prior consent of Spark.

4.4.2 **Costs.** The cost to obtain and maintain all necessary regulatory filings and Regulatory Approvals for Luxturna will be borne by [**], with the exception of the filing fees and all other costs related to obtaining the EU Regulatory Approval of Luxturna, including any activities required by Sections 4.4.1(a)(ii)(1)(a) and 4.4.1(a)(ii)(2) (which costs shall be borne by [**]) but excluding any activities required by Section 4.4.1(a)(ii)(1)(b) (which costs shall be borne by [**]).

4.5 **Adverse Event and Product Complaint Reporting Procedures; Pharmacovigilance.**

4.5.1 The Parties shall enter into a pharmacovigilance agreement (the “Pharmacovigilance Agreement”) for Luxturna applying to the Novartis Territory and the Spark Territory within [**] after the Effective Date, but no later than when Novartis commences any clinical study of Luxturna. Such Pharmacovigilance Agreement shall contain the specific terms, conditions and obligations of the Parties with respect to the collection, reporting and monitoring of all adverse drug reactions, adverse events, medical inquires, and other relevant drug or related device safety matters with respect to Luxturna during the Term. Each Party acknowledges that its
obligations under the Pharmacovigilance Agreement shall include the obligations imposed on each Party by the applicable Law. Each Party will (a) provide the other Party with all complaints, non-serious and serious adverse event information, and safety data from clinical studies, including related communications with and from Regulatory Authorities, hospitals, physicians or patients, in its control necessary or desirable for the other Party to comply with all applicable Laws with respect to Luxturna and (b) report and provide access to such information to the other Party in such a manner and time so as to enable the other Party to comply with all applicable Laws.

4.5.2 Each Party has established (or shall establish) and shall maintain, at its cost, a global adverse event database. At the time agreed under the Pharmacovigilance Agreement, Spark shall make a one-time transfer to Novartis of the legacy data for Luxturna in Spark’s global adverse event database. This shall be provided in E2B format and/or CIOMS I format, understanding that certain elements will be redacted respecting appropriate data privacy laws. The Parties acknowledge that the transfer of data from the global adverse event database will require mutual cooperation between the Parties and the Parties will use reasonable efforts to complete this transfer as soon as possible. With effect from the Effective Date, Novartis shall have access to all data in Spark’s global adverse event database for use in the Novartis Territory and Spark shall have access to all data in Novartis’ global adverse event database for use in the Spark Territory. Novartis shall be responsible for submitting adverse events reports to the applicable Regulatory Authorities for the Novartis Territory, and Spark shall be responsible for submitting serious adverse events reports to the applicable Regulatory Authorities in the Spark Territory. In addition, each Party shall promptly notify the other if such Party becomes aware of any information or circumstance that is have a material adverse effect on the Development or Commercialization of Luxturna.

4.6 Decisions to Terminate or Suspend a Study Based on Safety Concerns. The Party sponsoring or controlling any clinical study of Luxturna may terminate or suspend such clinical study if (a) a Regulatory Authority or safety data review board for such clinical study has required such termination or suspension, or (b) such Party believes in good faith that such termination or suspension is warranted because of safety or tolerability risks to the study subjects. In either case, such Party shall promptly notify the other Party of such termination or suspension, and shall use all reasonable efforts to inform and consult with the other Party prior to taking such action.

ARTICLE 5
COMMERCIALIZATION

5.1 Diligence. Novartis shall use Diligent Efforts to Commercialize Luxturna in accordance with the approved label therefor in the Field in the Novartis Territory. Without limiting the foregoing, in the event (a) Novartis determines not to use Diligent Efforts, or (b) following written notice from Spark that Novartis has ceased to use Diligent Efforts and Novartis has failed to resume Diligent Efforts within [**] of the date of such written notice, to Commercialize or continue Commercialization of Luxturna in a Terminated Country, (i) Novartis may elect to forego or suspend Commercialization activities with respect to such Terminated Country upon notice to Spark, (ii) such election shall not be deemed a breach of Novartis’ obligations under this Agreement (including without limitation Section 5.1); (iii) such Terminated Country shall be excluded from the scope of the licenses granted to Novartis in Section 3.1.1 and 3.1.2, and thereafter the “Novartis
“Territory” shall be deemed to exclude such Terminated Country(ies) and the “Spark Territory” shall be deemed to include such Terminated Country(ies) and (iv) the consequences set forth in Section 10.7.3 shall apply with respect to such Terminated Country(ies).

5.2 **Product Trademarks.** Novartis, in consultation with the JSC, shall determine the Product Trademarks in the Novartis Territory. In connection therewith, Novartis may determine whether to use the LUXTURNA trademark for the Novartis Territory but shall not attempt, and shall have no authority to influence Spark’s branding strategy in the Spark Territory.

5.3 **Advertising and Promotional Materials.** Novartis shall develop and approve relevant written sales, promotion and advertising materials relating to Luxturna (“Promotional Materials”) for use in the Novartis Territory, which shall be consistent with the plans discussed at the JSC and with Novartis’ standard operating procedures, and compliant with applicable Laws and the provisions of the applicable Regulatory Approvals. Copies of all Promotional Materials used in the Novartis Territory will be archived by Novartis in accordance with Novartis’ standard operating procedures in accordance with applicable local Law.

5.4 **Pricing and Reimbursement.** Novartis and its Affiliates shall control and take the lead in all pricing and reimbursement approval proceedings relating to Luxturna in the Novartis Territory in accordance with the JSC-reviewed high-level general pricing and reimbursement strategy for the Novartis Territory. Novartis and its Affiliates shall be responsible for negotiating and shall have final decision-making authority in respect to the pricing and reimbursement for Luxturna in the Novartis Territory. Spark shall provide Novartis with reasonable access to data in Spark’s control, in the form Spark possesses such data, as is reasonably necessary or desirable to support Novartis to carry out health technology assessments (which may include, for example, [**]), provided that, Spark shall not be required to generate any further analyses or validation of any data, or otherwise to incur any costs or expense related to pricing and reimbursement after the Effective Date.

5.5 **Other Responsibilities.** Novartis shall be solely responsible for the following functions in the Novartis Territory:

5.5.1 managing all returns of Luxturna. If Luxturna sold in the Novartis Territory is returned to Spark, it shall promptly be shipped to a facility designated by Novartis; and

5.5.2 managing all aspects of Luxturna order processing, invoicing and collection, distribution, inventory and receivables.

5.6 **Manufacture and Supply.** Subject to the terms of the Supply Agreement, Spark shall retain the responsibility to Manufacture, and Novartis shall purchase from Spark, clinical and commercial supplies of Products (as defined in the Supply Agreement), and Spark shall supply Novartis’s clinical and commercial requirements of Products for the Novartis Territory. All Manufacturing and supply by Spark of Products for Development and Commercialization by Novartis shall be covered by the Supply Agreement and a quality agreement executed by the Parties as set forth in the Supply Agreement (the “Quality Agreement”).

-26-

ActiveUS 166647742v.1
ARTICLE 6
FINANCIAL PROVISIONS

6.1 Upfront Payments. Novartis shall pay Spark a non-refundable, non-creditable, one-time payment of one hundred five million dollars ($105,000,000) within five (5) Business Days following the Effective Date.

6.2 Milestones. Spark shall notify Novartis in writing of the achievement of milestone event I below and, in accordance with the timelines set forth in Section 6.4, Novartis shall notify Spark in writing of the achievement of each milestone event II and III below. Spark shall issue an invoice to Novartis for each corresponding milestone payment as set forth below. For clarity, each referenced milestone event may be attained only once, and in no event shall any milestone payment be earned or paid more than once. Novartis shall make the corresponding non-refundable, non-creditable, one-time payments to Spark in accordance with Section 6.4.3:

<table>
<thead>
<tr>
<th>Milestone Event</th>
<th>Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. EU Regulatory Approval*</td>
<td>$25,000,000</td>
</tr>
<tr>
<td>II. Achievement of aggregate Net Sales of Luxturna in [*] of $[**]</td>
<td>[**]</td>
</tr>
<tr>
<td>III. Achievement of aggregate Net Sales of Luxturna in [*] of $[**]</td>
<td>[**]</td>
</tr>
</tbody>
</table>

* With respect to the milestone payment in respect of EU Regulatory Approval, the milestone event shall not be triggered and Novartis shall have no obligation to pay such milestone payment (i) upon issuance of a conditional Regulatory Approval unless such conditional Regulatory Approval permits Novartis to Commercialize Luxturna within the EU, provided that in such event such milestone payment shall become payable once all conditions in such conditional Regulatory Approval that are required to be satisfied to permit Novartis to Commercialize Luxturna within the EU have been satisfied, or (ii) upon issuance of Regulatory Approval in the United Kingdom during a period of time when the United Kingdom is no longer a member state of the European Union.

6.3 Royalties. Novartis shall pay to Spark, on a Royalty Region-by-Royalty Region basis, a royalty of (a) [**] percent ([**]% in respect of Net Sales of Luxturna in such Royalty Region during the Base Royalty Term and (b) [**] percent ([**]% in respect of Net Sales of Luxturna in such Royalty Region during the Continued Royalty Term. For clarity, Novartis shall have no obligations to pay any royalty within a Royalty Region following the expiration of the Continued Royalty Term in such Royalty Region.

6.4 Reports; Invoices; Payments.

6.4.1 Within [**] after the end of each Calendar Quarter during the Royalty Term, Novartis shall submit to Spark a report providing (i) the Net Sales of Luxturna during such Calendar Quarter, (ii) a detailed calculation of the applicable royalties under Section 6.3, and (iii)
notification of any Net Sales milestone event set forth in Section 6.2 achieved during such Calendar Quarter;

6.4.2 Spark shall issue an invoice to Novartis for payments due pursuant to Section 6.3; and

6.4.3 Except as set forth in Sections 3.2.4 and 6.1, Novartis shall pay to Spark all undisputed amounts within [**] from receipt of an invoice therefor.

6.5 Records; Audits. Novartis shall keep, and shall cause its applicable Affiliates and Sublicensees to keep, complete, true and accurate records in accordance with its Accounting Standards of the items underlying Net Sales and amounts payable to Third Parties pursuant to any licenses or sublicenses granted pursuant to Section 3.2.4. Novartis and its applicable Affiliates and Sublicensees shall keep such books and records for at least [**] following the end of the Calendar Year to which they pertain. Spark will have the right [**], at its own expense, to have an independent, internationally-recognized, certified public accounting firm (the “Auditor”), selected by Spark and reasonably acceptable to Novartis, upon the written request of Spark, not more than [**] and not more frequently than [**] with respect to records covering any specific period of time, review such of the records of Novartis, its Affiliates and Sublicensees in the location(s) where such records are customarily maintained upon reasonable notice and during regular business hours, for the sole purpose of verifying the basis and accuracy of payments made under this Agreement by Novartis within the prior [**] period. Before beginning its audit, the Auditor shall execute an undertaking reasonably acceptable to Novartis by which the Auditor agrees to keep confidential all information reviewed during the audit. The Auditor shall have the right to disclose to the Parties only its conclusions regarding any payments owed under this Agreement. In addition, Spark shall only be entitled to audit the books and records of Novartis from the [**] in which the audit request is made. Spark agrees to hold in confidence all information received and all information learned in the course of any audit or inspection, except to the extent necessary to enforce its rights under this Agreement or to the extent required to comply with any applicable Law. The Auditor shall provide its audit report and basis for any determination to Novartis at the time such report is provided to Spark before it is considered final. If the review of such records reveals that the Novartis has failed to accurately report information pursuant to this Agreement, then Novartis shall promptly pay to Spark any resulting amounts due under this Agreement together with interest calculated in the manner provided in Section 6.9. If Novartis has underpaid by an amount greater than [**] percent (%%) of the amounts due for the period audited, Novartis shall also pay the reasonable costs of such review.

6.6 Tax Matters. Each Party shall be solely responsible for all net income taxes due with respect to payments received by such Party under this Agreement and for all of its other tax obligations. Novartis shall make all payments to Spark hereunder from accounts located within the United States or Switzerland and, except as otherwise required by then-applicable Law, shall not deduct or withhold any tax from any such payments. If then-applicable Law requires Novartis to deduct or withhold tax from any payment due to Spark hereunder, Novartis shall timely withhold and deduct the amount of such tax and pay it over to the relevant Governmental Authority, and shall promptly transmit to Spark an official tax certificate or other evidence of such payment sufficient to enable Spark to claim payment of such taxes. Novartis shall cooperate with Spark and shall use
reasonable efforts to lawfully avoid or reduce any deduction and withholding of tax in respect of any payments made to Spark hereunder or to secure a refund of any taxes so deducted and withheld. Novartis shall cooperate with Spark and shall use reasonable efforts to lawfully avoid or reduce indirect taxes arising in connection with this Agreement and the transactions contemplated hereby.

6.7 **Currency Exchange.** All payments to be made by Novartis to Spark shall be made in U.S. Dollars, to a Spark bank account able to receive U.S. Dollars. Net Sales amounts used to calculate royalties and milestones shall be converted to U.S. Dollars in accordance with Novartis’ then-current standard exchange rate methodology as applied in its external reporting for the conversion of foreign currency sales into U.S. Dollars.

