UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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, 2016

☐ 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 001-33451

Albireo Pharma, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of Incorporation or Organization)

90-0136863
(L.R.S. Employer Identification No.)

10 Post Office Square, Suite 502 South
Boston, MA
(Address of Principal Executive Offices)

02109
(Zip Code)

Registrant’s telephone number, including area code (857) 254-5555

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

Common Stock, par value $0.01 per share
The NASDAQ Capital Market

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 Section 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 ☐

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 (§232.405 of this chapter) 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 whether 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, or a smaller reporting company. See the definitions of “large accelerated filer,” “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐
Non-accelerated filer ☐ (Do not check if a smaller reporting company) Smaller reporting company ☒

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

The aggregate market value of the common stock of the registrant held by non-affiliates was approximately $19.9 million based on the price at which the common stock was last sold on The NASDAQ Capital Market on June 30, 2016.

The number of shares of the registrant’s common stock outstanding as of March 1, 2017, was 6,292,644.

Documents Incorporated by Reference

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant’s Proxy Statement for its 2017 Annual Meeting of Stockholders.
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## EXPLANATORY NOTE

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## SIGNATURES
On November 3, 2016, Albireo Pharma, Inc. (formerly Biodel Inc.), or the Company, completed its share exchange pursuant to the Amended and Restated Share Exchange Agreement, dated as of July 13, 2016, by and among the Company, Albireo Limited and the holders of shares and notes convertible into shares of Albireo Limited, or the Exchange Agreement. Pursuant to the Exchange Agreement, each holder of Albireo Limited shares or notes convertible into Albireo Limited shares exchanged their shares of Albireo Limited for newly issued shares of the Company’s common stock. This share exchange is referred to herein as the Transaction. As a result, Albireo Limited became a wholly owned subsidiary of the Company. Following the completion of the Transaction, the business of Albireo Limited became the business of the Company and the Company’s corporate name was changed from Biodel Inc. to Albireo Pharma, Inc. As a result of the Transaction, the Company’s board of directors decided to change the Company’s fiscal year end from September 30 to December 31. Unless otherwise noted, all references to common stock share and per share amounts in this Annual Report on Form 10-K have been retroactively adjusted to reflect the exchange of shares in the Transaction based on an exchange ratio of 0.06999 and, where applicable, a 1-for-30 reverse stock split effected by Biodel on November 3, 2016 prior to completion of the Transaction. As used herein, the words “we,” “us,” and “our” refer to Albireo Pharma, Inc. and its direct and indirect subsidiaries, as applicable. In addition, the word “Biodel” refers to the Company prior to the completion of the Transaction.
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act, that relate to future events or our future financial performance. Any forward-looking statement involves known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statement. Forward-looking statements include, among other things, statements about:

• the progress, scope, cost, duration or results of our development activities, nonclinical studies and clinical trials of A4250, elobixibat, A3384 or any of our other product candidates or programs, such as the target indication(s) for development, the size, design, population, conduct, cost, objective or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial (including our planned Phase 3 clinical trial of A4250 in patients with PFIC), for submission or approval of any regulatory filing (including a new drug application in Japan for elobixibat), for meeting with regulatory authorities, or, where applicable, for action or decision by EA Pharma;
• the potential benefits that may be derived from any of our product candidates;
• the timing of and our ability to obtain and maintain regulatory approval of our existing product candidates, any product candidates that we may develop, and any related restrictions, limitations, or warnings in the label of any approved product candidates;
• any payment that EA Pharma may make to us or any other action or decision that EA Pharma may make concerning our relationship with them;
• our future operations, financial position, revenues, costs, expenses, uses of cash, capital requirements or our need for additional financing; and
• our strategies, prospects, plans, expectations or objectives.

Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” “scheduled” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by any forward-looking statement to differ. The description of our Business set forth in Item 1, the Risk Factors set forth in Item 1A and our Management’s Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7, as well as other sections in this report, discuss some of the factors that could contribute to these differences.

Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various important factors, including our critical accounting policies and risks and uncertainties relating, among other things, to:

• whether preliminary data from our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis will be confirmed following database lock;
• whether the results of our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis will be sufficient to support advancement into a planned Phase 3 clinical trial of A4250 in patients with progressive familial intrahepatic cholestasis, or PFIC;
• whether the favorable findings from our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis will be predictive of results from future clinical trials, including our planned Phase 3 clinical trial of A4250 in patients with PFIC;
• the timing and outcomes of interactions with regulatory authorities in the United States and Europe regarding the planned Phase 3 program for A4250 in patients with PFIC;
• the Phase 3 program that will be required to support regulatory approval of A4250 to treat patients with PFIC in the United States and Europe;
• whether our current cash resources will be sufficient to fund our planned Phase 3 clinical trial of A4250 in patients with PFIC to completion;
• the clinical trial designs and endpoints for our planned Phase 3 clinical trial of A4250 in patients with PFIC, or that will otherwise be required to obtain marketing approval for A4250 to treat patients with PFIC or other pediatric cholestatic liver disease or for A3384 to treat bile acid malabsorption, or BAM;
• the conduct and results of clinical trials and nonclinical studies and assessments of A4250, elobixibat, A3384 or any of our other product candidates and programs, including the performance of third parties engaged to execute them and difficulties or delays in patient enrollment and data analysis;
• the size and growth of the markets and commercial opportunities for our product candidates, including A4250 in PFIC or other pediatric cholestatic liver diseases;
• whether A4250 will meet the criteria to receive a pediatric priority review voucher from the FDA and, if necessary, whether the pediatric priority review voucher program will be renewed beyond 2020;
• the significant control or influence that EA Pharma has over the development and commercialization of elobixibat in Japan and other licensed territories;
• whether we elect to seek a license or other partnering transaction with a third party for elobixibat in the United States or Europe;
• whether findings from nonclinical studies and clinical trials of IBAT inhibitors will be predictive of future clinical success for a future product candidate of ours in the treatment of nonalcoholic steatohepatitis, or NASH;
• the accuracy of our estimates regarding expenses, future revenues, uses of cash and capital requirements;
• our ability to obtain additional financing on reasonable terms, or at all;
• our ability to establish additional licensing, collaboration or similar arrangements on favorable terms and our ability to attract collaborators with development, regulatory and commercialization expertise;
• the success of competing third-party products or product candidates;
• our ability to successfully commercialize any approved product candidates, including their rate and degree of market acceptance;
• our ability to expand and protect our intellectual property estate;
• the timing and success of submission, acceptance and approval of regulatory filings, including in particular the new drug application submitted by EA Pharma in Japan for elobixibat for the treatment of chronic constipation