6.8 **Blocked Payments.** If, by reason of applicable Laws in any country, it becomes impossible or illegal for Novartis or its Affiliate or Sublicensee to transfer, or have transferred on its behalf, royalties or other payments to Spark, Novartis shall promptly notify Spark of the conditions preventing such transfer and such royalties or other payments shall be deposited in local currency in the relevant country to the credit of Spark in a recognized banking institution designated by Spark or, if none is designated by Spark within a period of [**], in a recognized banking institution selected by Novartis or its Affiliate or Sublicensee, as the case may be, and identified in a notice given to Spark pursuant to Section 12.3.

6.9 **Late Payments.** The paying Party shall pay interest to the receiving Party on the aggregate amount of any payment that is not paid on or before the date such payment is due under this Agreement at a rate per annum equal to the lesser of the prime or equivalent rate per annum quoted by *The Wall Street Journal* on the first Business Day after such payment is due, plus [**] percent ([**]%), or the highest rate permitted by applicable Law, calculated on the number of days such payment is paid after the date such payment is due, and compounded monthly.

6.10 **Resolution of Disputes.** If there is a dispute, claim or controversy relating to any financial obligation by one Party to the other Party pursuant to this Agreement, such Party shall provide such other Party with written notice setting forth in reasonable detail the nature and factual basis for such good-faith dispute and each Party agrees that it shall seek to resolve such dispute within [**] after the date such written notice is received. If no such resolution is reached by the Parties, the dispute shall be resolved through the procedures set forth in ARTICLE 11.

6.11 **No Guarantee.** Spark and Novartis acknowledge and agree that nothing in this Agreement shall be construed as representing an estimate or projection of anticipated sales of Luxturna in the Novartis Territory, and that the milestone events and Net Sales levels set forth in this Agreement or that have otherwise been discussed by the Parties are merely intended to define the milestone payments and royalty obligations to Spark in the event such milestone events or Net Sales level are achieved. Without prejudice to the express provisions of Sections 4.1 and 5.1, neither Party provides any representation, warranty or guarantee that (a) Development of Luxturna in the Novartis Territory will be successful, (b) Regulatory Approval for Luxturna in any specific country within the Novartis Territory will be sought or obtained, or (c) any other particular results will be achieved with respect to the Commercialization of Luxturna in the Novartis Territory hereunder or any specific country therein.
ARTICLE 7
INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION
AND RELATED MATTERS

7.1 Ownership of Intellectual Property.

7.1.1 Existing IP. Nothing in this Agreement shall affect Spark’s ownership of the Spark IP existing as the Effective Date or Novartis’ ownership of the Novartis IP existing as of the Effective Date, which in each case shall remain owned by the Party having such rights.

7.1.2 Arising IP. Each Party shall promptly notify the other Party of any new Intellectual Property created by such Party during the Term in the performance of this Agreement. Any such Intellectual Property shall be owned as follows:

(a) any such Intellectual Property that is solely conceived, reduced to practice, authored, created or developed (“Created”) by or on behalf of one Party or its Affiliates (and not by or on behalf of the other Party or its Affiliates) shall be owned by the Creating Party and shall be included with the Spark IP or Novartis IP, as applicable, and included in the licenses granted to the other Party pursuant to ARTICLE 3; and

(b) any other such Intellectual Property that is Created jointly by or on behalf of both of the Parties or their Affiliates shall be jointly owned by the Parties on the basis of each Party having an undivided interest in the whole (“Joint IP”). Subject to the terms and conditions of this Agreement, each Party shall have the right to exploit Joint IP as it may determine, without any duty to account to the other Party or obtain the other Party’s consent for any such exploitation, and shall provide such reasonable assistance to the other Party as may be required for it to enjoy the benefit of this Section 7.1.2(b).

(c) Questions of inventorship or authorship for purposes of determining whether new Intellectual Property created during the Term in the performance of this Agreement is Novartis IP, Spark IP, or Joint IP shall be resolved in accordance with United States patent or copyright Laws, as applicable.

7.2 Handling of Patent Rights.

7.2.1 By Novartis. Novartis shall have the sole right to Handle Patent Rights included in the Novartis IP worldwide (“Novartis Patent Rights”).

7.2.2 By Spark. Spark shall have the sole right to Handle Patent Rights included in the Spark IP worldwide (“Spark Patent Rights”).

7.2.3 Joint Patent Rights. The Parties will jointly control the Handling of Patent Rights included in the Joint IP (“Joint Patent Rights”). Spark shall have primary responsibility for Handling Joint Patent Rights in the Spark Territory and Novartis shall have primary responsibility for Handling Joint Patent Rights in the Novartis Territory. If a Party elects not to Handle any Joint Patent Right for which it has primary responsibility (or, after commencement of such Handling,
7.2.4 **Costs and Expenses.** The Party Handling any Patent Right under this Section 7.2 shall bear one hundred percent (100%) of the costs thereof.

7.2.5 **Cooperation.** Each Party agrees to cooperate with the other with respect to Handling Patent Rights pursuant to this Section 7.2. With respect to Joint Patent Rights, or any other Patent Right Covering Luxturna in the Field in the Novartis Territory, the Party responsible for Handling such Patent Rights shall provide the other Party with advance copies (which may be in draft form) of all material filings as well as copies of all material correspondence from the relevant patent office, in each case relating to such Patent Rights, and shall consider in good faith all comments from such other Party relating to such filings and correspondence.

7.3 **Third Party Infringement.**

7.3.1 **Notice.** Each Party shall promptly report in writing to the other Party during the Term any known or suspected (a) infringement of any of the Spark Patent Rights, Novartis Patent Rights or Joint Patent Rights, in each case that Cover Luxturna in the Field in the Novartis Territory or (b) other unauthorized use or violation of any of the Spark IP, Novartis IP or Joint IP, in each case relating to Luxturna in the Field in the Novartis Territory, of which such Party becomes aware, and shall provide the other Party with all available evidence supporting such known or suspected infringement or unauthorized use or violation.

7.3.2 **Enforcement Rights.** Subject to the provisions of any Third Party license agreement under which Spark’s rights in Spark IP or either Party’s rights in the Joint IP are granted:

(a) Novartis shall have the first right, but not the obligation, to institute, prosecute and control any action or proceeding that it believes is reasonably required to protect or otherwise enforce any of the Spark IP or Joint IP against Third Parties Developing, Manufacturing or Commercializing products that are competitive with Luxturna in the Field for the Novartis Territory through counsel of its own choice. Prior to instituting any such action or proceeding, Novartis will give Spark at least [**] notice of its intention to institute any such action or proceeding. Novartis shall consider in good faith any comments from Spark prior to instituting any such action or proceeding. If Novartis is not permitted (e.g., for local legal reasons) to bring such action and requests Spark to bring such action on Novartis’ behalf, then Spark shall bring such action at Novartis’ sole cost and expense. Notwithstanding the foregoing, Spark may elect to contribute [**] percent ([**]% of the costs and expenses of such action or proceeding by providing written notice to Novartis within [**] of the notice specified in Section 7.3.1. Should Spark elect to contribute [**] percent ([**]% of the costs and expenses of such action or proceeding, the Parties agree that there will be joint consensus decision-making relating to enforcement strategy for Luxturna in the Field for the Novartis Territory, provided that the Party controlling the action shall have final decision-making authority relating to such action so long as such Party does not settle any such action without
the prior written consent of the other Party, such consent not to be unreasonably withheld, conditioned or delayed.

(b) If Novartis fails to initiate a suit or take other appropriate action pursuant to Section 7.3.2(a) within [**] of the notice specified in Section 7.3.1 (or within [**] in the case of any action brought under a non-U.S. version of the Hatch-Waxman Act), then Spark may, in its discretion, initiate a suit or take other appropriate action against Third Parties Developing, Manufacturing or Commercializing products that are competitive with Luxturna in the Field in the Novartis Territory.

(c) Neither Party shall settle or compromise any action or proceeding under this Section 7.3.2 without the consent of the other Party, which consent shall not be unreasonably withheld.

7.3.3 Novartis Sole Right to Enforce. Subject to the provisions of any Third Party license agreement under which Novartis’ rights in Novartis IP are granted, Novartis shall have the sole right, but not the obligation, to initiate a suit or take other appropriate action that it believes is reasonably required to protect (i.e., prevent or abate actual or threatened infringement, unauthorized use, or violation of) or otherwise enforce any of the Novartis IP worldwide.

7.3.4 Spark Sole Right to Enforce. Subject to the provisions of any Third Party license agreement under which Spark’s rights in Spark IP or either Party’s rights in the Joint IP are granted, Spark shall have the sole right, but not the obligation, to initiate a suit or take other appropriate action that it believes is reasonably required to protect (i.e., prevent or abate actual or threatened infringement, unauthorized use, or violation of) or otherwise enforce (a) the Joint IP in the Spark Territory against Third Parties Developing, Manufacturing or Commercializing products that are competitive Luxturna in the Field, and (b) subject to Section 7.3.2, the Spark IP worldwide.

7.3.5 Conduct of Certain Actions; Costs. The Party initiating suit shall have the sole and exclusive right to select counsel for any suit initiated by it pursuant to Section 7.3.2, Section 7.3.3 or Section 7.3.4, but with regards to Section 7.3.2 Novartis will consider in good faith any comments on the choice of counsel received from Spark. If required under applicable Law in order for the initiating Party to initiate or maintain such suit, the other Party shall join as a party to the suit. Such other Party shall offer reasonable assistance to the initiating Party in connection therewith at no charge to the initiating Party except for reimbursement of reasonable out-of-pocket expenses incurred in rendering such assistance. The initiating Party shall assume and pay all of its own out-of-pocket costs incurred in connection with any litigation or proceedings initiated by it pursuant to Section 7.3.2, Section 7.3.3 and Section 7.3.4, including the fees and expenses of the counsel selected by it, unless Spark elects to contribute [**] percent ([**]%)] of the costs in accordance with Section 7.3.2. The other Party shall have the right to participate and be represented in any such suit by its own counsel at its own expense.

7.3.6 Recoveries. With respect to any suit or action referred to in Section 7.3.2, any recovery obtained as a result of any such proceeding, by settlement or otherwise, shall be applied in the following order of priority:
first, the Parties shall be reimbursed for all costs incurred in connection with such proceeding paid by
the Parties and not otherwise recovered; and

second, any remainder shall be [**].

7.3.7  **Patent Invalidity Claim**. If a Third Party at any time asserts a counterclaim to a patent infringement
claim initiated by a Party that any Spark Patent Right or Joint Patent Right that Covers Luxturna in the Field is invalid or otherwise
unenforceable (an “Invalidity Claim”), control of the response to such claim in the Field in the Novartis Territory shall, as between
the Parties, be determined in the same manner as enforcement rights with respect to such Patent Right are determined pursuant to
Section 7.3.2, with the time periods set forth in Section 7.3.2 shortened where necessary to provide Spark sufficient time to respond
without a loss of rights, and the non-controlling Party shall cooperate with the controlling Party in the preparation and formulation of
such response, and in taking other steps reasonably necessary to respond, to such Invalidity Claim. Neither Party shall settle or
compromise any Invalidity Claim without the consent of the other Party, which consent shall not be unreasonably withheld. If the
Invalidity Claim does not arise in connection with a suit or action referred to in Section 7.3.2(a), Control of and the costs and
expenses of responding to the Invalidity Claim shall be borne by the Party responsible for Handling the applicable Patent Right in
accordance with Section 7.2.

7.4  **Claimed Infringement**. If a Party becomes aware of any claim that the Development or Commercialization of Luxturna
infringes or otherwise violates the intellectual property rights of any Third Party, such Party shall promptly notify the other Party. In
any such instance, the Parties shall cooperate and shall mutually agree upon an appropriate course of action and any settlement of
such claim. Each Party shall have an equal right to participate in any settlement discussions that are held with such Third Parties. If
there is a dispute between the Parties as to whether or not a Third Party Patent Right Covers Luxturna, the Parties agree to select an
independent patent counsel reasonably acceptable to both Parties (the “Independent Patent Counsel”) to make such determination.
The Parties agree that if the Independent Patent Counsel determines that the subject Third Party Patent Right Covers Luxturna, they
will accept such determination for purposes of Section 3.2.4, if applicable. If the Independent Patent Counsel determines that the
subject Third Party Patent Right does not Cover Luxturna or is invalid, either Party may still obtain a license, but shall be solely
responsible for any payment obligation to the Third Party. Each Party shall provide to the other Party copies of any notices it
receives from any Third Party regarding any patent nullity actions, any declaratory judgment actions and any alleged infringement or
other violation of Third Party intellectual property rights relating to the Development or Commercialization of Luxturna. Such
notices shall be provided promptly, but in no event after more than [**] following receipt thereof. The Parties shall equally share the

7.5  **Patent Term Extensions**. The Parties shall cooperate, if necessary and appropriate, with each other in gaining patent
term extension (including those extensions available under the Supplementary Certificate of Protection of Member States of the EU
and other similar measures in any other country) wherever applicable to Patent Rights in the Novartis Territory Controlled by either
Party that Cover Luxturna in the Field. The Parties shall, if necessary and appropriate, use commercially reasonable efforts in good
faith to agree upon a joint strategy relating to patent term
extensions, but, in the absence of mutual agreement with respect to any extension issue in the Novartis Territory, the patent or the claims of the patent shall be selected on the basis of the scope, enforceability and remaining term of the patent in the relevant country or region. All filings and costs for such extensions shall be made by the Party responsible for Handling the applicable Patent Right in accordance with Section 7.2.

7.6 License Recordals. The Parties shall cooperate, if necessary and appropriate, with each other in recording any license agreements wherever applicable to Patent Rights in the Novartis Territory that Cover Luxturna in the Field at Novartis’ sole cost and expense.

7.7 Patent Marking. Each Party agrees to comply with the patent marking statutes in each country in which Luxturna is sold by such Party, its Affiliates or its Sublicensees.

7.8 Trademarks.

7.8.1 Each Party and its Affiliates shall retain all right, title and interest in and to its and their respective corporate names and logos.

7.8.2 Unless otherwise agreed in writing by the Parties, and subject to any Third Party rights in the relevant Trademarks, Spark shall own the trademark for the name and logo of LUXTURNA worldwide and Novartis shall own all other Product Trademarks in the Novartis Territory.

7.8.3 The Party owning a Trademark pursuant to this Section 7.8 shall be exclusively entitled to register and be the owner of the domain names corresponding to or containing such Trademark in any generic Top Level Domains (gTLDs), including the new and to be introduced gTLDs. The Party owning a Trademark shall also own all goodwill associated therewith throughout the world.

7.8.4 The Parties agree that each Party, its Affiliates and Sublicensees shall comply strictly with the other Party’s trademark style and usage standards that such other Party communicates to such Party from time to time in connection with the use by such Party, its Affiliates and Sublicensees of Trademarks Controlled by such other Party. The Parties agree that in the event of a Supply Transition Event, if Novartis elects to use Trademarks Controlled by Spark in connection with its branding strategy in the Novartis Territory, the Parties shall agree in good faith to reasonable and customary applicable trademark quality control standards.

7.8.5 Neither Party shall use any Product Trademark to identify any product other than Luxturna.

7.8.6 Novartis shall be solely responsible for Trademark matters in the Novartis Territory at Novartis’ cost, including decision-making, filing, litigation, customs registrations and enforcement, and Spark shall be solely responsible for implementing such strategy and Trademark matters, including Product Trademark matters in the Spark Territory at Spark’s cost, including decision-making, filing, litigation, customs registrations and enforcement. Novartis shall have the first right to enforce the Product Trademarks in the Novartis Territory, at Novartis’ cost
and with the reasonable information to and assistance of Spark, and Spark shall have the first right to enforce the Product Trademarks in the Spark Territory, at Spark’s cost and with the reasonable information to and assistance of Novartis.

7.8.7 If either Party becomes aware of any infringement of any Product Trademark by a Third Party, such Party shall promptly notify the other Party. The Parties shall cooperate and inform each other of relevant activities in their respective territory and consider in good faith the other Party’s feedback if there is the potential for an impact to the other Party’s territory.

7.8.8 Except as otherwise stated in this Agreement, Novartis shall not, and shall ensure that its Affiliates and Sublicensees do not, without Spark’s prior written approval, use or seek to register any Trademark or domain name consisting of, or containing “Luxturna” or any other Product Trademark of Spark.

ARTICLE 8
CONFIDENTIALITY AND PUBLICITY

8.1 Confidential Information. Subject to the other provisions of this ARTICLE 8, each Party agrees to keep in confidence and not to disclose to any Third Party, or use for any purpose, except pursuant to, and in order to carry out, the terms and objectives of this Agreement, any Confidential Information of the other Party. As used herein, “Confidential Information” means confidential strategy, development plans, research information, manufacturing and technical information, technology, devices, products, clinical trial designs, clinical and pre-clinical data or other business information, objectives or technical information in any form or medium of a Party or its Affiliates disclosed by or on behalf of a Party in connection with this Agreement, whether prior to, on or following the Effective Date and whether disclosed orally, electronically, by observation or in writing. The terms of this Agreement and the Supply Agreement shall be considered Confidential Information hereunder. The restrictions on the disclosure and use of Confidential Information set forth in the first sentence of this Section 8.1 shall not apply to any Confidential Information that:

8.1.1 was known by the receiving Party prior to disclosure by the disclosing Party hereunder (as evidenced by the receiving Party’s written records or other competent evidence);

8.1.2 is or becomes generally known or part of the public domain through no fault of the receiving Party;

8.1.3 is disclosed to the receiving Party by a Third Party having a legal right to make such disclosure without violating any confidentiality or non-use obligation that such Third Party has to the disclosing Party; or

8.1.4 is independently developed by personnel of the receiving Party who did not have access to the other Party’s Confidential Information (as evidenced by the receiving Party’s written records or other competent evidence).
In addition, if either Party is required to disclose Confidential Information of the other Party by applicable Law or legal process, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange, including Nasdaq, such Party shall comply with Section 8.5.4.

8.2 Employee, Consultant and Advisor Obligations. Each Party agrees that it and its Affiliates shall provide or permit access to Confidential Information received from the other Party and such Party’s Affiliates and representatives only to the receiving Party’s employees, consultants, advisors, licensees and permitted subcontractors, licensees and distributors, and to the employees, consultants, advisors and permitted subcontractors, licensees and distributors of the receiving Party’s Affiliates, who in such Party’s reasonable judgment have a need to know such Confidential Information to assist the receiving Party with the activities contemplated by this Agreement and who are subject to obligations of confidentiality and non-use with respect to such Confidential Information substantially equivalent to the obligations of confidentiality and non-use of the receiving Party pursuant to Section 8.1.

8.3 Permitted Disclosures. Either Party may disclose Confidential Information (a) to bona fide potential investors, licensees, licensors, collaborators, lenders and acquirors/acquirees, and to such Party’s consultants and advisors, the existence and terms of this Agreement to the extent necessary in connection with a proposed equity or debt financing of such Party, an actual or proposed license, collaboration or similar arrangement, or a proposed acquisition or business combination, (b) to bona fide potential Sublicensees or and distributors, so long as such recipients are bound in writing to maintain the confidentiality of such information in accordance with the terms of this Agreement, and (c) as reasonably necessary in connection with the prosecution and maintenance of Patent Rights as contemplated by this Agreement, in connection with regulatory filings made with Regulatory Authorities with respect to Luxturna, or in connection with the prosecuting or defending of any legal proceeding, as contemplated by this Agreement.

8.4 Responsibility for Compliance. Spark or Novartis, as applicable, shall remain responsible for any failure by any Person to whom such Party discloses the other Party’s Confidential Information pursuant to Section 8.2 or Section 8.3 to treat such information as required under Section 8.1 (as if such Person were a Party directly bound to the requirements of Section 8.1).

8.5 Publicity.

8.5.1 The Parties shall issue press releases as set forth on Exhibit 8.5.1 hereto following the Effective Date.

8.5.2 Neither Party shall, without the prior written consent of the other Party, not to be unreasonably withheld or delayed, issue any other press release or make any public announcement (whether verbally or in writing) to any Third Party that (a) references the other Party (other than pre-agreed language for ownership of trademarks); (b) references joint activities under this Agreement; or (c) relates to this Agreement or the other Party. A Party’s consent shall not be required to the extent such press release or public announcement that (i) subject to Section 8.5.4, is required by securities law disclosure requirements or otherwise required by applicable Laws, or legal process, in which event the Party issuing such press release or making such public

-36-
announcement will, to the extent possible, provide the other Party with advance notice and a draft thereof and reasonably consider any timely comment with respect thereto provided by such other Party or (ii) is of any subject matter included in any prior press release or public announcement.

8.5.3 Subject to the last sentence of Section 8.5.2, any Party proposing to make a press release or public announcement requiring the other Party’s consent shall provide the proposed text to the other Party for its review prior to the date of disclosure. The reviewing Party shall respond to the other Party’s proposal no later than [**] after the proposing Party’s delivery of the proposed text, and may condition its consent on the publishing Party’s agreement to implement the reviewing Party’s reasonable revisions to the proposed text.

8.5.4 A Party may disclose this Agreement and its terms, and material developments or material information generated under this Agreement, in securities filings with the U.S. Securities and Exchange Commission (or equivalent foreign agency) to the extent required by applicable Law after complying with the procedure set forth in this Section 8.5.4.

(a) In such event, the Party seeking such disclosure will prepare a draft confidential treatment request and proposed redacted version of this Agreement to request confidential treatment for this Agreement, and the other Party agrees to promptly (and in any event, no more than [**] after receipt of such confidential treatment request and proposed redactions (or such lesser period of time as required by applicable Law)) give its input in a reasonable manner in order to allow the Party seeking disclosure to file its request within the time lines prescribed by applicable Law. The Party seeking such disclosure shall exercise reasonable efforts to obtain confidential treatment of this Agreement from the U.S. Securities and Exchange Commission (or equivalent foreign agency) as represented by the redacted version reviewed by the other Party.

(b) Further, each Party acknowledges that the other Party may be legally or by stock exchange rules required to make public disclosures (including in filings with Government Authorities or stock exchanges) of the terms of this Agreement or certain material developments or material information generated under this Agreement and agrees that each Party may make such disclosures as required by law or by stock exchange rules, provided that the Party seeking such disclosure first provides the other Party a copy of the proposed disclosure, except where prohibited by applicable Law, and provided further that (except to the extent that the Party seeking disclosure is required to disclose such information to comply with applicable Law and rules) if the other Party demonstrates to the reasonable satisfaction of the Party seeking disclosure, within [**] of such Party’s providing the copy (or such lesser period of time as required by applicable Law), that the public disclosure of previously undisclosed information will materially adversely affect the Development or Commercialization of Luxturna (including with respect to such Party’s Intellectual Property protection strategy), the Party seeking disclosure will remove from the disclosure such specific previously undisclosed information as the other Party shall reasonably request to be removed.

8.6 Publications.

8.6.1 Subject to this Section 8.6, either Party may publish or present the results of Development carried out by such Party on Luxturna following review by the other Party.
for patentability and protection of such other Party’s Confidential Information and potential impact on its plans for Development and Commercialization of Luxturna, provided that, Novartis’ review and publication rights under this Section 8.6.1 shall commence upon EU Regulatory Approval.

8.6.2 Each Party shall provide the other Party with a copy of each proposed publication pursuant to Section 8.6.1 at least [**] in advance of submission for publications in peer-reviewed publications and at least [**] in advance of submission for posters, abstracts and oral presentations or scientific publications. If a proposing Party does not receive feedback from the other Party during the applicable review period, then it is deemed that there is a non-objection by the receiving Party to the content of such publication.

8.6.3 The Parties will cooperate to remove a Party’s Confidential Information following such Party’s request and reasonably cooperate on timing for late-breaking or otherwise urgent submission requirements and to minimize any impact on the reviewing Party’s plans for Development and Commercialization of Luxturna. A reviewing Party, acting in good faith, may delay publication of a publication proposed pursuant to Section 8.6.2 above for up to [**] to secure related Intellectual Property rights in the subject matter of the publication.

8.7 No Liability for Public Disclosures by Other Party. Nothing in this Agreement shall be construed to impose upon either Party any liability or other obligation (either to the other Party or to any other Person) with respect to any press release, publication or other form of public disclosure or statement of the other Party.

ARTICLE 9
REPRESENTATIONS AND WARRANTIES; CERTAIN COVENANTS; INDEMNIFICATION

9.1 Authority. Spark and Novartis each represents and warrants to the other Party that, as of the Effective Date, it is a corporation duly organized, validly existing, and in good standing under the laws of its jurisdiction of formation and it has full right, power and authority to enter into this Agreement and to perform its respective obligations under this Agreement that it has the right to grant to the other the licenses granted pursuant to this Agreement, and that it has taken all corporate action required by applicable Law and its organizational documents to authorize the execution and delivery of this Agreement and the consummation of the transactions contemplated by this Agreement.

9.2 Consents. Spark and Novartis each represents and warrants to the other Party that, as of the Effective Date, except for any Regulatory Approval, pricing or reimbursement approval or similar approval necessary for the Development or Commercialization of Luxturna, all necessary consents, approvals and authorizations of all Governmental Authorities and other Persons required to be obtained by it as of the Effective Date in connection with the execution, delivery and performance of this Agreement have been obtained by the Effective Date.

9.3 No Conflict. Spark and Novartis each represents and warrants to the other Party that, as of the Effective Date, the execution and delivery of this Agreement by such Party, the performance of such Party’s obligations hereunder and the licenses granted or to be granted by such
Party pursuant to this Agreement (a) do not conflict with or violate any requirement of any Law existing as of the Effective Date applicable to such Party, (b) do not conflict with or result in a breach of any provision of its organizational documents, and (c) do not materially conflict with, violate, breach or constitute a default under any contractual obligation of such Party or any of its Affiliates existing as of the Effective Date.

9.4 **Enforceability.** Spark and Novartis each represents and warrants to the other Party that, as of the Effective Date, this Agreement is a legal and valid obligation binding upon it and is enforceable against it in accordance with its terms.

9.5 **No Debarment.** (a) Spark represents, warrants and covenants to Novartis that as of the Effective Date, neither Spark nor any of its Affiliates, nor, to its knowledge, any other Person involved in the Development of Luxturna prior to the Effective Date, has been debarred or is subject to debarment pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act or comparable Laws in the Novartis Territory, as applicable, and (b) Spark and Novartis each represents, warrants and covenants to the other Party that neither such Party nor any of its Affiliates will knowingly use in any capacity, in connection with the Development of Luxturna, any Person who has been debarred pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act, or who is the subject of a conviction described in such section, or comparable Laws in the Novartis Territory, as applicable. Each Party agrees to inform the other Party in writing immediately if it or any Person who is performing services hereunder is debarred or is the subject of a conviction described in Section 306 or comparable Laws in the Novartis Territory, as applicable, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to the best of such Party’s knowledge, is threatened, relating to the debarment or conviction of such Party or any Person used in any capacity by such Party or any of its Affiliates in connection with the Development of Luxturna.

9.6 **Employment.** The purpose of this Agreement is simply the grant to Novartis of an exclusive right and license to Develop, have Developed, Commercialize and have Commercialized Luxturna in the Field for the Novartis Territory as set out in Section 3.1 hereof. For the avoidance of any doubt, Novartis will not be acquiring any business or any business assets from **:

9.6.1 Each Party shall notify the other in writing within ** from becoming aware of the same;

9.6.2 Novartis, **and Spark ** Novartis ** Novartis ** Novartis ** Spark ** Novartis ** Novartis Novartis ** Novartis ** Spark **.

9.7 **Other Products.** If, within ** following the Effective Date, Novartis or any of its Affiliates Commercializes any Gene Therapeutic, other than Luxturna, in any country within the Novartis Territory, for treatment, prevention, cure or control of RPE65-mediated retinitis pigmentosa or Leber’s Congenital Amaurosis in humans, Spark, in its discretion, and upon notice to Novartis, may elect to ** mutatis mutandis .

9.8 **Additional Representations, Warranties and Covenants of Spark.** Spark represents, warrants and covenants to Novartis that, as of the Effective Date:
9.8.1 To Spark’s knowledge, Spark has the right to use and disclose and to enable Novartis to use and disclose (in each case under appropriate conditions of confidentiality) all Know-How and Confidential Information included in the Spark IP in the Field in the Novartis Territory.

9.8.2 To Spark’s knowledge, the Development, Manufacture, use and Commercialization of Luxturna does not infringe the Patent Rights or misappropriate the Know-How of any Third Party. To Spark’s knowledge it has not received any written notice of an alleged, threatened or actual claim of infringement or misappropriation.

9.8.3 Spark has not initiated or been involved in any proceedings or Claims in which it alleges that any Third Party is or was infringing or misappropriating any Spark IP, nor have any such proceedings been threatened by Spark.

9.8.4 To Spark’s knowledge, the Spark IP comprises all of the intellectual property rights used by Spark, its Affiliates, consultants and contractors in the Development of Luxturna prior to the Effective Date.

9.8.5 Spark has not granted any license to any Third Party under the Spark IP that is inconsistent with the licenses granted to Novartis hereunder, and, except as identified in Section 3.1.6, there are no agreements or arrangements to which Spark or any of its Affiliates is a party relating to Luxturna or the Spark IP that would limit the rights granted to Novartis under this Agreement or that restrict or will result in a restriction on Novartis’ ability to Develop, Manufacture (to the extent permitted pursuant to this Agreement), use or Commercialize Luxturna in the Novartis Territory as permitted under this Agreement.

9.8.6 All of Spark and its Affiliates’ employees and officers employed prior to the Effective Date, and all consultants who have participated or continue to participate in the Development of Luxturna, have executed agreements or have existing obligations under applicable Laws requiring assignment to Spark of all inventions necessary for the Development or Commercialization of Luxturna which were made during the course of and as the result of their association with Spark (or any Spark Affiliate), excluding any such inventions that have been licensed to Spark pursuant to an Existing Spark Agreement, and all such employees, officers and consultants have executed agreements or have existing obligations under applicable Laws obligating such Persons to maintain as confidential Spark and its Affiliates’ Confidential Information as well as confidential information of other Persons (including Novartis and its Affiliates) which such Person has or may receive.

9.8.7 Spark will conduct all of its activities under this Agreement consistent with Law and prevailing industry practices.

9.9 Additional Representations, Warranties and Covenants of Novartis. Novartis represents, warrants and covenants to Spark that, as of the Effective Date:

9.9.1 Novartis has not granted any license to any Third Party that is inconsistent with the licenses granted or to be granted to Spark hereunder.

9.9.2 All of its employees, officers, and consultants have executed agreements or have existing obligations under applicable Laws requiring assignment to Novartis of all inventions made during the course of and as the result of their association with Novartis and obligating the individual to maintain as confidential Novartis’ Confidential Information as well as confidential information of other Persons (including Spark and its Affiliates) which such individual may receive, to the extent required to support Novartis’ obligations under this Agreement.

9.9.3 Novartis will conduct all of its activities under this Agreement consistent with Law and prevailing industry practices.

9.10 No Implied Warranties. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY, AND EACH PARTY HEREBY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT WITH RESPECT TO THE PRODUCTS. THE PARTIES AGREE THAT MILESTONE EVENTS AND NET SALES LEVELS SET OUT IN THIS AGREEMENT OR THAT HAVE OTHERWISE BEEN DISCUSSED BY THE PARTIES AS OF THE EFFECTIVE DATE ARE MERELY INTENDED TO DEFINE THE MILESTONE PAYMENTS AND ROYALTY OBLIGATIONS IF SUCH MILESTONE EVENTS OR NET SALES LEVELS ARE ACHIEVED. NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY, EITHER EXPRESS OR IMPLIED, THAT IT WILL BE ABLE TO SUCCESSFULLY DEVELOP OR COMMERCIALIZE ANY PRODUCT OR, IF COMMERCIALIZED, THAT ANY PARTICULAR SALES LEVEL OF SUCH PRODUCT WILL BE ACHIEVED AT ALL OR WITHIN ANY COUNTRY OR JURISDICTION WITHIN SUCH PARTY’S RESPECTIVE TERRITORY.
9.11 **Indemnification**.

9.11.1 **By Spark.** Spark shall indemnify, defend and hold harmless Novartis, its Affiliates and their respective directors, officers, employees and agents (collectively, the “Novartis Indemnified Parties”), from, against and in respect of any and all Claims, to the extent arising out of or resulting from:

(a) any uncured breach of any representation, warranty or covenant made by Spark in this Agreement;

(b) the Development or Commercialization by Spark, its Affiliates and Sublicensees of Luxturna in the Spark Territory;

(c) the gross negligence, intentional misconduct or violation of Law by or of Spark or any of the other Spark Indemnified Parties;

(d) any acts or omissions by or of Spark or any Spark Affiliate in relation to any of their respective employees prior to the Effective Date for which Novartis or any Novartis Affiliate is or becomes liable by operation of applicable Law;

provided that, in the case of each of clauses (a)–(d) above, Spark shall not be obliged to so indemnify, defend and hold harmless the Novartis Indemnified Parties for any Claims to the extent Novartis has an obligation to indemnify Spark Indemnified Parties under Section 9.11.2 or to the extent such Claims arise out of or result from the gross negligence, willful misconduct or violation of Law of or by Novartis or any of the other Novartis Indemnified Parties other than any refusal by Novartis or any Novartis Affiliate to employ any employee of Spark or any Spark Affiliate, until the date it is ordered to do so by a competent Government Authority, who was prior to the Effective Date assigned to working on Luxturna and/or any dismissal by Novartis or any Novartis Affiliate of any such employee who claims that their contract of employment has transferred to Novartis by operation of Law or any failure by Novartis or any Novartis Affiliate pursuant to applicable Law to furnish Spark or any Spark Affiliate with required information in respect of such employees.

9.11.2 **By Novartis.** Novartis shall indemnify, defend and hold harmless Spark, its Affiliates and their respective directors, officers, employees and agents (collectively, the “Spark Indemnified Parties”), from, against and in respect of any and all Claims to the extent arising out of or resulting from:

(a) any uncured breach of any representation, warranty or covenant made by Novartis in this Agreement;

(b) the Development or Commercialization by Novartis, its Affiliates and Sublicensees of Luxturna in the Novartis Territory;

(c) the gross negligence, intentional misconduct or violation of Law by or of Novartis or any of the other Novartis Indemnified Parties; or
(d) any acts or omissions by or of Novartis or any Novartis Affiliate arising after the Effective Date in relation to any to individuals employed by Spark prior to the Effective Date and subsequently hired or engaged by Novartis or any Novartis Affiliate other than a refusal by Novartis or any Novartis Affiliate to employ a former employee of Spark or any Spark Affiliate, until the date it is ordered to do so by a competent Government Authority, or the termination of employment of any such former employee of Spark or any Spark Affiliate by Novartis or any Novartis Affiliate in circumstances where Section 9.6 applies; provided that, in the case of each of clauses (a)–(d) above, Novartis shall not be obliged to so indemnify, defend and hold harmless the Spark Indemnified Parties for any Claims to the extent Spark has an obligation to indemnify Novartis Indemnified Parties under Section 9.11.1 or to the extent such Claims arise out of or result from the gross negligence, willful misconduct or violation of Law of or by Spark or any of the other Spark Indemnified Parties.

In the event that the licenses granted by Spark hereunder expand to include the Spark Manufacturing IP, to the extent that Novartis is exercising a sublicense to Patent Rights licensed to Spark pursuant to the CHOP Agreement, Novartis shall indemnify, defend and hold harmless HHMI, its trustees, officers, employees and agents as set forth in Section 11.7 of the CHOP Agreement.

9.11.3 Claims for Indemnification.

(a) A Person entitled to indemnification under this Section 9.11 (an “Indemnified Party”) shall give prompt written notification to the Party from whom indemnification is sought (the “Indemnifying Party”) of any Claim or fact in respect of which the Indemnified Party may base a claim for indemnification hereunder (it being understood and agreed, however, that the failure by an Indemnified Party to give notice of a Claim as provided in this Section 9.11 shall not relieve the Indemnifying Party of its indemnification obligation under this Agreement except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure to give notice). Such notice (the “Indemnification Claim Notice”) shall contain a description of the Claim and the nature and amount of the Claim (to the extent that the nature and amount of such Claim is known at such time). Upon the request of the Indemnifying Party, the Indemnified Party shall furnish promptly to the Indemnifying Party copies of all correspondence, communications and official documents (including court documents) received or sent in respect of such Claim.

(b) Within [**] after delivery of such notification, the Indemnifying Party shall assume control of the defense of such action, suit, proceeding or claim with counsel reasonably satisfactory to the Indemnified Party. The assumption of the defense of a Claim by the Indemnifying Party shall not be construed as acknowledgement that the Indemnifying Party is liable to indemnify any indemnitee in respect of the Claim, nor shall it constitute a waiver by the Indemnifying Party of any defenses it may assert against any Indemnified Party’s claim for indemnification. If it is ultimately decided that the Indemnifying Party is not obligated to indemnify or hold an indemnitee harmless from and against the Claim, the Indemnified Party shall reimburse the Indemnifying Party for any and all costs and expenses (including reasonable attorneys’ fees and costs of suit) incurred by the Indemnifying Party in its defense of the Claim. If the Indemnifying Party does not give written notice to the Indemnified Party, within [**] after receipt of the Indemnification Claim Notice,
of the Indemnifying Party’s election to assume the defense and handling of such Claim, the provisions of clause (f) below shall govern.

(c) The Indemnified Party may participate in, but not control, any such Claim at its own expense; provided that if the Indemnified Party reasonably concludes, based on advice from counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such Claim, the Indemnifying Party shall be responsible for the reasonable fees and expenses of counsel to the Indemnified Party solely in connection therewith. The Indemnifying Party shall also cooperate with the Indemnifying Party in the defense of such Claim, including by furnishing such records, information and testimony, providing witnesses and attending such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith, providing access during normal business hours to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Claim, and making the Indemnified Party, the indemnitees and its and their employees and agents available on a mutually convenient basis to provide additional information and explanation of any records or information provided, all at the Indemnifying Party’s expense.

(d) The Indemnifying Party shall keep the Indemnified Party advised of the status of such Claim and the defense thereof and shall consider recommendations made by the Indemnified Party with respect thereto.

(e) The Indemnified Party shall not agree to any settlement of such Claim without the prior written consent of the Indemnifying Party. The Indemnifying Party shall have the right to settle such Claim on any terms the Indemnifying Party chooses; provided that it shall not, without the prior written consent of the Indemnified Party, agree to a settlement of any Claim which could lead to liability or create any financial or other obligation on the part of the Indemnified Party for which the Indemnified Party is not entitled to indemnification hereunder or which admits any wrongdoing or responsibility for the Claim on behalf of the Indemnified Party.

(f) If the Indemnifying Party does not give written notice to the Indemnified Party as set forth in Section 9.11.3(b) or fails to conduct the defense and handling of any Claim in good faith after having assumed such, the Indemnified Party may, at the Indemnifying Party’s expense, select counsel reasonably acceptable to the Indemnifying Party in connection with conducting the defense and handling of such Claim and defend or handle such Claim in such manner as it may deem appropriate. In such event, the Indemnified Party shall keep the Indemnifying Party timely apprised of the status of such Claim and shall not settle such Claim without the prior written consent of the Indemnifying Party, which consent shall not be unreasonably withheld. If the Indemnified Party defends or handles such Claim, the Indemnifying Party shall cooperate with the Indemnified Party, at the Indemnified Party’s request but at no expense to the Indemnified Party, and shall be entitled to participate in the defense and handling of such Claim with its own counsel and at its own expense.

9.12 Direct Claims for Breach. If a Party believes it has been damaged directly (i.e., not arising from a Claim of a Third Party), such Party shall provide a Notice of Dispute to the other pursuant to Section 12.3 of this Agreement. All such disputes shall be governed by ARTICLE 11
of this Agreement. For clarity, this Section 9.12 is not intended to limit any other right or remedy of a Party with respect to this Agreement.

9.13 Integration of this Agreement and Supply Agreement. Spark and Novartis each acknowledge that the Supply Agreement and this License Agreement were entered into as part of one integrated transaction. As such, in the case of a claim for damages or indemnification, neither Spark nor Novartis shall assert that the performance and/or payment under one agreement was separate and apart from payment and/or performance under the other agreement.

9.14 Measure of Damages. Neither Party shall have liability to the other under this Agreement, whether pursuant to Section 9.11, ARTICLE 11 or otherwise, in contract, tort or otherwise, for [**]; provided that the foregoing limitation shall not apply to any such damages paid or payable to Third Parties in connection with an indemnifiable Claim pursuant to Section 9.11 or in the case of gross negligence or fraud.

9.15 No Exclusion. Neither Party excludes any liability for death or personal injury caused by its negligence or that of its employees, agents or subcontractors to the extent such exclusion is prohibited by applicable Law.

ARTICLE 10
TERM AND TERMINATION

10.1 Term. Unless terminated earlier in accordance with this ARTICLE 10, this Agreement shall remain in force for the period commencing on the Effective Date and ending on the expiration of the last to expire Royalty Term (the “Term”).

10.2 Termination for Material Breach. Upon any material breach of this Agreement by a Party (the “Breaching Party”), the other Party (the “Non-Breaching Party”) may give written notice to the Breaching Party specifying the claimed particulars of such breach. The Breaching Party shall have a period of [**] after such notice if such material breach is a breach of a payment obligation or [**] after such notice in the case of any other material breach in which to cure such breach; provided that, if such breach other than a payment breach is capable of being cured and cannot be cured within such [**] period, and the Breaching Party notifies the Non-Breaching Party within such period that it has initiated actions to cure such breach and thereafter diligently pursues such actions, the Breaching Party shall have such additional period as is reasonable in the circumstances, but in no event longer than [**] after the end of the original cure period, to cure such breach. Any termination by any Party under this Section 10.2 and the effects of termination provided in this ARTICLE 10 shall be without prejudice to any damages or other legal or equitable remedies to which it may be entitled from the other Party. If the Breaching Party fails to cure the breach within the time period set forth above, the Non-Breaching Party shall have the right thereafter to terminate this Agreement effective immediately by giving written notice to the Breaching Party to such effect; provided that the Non-Breaching Party may, by notice to the Breaching Party, designate a later date for such termination in order to facilitate an orderly transition of activities relating to Luxturna or elect not to terminate this Agreement.

-44-
10.3 **Termination for Insolvency.** Each Party shall have the right to terminate this Agreement upon written notice to the other Party if an Insolvency Event occurs with respect to such other Party. In any event when a Party first becomes aware of the likely occurrence of any Insolvency Event in regard to that Party, it shall promptly so notify the other Party in sufficient time to give the other Party sufficient notice to protect its interests under this Agreement.

10.4 **Termination by Novartis for Convenience.** Novartis shall have the right to terminate this Agreement upon one (1) year’s prior written notice to Spark. Following such notice of termination, Spark may elect to accelerate the effective date of such termination to any time earlier than the end of such one-year notice period upon written notice to Novartis specifying such earlier termination date; provided that such earlier date is consistent with the orderly wind down set forth in Section 10.7.2(i).

10.5 **Termination by Novartis for Breach of Supply Agreement.** In the event Novartis terminates the Supply Agreement in full pursuant to Section 14.2 thereof due to an uncured material breach by Spark, Novartis may, upon thirty (30) days’ prior written notice to Spark, terminate this Agreement, provided that Novartis may not terminate this Agreement if, following a Supply Transition Event, Novartis assumes the right to Manufacture Luxturna pursuant to Article 9 of the Supply Agreement as a consequence of such Supply Transition Event.

10.6 **Termination by Novartis for Change in Control of Spark.** Novartis may, upon sixty (60) days’ prior written notice to Spark, to be given by Novartis within thirty (30) days following the earliest public announcement of such event, unilaterally terminate this Agreement following a Spark Change in Control.

10.7 **Effects of Termination.**

10.7.1 **Spark Material Breach, Insolvency, Breach of Supply Agreement.** In the event Novartis has the right to terminate this Agreement pursuant to Section 10.2 (Material Breach), 10.3 (Insolvency) or 10.5 (Breach of Supply Agreement), Novartis may elect, in its sole discretion, to terminate this Agreement in accordance with the specific notice and timing requirements set forth in Section 10.2, 10.3 or 10.5, as applicable:

(a) In the event Novartis exercises any such right to terminate:

   (i) Novartis may pay for and take receipt of Product in respect of orders already placed pursuant to the Supply Agreement;

   (ii) Novartis may continue to exercise the license granted pursuant to Section 3.1.1 to Commercialize such Product until supply is exhausted (including supply obtained pursuant to Section 10.7.1(a)(i)), and [**];

   (iii) Novartis shall have no obligation to pay the [**];

   (iv) Novartis shall wind down, or if requested by Spark and at Spark’s cost, transition to Spark or its designee, any clinical study of Luxturna as to which Novartis

-45-

ActiveUS 166647742v.1
is the regulatory sponsor that is ongoing as of the effective date of termination to the extent such clinical study was being carried out by Novartis or funded by Novartis immediately prior to termination of this Agreement;

(v) the licenses granted to Novartis in Section 3.1 shall terminate upon exhaustion of the Product referenced in Section 10.7.1(a)(i) (except as set forth in Section 10.7.4) and the licenses granted to Spark in Section 3.2 shall expand to cover the Novartis Territory upon the effective date of termination and survive;

(vi) Novartis shall promptly transfer on an as-is, where-is basis to Spark or Spark’s designee possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of Luxturna, to the extent permitted under applicable Law, and Novartis shall reasonably cooperate, at no additional out-of-pocket cost to Novartis, with requests by Spark for assistance necessary to facilitate Spark’s assumption of regulatory responsibilities for Luxturna in the applicable countries in which direct transfer is not permitted;

(vii) Novartis shall promptly provide Spark with a summary of all Third Party agreements relating to the Development or Commercialization of Luxturna to which Novartis is a party and shall transfer to Spark any such Third Party agreements solely relating to the Development or Commercialization of Luxturna that Spark requests be assigned, to the extent such transfer is permitted thereunder; with respect to each agreement relating to the Development or Commercialization of Luxturna that is not transferred to Spark, at Spark’s request, Novartis shall reasonably facilitate a direct introduction between Spark and the Third Party counterparty to such agreement;

(viii) the Related Agreements shall terminate, subject to any surviving obligations set forth therein;

(ix) Novartis shall execute all documents and take all such further actions as may be reasonably requested by Spark in order to give effect to the foregoing clauses in this Section 10.7.1;

(x) the Parties shall agree upon an orderly wind down of Development and Commercialization activities hereunder (including those activities being performed by their Affiliates, Sublicensees or Third Party contractors and any ongoing supply obligations) and each Party shall make all payments due and owing to one another and to Third Parties, provided that unless otherwise agreed or required under applicable Laws, all such transitional activities and obligations shall cease with effect from the [**] of the date of termination of this Agreement; and

(xi) Novartis’ performance of transition activities pursuant to Sections 10.7.1(a)(iv) through 10.7.1(a)(x) and the expansion of licenses pursuant to Section 10.7.1(a)(v) (collectively, the “Post-Termination Obligations.”) is conditioned on the Parties, within [**] of the effective date of termination, negotiating in good faith commercially reasonable terms.
therefor, taking into further account the overall circumstances of the particular termination, Novartis’ ability to achieve a reasonable economic return and the residual value of the Novartis Territory rights to Luxturna at the time of termination.

(b) In the event Novartis has any such right to terminate this Agreement, but declines to exercise such right:

(i) Novartis shall provide written notice to Spark that it intends to exercise its rights under this Section 10.7.1(b) (within [**] after such termination would otherwise become effective);

(ii) Novartis may exercise the provisions of Article 9 of the Supply Agreement (which rights include the rights to receive and assume responsibility for supply or have such responsibility transitioned to a Third Party contractor);

(iii) Novartis may continue to order and take receipt of Product in accordance with the Supply Agreement and shall continue to pay royalties in accordance with Section 6.3 with respect to such Product (subject, if applicable, to the specific modifications set forth in Section 10.7.1(b)(iv)); and

(iv) If, following an applicable Supply Transition Event that is a basis for such termination, Novartis assumes control of Manufacturing of Luxturna pursuant to Article 9 of the Supply Agreement, then commencing with Novartis’s assumption of Manufacturing, the royalty rate during the balance of the Base Royalty Term, if any, shall be reduced to [**] percent ([**]% of the royalty rate that would otherwise apply pursuant to Section 6.3 and the royalty rate during the Continued Royalty Term shall be reduced to [**]%, and Novartis shall be entitled to offset against all royalties due and payable to Spark the actual, documented costs incurred by Novartis in transferring Manufacturing from Spark to Novartis (or its designee) pursuant to Section 9 of the Supply Agreement.

10.7.2 Termination in Full by Spark for Novartis Material Breach or Insolvency; Termination by Novartis for Convenience or Change of Control. In the event of any termination of this Agreement by Spark in full pursuant to Section 10.2 (Material Breach) or Section 10.3 (Insolvency), or by Novartis pursuant to Section 10.4 (Convenience) or Section 10.6 (Change of Control), the following provisions of this Section 10.7.2 shall apply:

(a) Novartis shall pay for and take receipt of orders already placed, completed and/or in process pursuant to the Supply Agreement;

(b) With respect to the Fixed Facility Fee:

(i) in the event of termination by Spark pursuant to Section 10.2 (Material Breach) or Section 10.3 (Insolvency), Novartis shall be obligated to pay the Fixed Facility Fee in respect of [**]. Novartis shall pay the Fixed Facility Fee for each such Calendar Year on or before December 31 of the applicable Calendar Year; and
in the event of termination by Novartis pursuant to Section 10.4 (Convenience), Novartis shall be obligated to pay the Fixed Facility Fee in respect of [**]; provided, however, that if Spark enters into an arrangement with a Third Party to Develop or Commercialize Luxturna in all or a portion of the Novartis Territory, Novartis shall only be obligated to pay the Fixed Facility Fee in respect of [**]. Novartis shall pay the Fixed Facility Fee for each such Calendar Year on or before December 31 of the applicable Calendar Year; and

in the event of termination by Novartis pursuant to Section 10.6 (Change of Control), Novartis shall only pay the Fixed Facility Fee in respect of [**]. Novartis shall pay the Fixed Facility Fee on or before December 31 of such Calendar Year.

(c) Novartis shall wind down, or if requested by Spark and at Spark’s cost, transition to Spark or its designee, any clinical study of Luxturna as to which Novartis is the regulatory sponsor that is ongoing as of the effective date of termination to the extent such clinical study was being carried out by Novartis or funded by Novartis immediately prior to termination of this Agreement;

(d) the licenses granted to Novartis in Section 3.1 shall terminate (except as set forth in Section 10.7.4) and the licenses granted to Spark in Section 3.2 shall expand to cover the Novartis Territory and survive;

(c) Novartis shall promptly transfer on an as-is, where-is basis to Spark or Spark’s designee possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of Luxturna, to the extent permitted under applicable Law, and Novartis shall reasonably cooperate, at no additional out-of-pocket cost to Novartis, with requests by Spark for assistance necessary to facilitate Spark’s assumption of regulatory responsibilities for Luxturna in the applicable countries in which direct transfer is not permitted;

(f) Novartis shall promptly provide Spark with a summary of all Third Party agreements relating to the Development or Commercialization of Luxturna to which Novartis is a party and shall transfer to Spark any such Third Party agreements solely relating to the Development or Commercialization of Luxturna that Spark requests be assigned, to the extent such transfer is permitted thereunder; with respect to each agreement relating to the Development or Commercialization of Luxturna that is not transferred to Spark, at Spark’s request, Novartis shall reasonably facilitate a direct introduction between Spark and the Third Party counterparty to such agreement;

(g) the Related Agreements shall terminate, subject to any surviving obligations set forth therein;

(h) Novartis shall execute all documents and take all such further actions as may be reasonably requested by Spark in order to give effect to the foregoing clauses in this Section 10.7.2; and

-48-
the Parties shall agree upon an orderly wind down of Development and Commercialization activities hereunder (including those activities being performed by their Affiliates, Sublicensees or Third Party contractors and any ongoing supply obligations) and each Party shall make all payments due and owing to one another and to Third Parties, provided that unless otherwise agreed or required under applicable Laws, all such transitional activities and obligations shall cease with effect from the [**] of the date of termination of this Agreement.

10.7.3 Partial Termination. In the event of partial termination of this Agreement with respect to a Terminated Country pursuant to Section 4.1 or Section 5.1, the following provisions of this Section 10.7.3 shall apply:

(a) Novartis shall wind down, or if requested by Spark and at Spark’s cost, transition to Spark or its designee, any clinical study of Luxturna as to which Novartis is the regulatory sponsor that is ongoing as of the effective date of such partial termination to the extent such clinical study was being carried out by Novartis or funded by Novartis for the Terminated Country immediately prior to such partial termination;

(b) the licenses granted to Novartis in Section 3.1 shall terminate with respect to such Terminated Country (except as set forth in Section 10.7.4) and the licenses granted to Spark in Section 3.2 shall expand to cover such Terminated Country;

(c) Novartis shall promptly transfer on an as-is, where-is basis to Spark or Spark’s designee possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of Luxturna in such Terminated Country, to the extent permitted under applicable Law, and Novartis shall reasonably cooperate, at no additional out-of-pocket cost to Novartis, with requests by Spark for assistance necessary to facilitate Spark’s assumption of regulatory responsibilities for Luxturna in such Terminated Country if direct transfer is not permitted; provided, however, that if the Regulatory Approval covers both a Terminated Country and other non-terminating jurisdictions within the Novartis Territory, Novartis shall retain the Regulatory Approval but shall take such steps as are reasonably practicable under applicable Laws to enable Spark to market Luxturna in the Terminated Country as if it were the holder of a Regulatory Approval in such Terminated Country alone;

(d) Novartis shall promptly provide Spark with a summary of all Third Party agreements relating to the Development or Commercialization of Luxturna to which Novartis is a party and shall transfer to Spark any such Third Party agreements solely relating to the Development or Commercialization of Luxturna for such Terminated Country that Spark requests be assigned, to the extent such transfer is permitted thereunder; with respect to each agreement relating to the Development or Commercialization of Luxturna for such Terminated Country that is not transferred to Spark, at Spark’s request, Novartis shall reasonably facilitate a direct introduction between Spark and the Third Party counterparty to such agreement;
(c) Novartis shall execute all documents and take all such further actions as may be reasonably requested by Spark in order to give effect to the foregoing clauses in this Section 10.7.3; and

(f) the Parties shall agree upon an orderly wind down of Development and Commercialization activities with respect to such Terminated Country (including those activities being performed by their Affiliates, Sublicensees or Third Party contractors and any ongoing supply obligations) and each Party shall make all payments due and owing to one another and to Third Parties, provided that unless otherwise agreed or required under applicable Laws, all such transitional activities and obligations shall cease with effect from the [**] of the date of such partial termination of this Agreement.

10.7.4 Survival of Novartis Licenses. The licenses granted to Novartis under this Agreement shall survive (i) to the extent necessary for Novartis to perform its post-termination obligations under this ARTICLE 10, and (ii) as provided in Section 3.1.3.

10.7.5 Post-Expiration Supply. Upon expiration of the last to expire Royalty Term, the Parties shall meet and discuss the post-expiration provision of Product supply and Spark agrees to consider, in good faith, any request of Novartis to enter into a new supply arrangement. In the event the Parties cannot agree on a post-expiration supply arrangement, Spark shall transition Manufacture to Novartis, its Affiliate or a Third Party contract manufacturer pursuant to Section 9.2(e) of the Supply Agreement.

10.8 Return of Confidential Information. Within [**] following the expiration or termination of this Agreement, except to the extent and for so long as a Party retains license rights under this Agreement, each Party shall deliver to the other Party, or at the delivering Party’s option destroy, any and all Confidential Information of the other Party in its possession, except for one copy which may be retained in its confidential files for archive purposes and subject to any copies remaining on its standard computer back-up devices (which copies the Party agrees not to access after termination).

10.9 Survival. In the event of any expiration or termination of this Agreement, (a) all financial obligations under ARTICLE 6 (i) that have accrued as of the effective date of such expiration or termination, whether or not they have become due, shall remain in effect and (ii) shall continue to apply with respect to Net Sales of Luxturna supplied by Spark pursuant to the Supply Agreement after the effective date of such expiration or termination and (b) the provisions set forth in Sections 3.1.3, 3.2.1(b) (with respect to the Spark Territory and, to the extent provided in Section 10.7, with respect to the Novartis Territory), 3.2.1(c), 3.2.2 (with respect to the Spark Territory and, to the extent provided in Section 10.7, with respect to the Novartis Territory), 6.5, 6.6, 6.7, 6.8, 6.9, 6.10, 7.1, 7.8.1, 7.8.2, ARTICLE 8 (except for Sections 8.5 and 8.6), Sections 9.6.2, 9.10, 9.11, 9.12, 9.13, 9.14, 9.15, 10.7, 10.8, 10.9, ARTICLE 11 and ARTICLE 12 (and defined terms necessary to interpret the foregoing), shall survive.

ARTICLE 11
DISPUTE RESOLUTION

-50-
11.1 **In General.** If any dispute or disagreement arises between Novartis and Spark in respect of this Agreement or any Related Agreement, they shall follow the following procedures in an attempt to resolve the dispute or disagreement:

11.1.1 The Party claiming that such a dispute exists shall give notice in writing to the other Party of the nature of the dispute (a “**Notice of Dispute.**”)

11.1.2 Within [**] of receipt of a Notice of Dispute, the Alliance Managers shall meet and use reasonable efforts to resolve the dispute. If the Alliance Managers are unable to resolve the dispute within [**] of such initial meeting, they shall refer the matter to the JSC, which shall meet and use reasonable efforts to resolve the dispute. If the JSC has been disbanded or is unable to resolve the dispute within [**] of such referral, the Executive Officers (or a designate of the Executive Officer) of each Party shall meet in person or by teleconference and exchange written summaries reflecting, in reasonable detail, the nature and extent of the dispute, and at this meeting, they shall use their reasonable efforts to resolve the dispute.

11.1.3 If within [**] the dispute has not been resolved by the Executive Officers, or if, for any reason, the meeting described in Section 11.1.2 has not been held within [**] of initial receipt of the Notice of Dispute, then, subject to Section 11.2, the Parties agree that either Party may initiate litigation to resolve the dispute.

11.2 **Equitable Relief.** Nothing in this Agreement shall limit the right of either Party to seek to obtain in any court of competent jurisdiction any equitable or interim relief or provisional remedy, including injunctive relief.

11.3 **Survival.** The provisions of this ARTICLE 11 shall survive for [**] from the date of termination or expiration of this Agreement.

**ARTICLE 12**

**MISCELLANEOUS**

12.1 **Choice of Law.** This Agreement shall be governed by and interpreted under the Laws of the State of Delaware, United States, excluding: (a) any provision thereof that would apply the Law of any other jurisdiction; (b) the United Nations Conventions on Contracts for the International Sale of Goods; (c) the 1974 Convention on the Limitation Period in the International Sale of Goods (the “**1974 Convention.**”); and (d) the Protocol amending the 1974 Convention, done at Vienna April 11, 1980.

12.2 **Jurisdiction and Venue.** Each Party irrevocably submits to the exclusive jurisdiction of the United States District Court for the District of Delaware for the purposes of any suit, action or other proceeding arising out of this Agreement. Each Party agrees to commence any such action, suit or proceeding in the United States District Court for the District of Delaware or if such suit, action or other proceeding may not be brought in such court for jurisdictional reasons, in the Superior Court of the State of Delaware, Wilmington. Each Party irrevocably and unconditionally waives any objection to the laying of venue of any such action, suit or proceeding arising out of this Agreement in the United States District Court for the District of Delaware (or the Superior Court
the State of Delaware, Wilmington, as applicable), and hereby and thereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum. For the avoidance of doubt, both Parties hereby irrevocably waive any right they may have to a trial by jury arising from any dispute under this Agreement.

12.3 Notices. All notices, instructions and other communications hereunder or in connection herewith shall be in writing, shall be sent to the address specified in this Section 12.3 and shall be: (a) delivered personally; (b) transmitted by facsimile; or (c) sent via a reputable international overnight delivery service. Any such notice, instruction or communication shall be deemed to have been delivered (i) upon receipt if delivered by hand or when transmitted with electronic confirmation of receipt, if transmitted by facsimile (if such transmission is on a Business Day; otherwise, on the next Business Day following such transmission), provided that an original document is sent via an internationally recognized overnight delivery service (receipt requested), or (ii) one (1) Business Day after it is sent via a reputable international overnight delivery service.

If to Spark:
Spark Therapeutics, Inc.
3737 Market Street, Suite 1300
Philadelphia, PA 19104
USA
Attention: General Counsel
Facsimile: [**]

With copy to:
WilmerHale LLP
60 State Street
Boston, MA 02109
USA
Attention: Steven D. Barrett, Esq.
Facsimile No.: (617) 526-5000

If to Novartis:
Novartis Pharma AG
Lichtstrasse 35
CH 4002 Basel
Switzerland
Attn: Head of Pharma BD&L
Fax: [**]

Novartis Pharma AG
Lichtstrasse 35
CH-4002 Basel
Switzerland
Attn: General Counsel
Fax [**]

With a copy to:
Arnold & Porter Kaye Scholer LLP
250 West 55th Street
New York, NY 10019-9710
Attention: Derek M. Stoldt, Esq.
Facsimile No.: [**]

-52-
or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith.

12.4 **Severability.** If, under applicable Law, any provision of this Agreement is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision of this Agreement (such invalid or unenforceable provision, a “Severed Clause”), this Agreement shall endure except for the Severed Clause. The Parties shall consult one another and use reasonable, good faith efforts to agree upon a valid and enforceable provision that is a reasonable substitute for the Severed Clause in view of the intent of the Severed Clause and this Agreement.

12.5 **Integration.** This Agreement constitutes the entire agreement between the Parties hereto with respect to the subject matter of this Agreement and supersedes all previous agreements, whether written or oral including, without limitation, that certain Mutual Non-Disclosure Agreement by and between Novartis and Spark, dated September 27, 2017 (the “CDA”), which obligations between Novartis and Spark are hereby terminated as of the Effective Date, provided that the rights and obligations of the Parties in Section 8 of the CDA shall survive as set forth therein. The Parties acknowledge and agree that, as of the Effective Date, all Confidential Information (as defined in the CDA) disclosed by a Party pursuant to the CDA shall be considered Confidential Information of such Party and subject to the terms set forth in this Agreement. This Agreement may be amended only in writing signed by properly authorized representatives of each of Spark and Novartis. In the event of any conflict between a substantive provision of this Agreement and any Exhibit hereto or any Related Agreement, the substantive provision of this Agreement shall prevail.

12.6 **Independent Contractors; No Agency.** Neither Party shall have any responsibility for the hiring, firing or compensation of the other Party’s employees or for any employee benefits. No employee or representative of a Party shall have any authority to bind or obligate the other Party to this Agreement for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on the other Party without said Party’s written approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, each Party’s legal relationship under this Agreement to the other Party shall be that of independent contractor. Nothing contained in this Agreement shall be deemed to constitute a partnership, joint venture, or legal entity of any type between Spark and Novartis, or to constitute one as the agent of the other. Moreover, each Party agrees not to construe this Agreement, or any of the transactions contemplated hereby, as a partnership for any tax purposes.

12.7 **Assignment; Successors.** Neither Party will assign, transfer or novate this Agreement without the prior written consent of the other Party, except assignment or transfer will be permitted by notice in writing, and without the prior written consent of the other Party, to: (a) any of the assigning Party’s Affiliates; or (b) a purchaser of a substantial part of a Party’s assets or business relating to the subject matter of this Agreement. This Agreement shall be binding upon, and shall inure to the benefit of, all successors and permitted assigns. Any permitted assignee will assume all obligations of its assignor under this Agreement. Any assignment, transfer or novation made in violation of this Section 12.7 shall be wholly void and invalid, the assignee, transferee or successor shall acquire no rights whatsoever, and the non-assigning Party shall not recognize, nor shall it be required to recognize, the assignment, transfer or novation.
12.8 **Performance by Other Persons.** Subject to Section 3.1.5, each Party may exercise its rights and perform its obligations under this Agreement itself or through any of its Affiliates or permitted Sublicensees, and may subcontract its Development and Commercialization activities hereunder as it deems appropriate without the other Party’s consent (including to distributors or wholesalers in the ordinary course of business). Each Party shall be responsible for the performance and compliance with this Agreement of its Affiliates, permitted Sublicensees, authorized agents and subcontractors.

12.9 **Force Majeure.** No Party shall be liable for failure of or delay in performing obligations set forth in this Agreement, and no Party shall be deemed in breach of its obligations, if such failure or delay is due to any natural disaster, explosion, fire, flood, act of nature (including tornadoes, thunderstorms, earthquakes, typhoons, hurricanes, and tsunamis), war, hostilities between nations, civil commotions, terrorism, riots, embargo, losses or shortages of power, [*]**, sabotage, or any other cause reasonably beyond the control of such Party. The Party affected by such force majeure shall provide the other Party with full particulars thereof as soon as it becomes aware of the same (including its good faith estimate of the likely extent and duration of the interference with its activities), and will use commercially reasonable efforts in good faith to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable. If the performance of any such obligation under this Agreement is delayed owing to such a force majeure for any continuous period of more than [*]**, the Parties will consult with respect to an equitable solution, including the possibility of the mutual termination of this Agreement.

12.10 **No Third Party Beneficiaries.** Except for Indemnified Parties as set forth in Section 9.11, this Agreement shall not be construed as conferring any rights or remedies upon any Person other than the Parties and their respective successors and permitted assigns.

12.11 **Execution in Counterparts; Facsimile Signatures.** This Agreement may be executed in counterparts, each of which counterparts, when so executed and delivered, shall be deemed to be an original, and all of which counterparts, taken together, shall constitute one and the same instrument even if both Parties have not executed the same counterpart. Signatures provided electronically by PDF or facsimile transmission shall be deemed to be original signatures.

12.12 **English Language.** This Agreement is written and executed in the English language. Any translation into any other language shall not be an official version of this Agreement and in the event of any conflict in interpretation between the English version and such translation, the English version shall prevail.

12.13 **Expenses.** Except as otherwise expressly provided in this Agreement, each Party shall pay the fees and expenses of its respective lawyers and other experts and all other expenses and costs incurred by such Party incidental to the negotiation, preparation, execution and delivery of this Agreement.

12.14 **Cumulative Remedies.** No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

[Signature page follows]
IN WITNESS WHEREOF, Spark and Novartis have caused this Agreement to be duly executed by their authorized representatives, in duplicate as of the Effective Date.

**NOVARTIS PHARMA AG**

By: /s/ Marc Ceulemans
Name: Marc Ceulemans
Title: Head Strategic Venture Capital Fund & Pharma Equities

By: /s/ Bartosz Dzikowski
Name: Bartosz Dzikowski
Title: Authorized Signatory
IN WITNESS WHEREOF, Spark and Novartis have caused this Agreement to be duly executed by their authorized representatives, in duplicate as of the Effective Date.

SPARK THERAPEUTICS, INC.

By: /s/ Jeffrey D. Marrazzo

Name: Jeffrey D. Marrazzo
Title: CEO
License Agreement, by and between Spark (formerly AAvenue Therapeutics, LLC) and The Children’s Hospital of Philadelphia, dated October 14, 2013, as amended by that certain (i) License Agreement Amendment, dated December 26, 2013, (ii) License Agreement Amendment No. 2, dated May 16, 2014, (iii) License Agreement Amendment No. 3, dated December 5, 2014, and (iv) License Agreement amendment No. 4, dated October 8, 2015, and as supplemented by that certain License Agreement by and between Spark and The Children’s Hospital of Philadelphia dated on or about November 20, 2015 (collectively, the “CHOP Agreement”).

Amended and Restated Patent License Agreement, by and between Spark and The Trustees of the University of Pennsylvania, dated December 31, 2015 (the “UPenn Agreement”).

Patent License Agreement, by and between Spark Therapeutics, Inc. and The National Institutes of Health, dated December 26, 2014 (the “NIH Agreement”).
5.1 Prior to the First Commercial Sale, at NIH's reasonable request and to the extent reasonably available and already existing on-hand at Licensee's facilities, the Licensee agrees to provide the NIH with reasonable quantities of Licensed Products or materials made through the Licensed Processes solely for NIH's internal non-commercial research use only. The NIH may not transfer any Licensed Products obtained pursuant to this paragraph to any third party without the prior written consent of Licensee.

5.2 The Licensee agrees that products used or sold in the United States embodying Licensed Products or produced through use of Licensed Processes shall be manufactured substantially in the United States, unless a written waiver is obtained in advance from the NIH.

***

8.1 The Licensee agrees to keep accurate and correct records of Licensed Products, if any, made, used, sold, or imported and Licensed Processes practiced under this Agreement appropriate to determine the amount of royalties due the NIH. These records shall be retained for at least [**] following a given reporting period and shall be available during normal business hours for inspection, at the expense of the NIH, by an accountant or other designated auditor selected by the NIH for the sole purpose of verifying reports and royalty payments hereunder. The accountant or auditor shall only disclose to the NIH information relating to the accuracy of reports and royalty payments made under this Agreement. If an inspection shows an underreporting or underpayment in excess of [**] percent ([**]%) for any twelve (12) month period, then the Licensee shall reimburse the NIH for the cost of the inspection at the time the Licensee pays the unreported royalties, including any additional royalties as required by Paragraph 9.7. All royalty payments required under this Paragraph shall be due within [**] of the date the NIH provides the Licensee notice of the payment due.

***

10.1 The Licensee shall use its reasonable commercial efforts to bring the Licensed Products and Licensed Processes to Practical Application. "Reasonable commercial efforts" for the purposes of this provision shall include reasonable efforts to adhere to the Commercial Development Plan in Appendix E and toward the performance of the Benchmarks in Appendix D. The efforts of any sublicensee shall be considered the efforts of the Licensee.

10.2 Upon the First Commercial Sale, until the expiration or termination of this Agreement, the Licensee shall use its reasonable commercial efforts to make Licensed Products and Licensed Processes reasonably accessible to the United States public.

***
12.5 The Licensee shall indemnify and hold the NIH, its employees, students, fellows, agents, and consultants harmless from and against all liability, demands, damages, expenses, and losses, including but not limited to death, personal injury, illness, or property damage in connection with or arising out of:

(a) the use by or on behalf of the Licensee, its directors, employees, or third parties of any Licensed Patent Rights; or

(b) the design, manufacture, distribution, or use of any Licensed Products, Licensed Processes or materials by the Licensee, or other products or processes developed in connection with or arising out of the Licensed Patent Rights.

* * *

13.7 The NIH reserves the right according to 35 U.S.C. §209(d)(3) to terminate or modify this Agreement if it is determined that the action is necessary to meet the requirements for public use specified by federal regulations issued after the date of the license and these requirements are not reasonably satisfied by the Licensee.

13.8 Within [**] of receipt of written notice of the NIH's unilateral decision to modify or terminate this Agreement, the Licensee may, consistent with the provisions of 37 C.F.R.) i404.1 l, appeal the decision by written submission to the designated the NIH official. The decision of the designated the NIH official shall be the final agency decision. The Licensee may thereafter exercise any and all administrative or judicial remedies (or both) that may be available.

13.9 Within [**] of expiration or termination of this Agreement under this Article 13, a final report shall be submitted by the Licensee. Any royalty payments, including those incurred but not yet paid (such as the full minimum annual royalty), and those related to patent expense, due to the NIH shall become immediately due and payable upon termination or expiration. Unless otherwise specifically provided for under this Agreement, upon termination or expiration of this Agreement, the Licensee shall return all Licensed Products or other materials included within the Licensed Patent Rights to the NIH or provide the NIH with written certification of the destruction thereof. The Licensee may not be granted additional NIH licenses if the final reporting requirement is not fulfilled.
Novartis exclusively licenses first ophthalmology gene therapy in all markets outside the US, a milestone for patients with rare inherited vision loss

- Novartis enters into a licensing and supply agreement to develop, register and commercialize investigational gene therapy voretigene neparvovec outside the US; Spark Therapeutics retains US rights for LUXTURNA™ (voretigene neparvovec-rzyl)

- Voretigene neparvovec is an investigational one-time gene therapy to restore functional vision for patients with biallelic mutations of the RPE65 gene

- This investigational therapy provides patients with a working copy of the RPE65 gene to treat otherwise progressive vision loss that typically leads to blindness

Basel, January 24, 2018 – Novartis today announced a licensing agreement with Spark Therapeutics covering development, registration and commercialization rights to voretigene neparvovec in markets outside the US. Voretigene neparvovec, known as LUXTURNA™ (voretigene neparvovec-rzyl) in the US, received FDA approval on December 19, 2017 as a one-time gene therapy to restore functional vision in children and adult patients with biallelic mutations of the RPE65 (retinal pigment epithelial 65 kDa protein) gene \(^1\). The market authorization application (MAA) with the European Medicines Agency (EMA) was filed on July 31, 2017. Currently there is no existing therapy for this disease outside the US.

“No otherwise healthy child should have to go blind due to this devastating disease. Gene therapy is a promising new avenue to potentially address this unmet need,” said Shreeram Aradhye, Global Head of Medical Affairs and Chief Medical Officer, Novartis Pharmaceuticals. “This collaboration builds on our commitment to ophthalmology. We look forward to leveraging our global presence to ensure that patients outside the US have access to this potentially life-changing treatment.”

Novartis will make an upfront payment as well as pay milestones and royalties to Spark Therapeutics reflective of the late stage of the opportunity. Spark Therapeutics retains exclusive rights for LUXTURNA™ in the US and will retain responsibility for obtaining EMA approval. Commercialization rights will be transferred to Novartis upon successful completion of registration and issuance of market authorization. Novartis has exclusive rights to pursue development, registration and commercialization in all other countries outside the US. Spark Therapeutics will be responsible for the supply of voretigene neparvovec worldwide under a separate manufacturing and supply agreement with Novartis.

Mutations in the RPE65 gene lead to reduced or absent levels of RPE65 isomeroxydrolase activity, blocking the visual cycle and resulting in progressive vision loss and ultimately,
blindness. Only a few thousand people worldwide are affected by this ultra-orphan condition. Pending approval, Novartis will work with physicians to establish new approaches to facilitating diagnosis and treatment at specialized treatment centers.

About Novartis in ophthalmology

Novartis is a leading ophthalmology company, with therapies that treat both front and back of the eye disorders, including retina diseases, glaucoma, dry eye and other external eye diseases. In 2016, approximately 200 million patients worldwide were treated with Novartis ophthalmic products.

About LUXTURNAM

LUXTURNAM is an adeno-associated virus (AAV) vector-based gene therapy indicated in the United States for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician. Mutations in the RPE65 (retinal pigment epithelial 65 kDa protein) gene lead to reduced or absent levels of RPE65 isomerohydrolase activity, blocking the visual cycle and resulting in impairment of vision. Injection of LUXTURNAM into the subretinal space results in transduction of some retinal pigment epithelial cells with a cDNA encoding normal human RPE65 protein, thus providing the potential to restore the visual cycle.

The safety data reflect exposure to LUXTURNAM in two clinical trials consisting of 41 subjects (81 eyes) with confirmed biallelic RPE65 mutation-associated retinal dystrophy. 40 of the 41 subjects received sequential subretinal injections to each eye. The efficacy in pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy was evaluated in an open-label, two-center, randomized trial. The average age of the 31 randomized subjects was 15 years (range 4 to 44 years), including 64% pediatric subjects (n=20, age from 4 to 17 years) and 36% adults (n=11). The efficacy of LUXTURNA was established on the basis of multi-luminance mobility testing (MLMT) score change from Baseline to Year 1.

Indication and Important Safety Information

LUXTURNA (voretigene neparvovec-rzyl) is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

Patients must have viable retinal cells as determined by the treating physicians.

Warnings and Precautions

- **Endophthalmitis** may occur following any intraocular surgical procedure or injection. Use proper aseptic injection technique when administering LUXTURNA, and monitor for and advise patients to report any signs or symptoms of infection or inflammation to permit early treatment of any infection.

- **Permanent decline in visual acuity** may occur following subretinal injection of LUXTURNA. Monitor patients for visual disturbances.

- **Retinal abnormalities** may occur during or following the subretinal injection of LUXTURNA, including macular holes, foveal thinning, loss of foveal function, foveal dehiscence, and retinal hemorrhage. Monitor and manage these retinal abnormalities appropriately. Do not administer LUXTURNA in the immediate vicinity of the fovea. Retinal abnormalities may occur during or following vitrectomy, including retinal tears, epiretinal membrane, or retinal detachment. Monitor patients during and following the injection to permit early treatment of these retinal abnormalities. Advise patients to report any signs or symptoms of retinal tears and/or detachment without delay.

- **Increased intraocular pressure** may occur after subretinal injection of LUXTURNA. Monitor and manage intraocular pressure appropriately.

- **Expansion of intraocular air bubbles** Instruct patients to avoid air travel, travel to high elevations or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. It may take one week or more following injection for the air bubble to
dissipate. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through ophthalmic examination.

**Cataract** Subretinal injection of LUXTURNA, especially vitrectomy surgery, is associated with an increased incidence of cataract development and/or progression.

**Adverse Reactions**

- In clinical studies, ocular adverse reactions occurred in 66% of study participants (57% of injected eyes), and may have been related to LUXTURNA, the subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products.
- The most common adverse reactions (incidence ≥ 5% of study participants) were conjunctival hyperemia (22%), cataract (20%), increased intraocular pressure (15%), retinal tear (10%), dellen (thinning of the corneal stroma) (7%), macular hole (7%), subretinal deposits (7%), eye inflammation (5%), eye irritation (5%), eye pain (5%), and maculopathy (wrinkling on the surface of the macula) (5%).

**Immunogenicity**

Immune reactions and extra-ocular exposure to LUXTURNA in clinical studies were mild. No clinically significant cytotoxic T-cell response to either AAV2 or RPE65 has been observed. Study participants received systemic corticosteroids before and after subretinal injection of LUXTURNA to each eye, which may have decreased the potential immune reaction to either AAV2 or RPE65.

**Pediatric Use**

Treatment with LUXTURNA is not recommended for patients younger than 12 months of age, because the retinal cells are still undergoing cell proliferation, and LUXTURNA would potentially be diluted or lost during the cell proliferation. The safety and efficacy of LUXTURNA have been established in pediatric patients. There were no significant differences in safety between the different age subgroups.

Please see the full US Prescribing Information for LUXTURNA here.

**Disclaimer**

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “promising,” “potentially,” “builds on,” “commitment,” “potential,” “will,” “look forward,” “investigational,” “currently,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for voretigene neparvovec and the other investigational and approved products described in this press release, or regarding potential future revenues from such products, or regarding the licensing agreement and the manufacturing and supply agreement with Spark Therapeutics. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that voretigene neparvovec or the other investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. Neither can there be any guarantee that Spark Therapeutics will successfully manufacture and supply voretigene neparvovec; or in sufficient quantities, or in a timely fashion, under the manufacturing and supply agreement. Nor can there be any guarantee that Novartis will successfully establish new specialized treatment centers. Neither can there be any guarantee that we will achieve any or all of the intended goals and objectives of either or both of the licensing and manufacturing and supply agreements, or that such agreements will be commercially successful. In particular, our expectations regarding the licensing agreement, the manufacturing and supply agreement, voretigene neparvovec and the other investigational and approved products described in this press release could be affected by, among other things, regulatory actions or delays or government regulation generally; the ability of Spark Therapeutics to successfully manufacture and supply voretigene neparvovec;
the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; safety, quality or manufacturing issues; potential or actual data security and data privacy issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

References

Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Amy Wolf
Global Head Novartis Ophthalmology
+41 61 696 5894 (direct)
+41 79 576 0723 (mobile)
amy.wolf@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central
Samir Shah 41 61 324 7944
Pierre-Michel Bringer 41 61 324 1065
Thomas Hungerbuehler 41 61 324 8425
Isabella Zinck 41 61 324 7188

North America
Richard Pulik 1 212 830 2448
Cory Twining 1 212 830 2417
Spark Therapeutics Enters into a Licensing and Supply Agreement for Investigational Voretigene Neparvovec Outside the U.S.

Novartis Pharmaceuticals will commercialize investigational voretigene neparvovec when and if approved in Europe and all other markets outside the U.S.; Spark Therapeutics retains U.S. commercial rights for LUXTURNA™ (voretigene neparvovec-ryzl)

Agreement leverages Novartis’ extensive ex-US ophthalmology capabilities and infrastructure to the benefit of patients outside of U.S.

Spark Therapeutics to receive $105 million as an upfront fee and is eligible to receive up to $65 million in milestone payments, as well as receive a royalty on net sales outside the U.S.

PHILADELPHIA, Jan. 24, 2018 (GLOBE NEWS) -- Spark Therapeutics (NASDAQ:ONCE), a fully integrated gene therapy company dedicated to challenging the inevitability of genetic disease, today announced it has entered into a licensing agreement with Novartis Pharmaceuticals to develop and commercialize investigational voretigene neparvovec outside the U.S., while Spark Therapeutics will continue to exclusively commercialize LUXTURNA™ (voretigene neparvovec-ryzl) in the U.S. Under the agreement, Spark Therapeutics will retain regulatory responsibility for obtaining European Medicines Agency approval for investigational voretigene neparvovec. Spark Therapeutics also entered into a separate agreement to manufacture and supply investigational voretigene neparvovec to Novartis. No other programs in Spark Therapeutics’ pipeline are part of this agreement.

Under the terms of the licensing agreement, Novartis will pay Spark Therapeutics $105 million in cash as an upfront fee. Spark Therapeutics is eligible to receive up to an additional $65 million in cash milestone payments based on near-term European Regulatory Agency (EMA) regulatory approval and initial sales outside the U.S. in certain markets. Spark Therapeutics is also entitled to receive royalty payments on net sales of investigational voretigene neparvovec outside the U.S.

“By leveraging Novartis’ large, existing commercial and medical infrastructure in ophthalmology, as well as its commitment to commercializing genetic-based medicines, we help ensure that more patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy who live outside the U.S., and importantly outside of Europe, have access to investigational voretigene neparvovec,” said Dan Faga, chief business officer, Spark Therapeutics. “We intend to use the proceeds from this transaction to continue to develop our robust pipeline of investigational gene therapies to create a path to a world where no life is limited by genetic disease.”

Indication and Important Safety Information for LUXTURNA

LUXTURNA™ (voretigene neparvovec-ryzl) is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

Patients must have viable retinal cells as determined by the treating physicians.
Warnings and Precautions

• Endophthalmitis may occur following any intraocular surgical procedure or injection. Use proper aseptic injection technique when administering LUXTURNA, and monitor for and advise patients to report any signs or symptoms of infection or inflammation to permit early treatment of any infection.

• Permanent decline in visual acuity may occur following subretinal injection of LUXTURNA. Monitor patients for visual disturbances.

• Retinal abnormalities may occur during or following the subretinal injection of LUXTURNA, including macular holes, foveal thinning, loss of foveal function, foveal dehiscence, and retinal hemorrhage. Monitor and manage these retinal abnormalities appropriately. Do not administer LUXTURNA in the immediate vicinity of the fovea. Retinal abnormalities may occur during or following vitrectomy, including retinal tears, epiretinal membrane, or retinal detachment. Monitor patients during and following the injection to permit early treatment of these retinal abnormalities. Advise patients to report any signs or symptoms of retinal tears and/or detachment without delay.

• Increased intraocular pressure may occur after subretinal injection of LUXTURNA. Monitor and manage intraocular pressure appropriately.

• Expansion of intraocular air bubbles Instruct patients to avoid air travel, travel to high elevations or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. It may take one week or more following injection for the air bubble to dissipate. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through ophthalmic examination.

• Cataract Subretinal injection of LUXTURNA, especially vitrectomy surgery, is associated with an increased incidence of cataract development and/or progression.

Adverse Reactions

• In clinical studies, ocular adverse reactions occurred in 66% of study participants (57% of injected eyes), and may have been related to LUXTURNA, the subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products.

• The most common adverse reactions (incidence ≥ 5% of study participants) were conjunctival hyperemia (22%), cataract (20%), increased intraocular pressure (15%), retinal tear (10%), dellen (thinning of the corneal stroma) (7%), macular hole (7%), subretinal deposits (7%), eye inflammation (5%), eye irritation (5%), eye pain (5%), and maculopathy (wrinkling on the surface of the macula) (5%).

Immunogenicity

Immune reactions and extra-ocular exposure to LUXTURNA in clinical studies were mild. No clinically significant cytotoxic T-cell response to either AAV2 or RPE65 has been observed. Study participants received systemic corticosteroids before and after subretinal injection of LUXTURNA to each eye, which may have decreased the potential immune reaction to either AAV2 or RPE65.

Pediatric Use

Treatment with LUXTURNA is not recommended for patients younger than 12 months of age, because the retinal cells are still undergoing cell proliferation, and LUXTURNA would potentially be diluted or lost during the cell proliferation. The safety and efficacy of LUXTURNA have been established in pediatric patients. There were no significant differences in safety between the different age subgroups.

Please see the full U.S. Prescribing Information for LUXTURNA here.
Clinical Trial Overview of LUXTURN™ (voretigene neparvovec-rzyl)

The safety and efficacy of LUXTURN were assessed in one open-label, dose-exploration Phase 1 safety study (n=12) and one open-label, randomized, controlled Phase 3 efficacy and safety study (n=31) in pediatric and adult participants (range 4 to 44 years) with biallelic RPE65 mutation-associated retinal dystrophy and sufficient viable retinal cells.

Of the 31 participants enrolled in the Phase 3 study, 21 were randomized to receive subretinal injection of LUXTURN and 10 were randomized to the control (non-intervention) group. One participant in the intervention group discontinued from the study prior to treatment and one participant in the control group withdrew consent and was discontinued from the study. All nine participants randomized to the control group elected to crossover and receive LUXTURN after one year of observation. All participants in these studies continue to be followed for long-term safety and efficacy. LUXTURN Phase 3 clinical trial data, including data from the intervention group of all randomized participants through the one-year time point has been previously reported in The Lancet.

The efficacy of LUXTURN in the Phase 3 study was established based on the multi-luminance mobility test (MLMT) score change from baseline to one year. MLMT was designed to measure changes in functional vision as assessed by the ability of a participant to navigate a course accurately and at a reasonable pace at seven different levels of illumination, ranging from 400 lux (corresponding to a brightly lit office) to one lux (corresponding to a moonless summer night). Each light level was assigned a score ranging from zero to six, with a higher score indicating that a participant could pass MLMT at a lower light level. A score of negative one was assigned to participants who could not pass MLMT at a light level of 400 lux. MLMT score change was defined as the difference between the score at baseline and the score at one year with a positive score change indicating that a participant was able to complete MLMT at a lower light level. Additional clinical outcomes included white light full-field light sensitivity threshold (FST) testing and visual acuity.

LUXTURN Phase 3 clinical study results showed a statistically significant difference between the intervention group (n=21) and control participants (n=10) at one year in median bilateral MLMT score change (intervention minus control group difference of 2; \( p =0.001 \)) and median first-treated eye MLMT score change (intervention minus control group difference of 2; \( p =0.003 \)). After crossing over to receive LUXTURN, participants in the control group showed a similar response to those in the intervention group. The median bilateral MLMT score change of two was observed for the intervention group at the 30-day timepoint. This change score has been sustained for at least three years for the original intervention group and at least two years in the crossover group in the Phase 3 clinical study. In addition, participants who received LUXTURN showed a statistically significant improvement from baseline to one year in white light FST in the intervention group compared to the control group. The change in visual acuity from baseline to one year was not significantly different between the intervention and control participants.

The U.S. Prescribing Information for LUXTURN includes the following Warnings and Precautions: endophthalmitis; permanent decline in visual acuity; retinal abnormalities; increased intraocular pressure; expansion of intraocular air bubbles; and cataract. The most common adverse reactions (incidence ≥ 5%) were conjunctival hyperemia, cataract, increased intraocular pressure, retinal tear, dellen (thinning of the
corneal stroma), macular hole, subretinal deposits, eye inflammation, eye irritation, eye pain and maculopathy (wrinkling on the surface of the macula).

About Spark Therapeutics
At Spark Therapeutics, a fully integrated company committed to discovering, developing and delivering gene therapies, we challenge the inevitability of genetic diseases, including blindness, hemophilia and neurodegenerative diseases. We have successfully applied our technology in the first FDA-approved gene therapy in the U.S. for a genetic disease, and currently have three programs in clinical trials, including product candidates that have shown promising early results in patients with hemophilia. At Spark, we see the path to a world where no life is limited by genetic disease. For more information, visit www.sparktx.com, and follow us on Twitter and LinkedIn.

Spark Cautionary Note on Forward-looking Statement
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the company's product LUXTURNA™ (voretigene neparvovec-rzyl). The words "anticipate," "believe," "expect," "intend," "may," "plan," "predict," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that: (i) the licensing and supply agreement will not facilitate faster access to voretigene neparvovec for patients globally who do not have access to genetically based treatment options, (ii) our MAA submitted for LUXTURNA may not be approved by EMA; (iii) voretigene neparvovec may not be approved in any markets outside of the U.S.; (iv) upon approval, Novartis may not be successful in commercializing or selling voretigene neparvovec in one or more markets; and (v) we may not receive any additional milestone or royalty payments from Novartis. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and other filings we make with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Spark undertakes no duty to update this information unless required by law.

Investor Contact: Media Contact:
Ryan Asay                        Monique da Silva
Ryan.asay@sparktx.com                        Monique.dasilva@sparktx.com
(215) 239-6424                        (215) 282-7470

# # #
The following is a list of subsidiaries of the Company as of December 31, 2017:

<table>
<thead>
<tr>
<th>Name</th>
<th>Jurisdiction of Incorporation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spark Therapeutics, Inc.</td>
<td>Delaware</td>
</tr>
<tr>
<td>Spark Therapeutics International Holdings, Inc.</td>
<td>Delaware</td>
</tr>
<tr>
<td>Spark Therapeutics Ireland Limited</td>
<td>Ireland</td>
</tr>
<tr>
<td>Spark Therapeutics UK Limited</td>
<td>England</td>
</tr>
<tr>
<td>Spark Therapeutics Argentina Limited</td>
<td>Argentina</td>
</tr>
<tr>
<td>Spark Therapeutics Switzerland Limited</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Spark Therapeutics Germany Limited</td>
<td>Germany</td>
</tr>
<tr>
<td>Spark Therapeutics France Limited</td>
<td>France</td>
</tr>
<tr>
<td>Spark Therapeutics Brazil Limited</td>
<td>Brazil</td>
</tr>
</tbody>
</table>
CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Spark Therapeutics, Inc.:

We consent to the incorporation by reference in the registration statements on Form S-8 (Nos. 333-201768, 333-210184, 333-215578, and 333-222569) and Form S-3 (Nos. 333-211841 and 333-211993) of Spark Therapeutics, Inc. of our report dated February 27, 2018, with respect to the consolidated balance sheets of Spark Therapeutics, Inc. and subsidiaries as of December 31, 2016 and 2017, and the related consolidated statements of operations and comprehensive income (loss), stockholders’ equity, and cash flows for each of the years in the three-year period ended December 31, 2017, and the related notes (collectively, the consolidated financial statements), and the effectiveness of internal control over financial reporting as of December 31, 2017, which report appears in the December 31, 2017 annual report on Form 10-K of Spark Therapeutics, Inc.

/s/ KPMG LLP

Philadelphia, Pennsylvania
February 27, 2018
CERTIFICATIONS

I, Jeffrey D. Marrazzo, certify that:

1. I have reviewed this Annual Report on Form 10-K of Spark Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting.
5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):
   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and
   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: February 27, 2018

By: /s/ Jeffrey D. Marrazzo
Jeffrey D. Marrazzo
Chief Executive Officer
(Principal Executive Officer)
CERTIFICATIONS

I, Stephen W. Webster, certify that:

1. I have reviewed this Annual Report on Form 10-K of Spark Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting.

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):
   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and
   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: February 27, 2018

By: /s/ Stephen W. Webster

Stephen W. Webster
Chief Financial Officer
(Principal Financial Officer)
CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Spark Therapeutics, Inc. (the “Company”) for the period ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I, Jeffrey D. Marrazzo, Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2018

By: /s/ Jeffrey D. Marrazzo

Jeffrey D. Marrazzo
Chief Executive Officer
(Principal Executive Officer)
CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Spark Therapeutics, Inc. (the “Company”) for the period ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I, Stephen W. Webster, Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 27, 2018

By: /s/ Stephen W. Webster

Stephen W. Webster
Chief Financial Officer
(Principal Financial Officer)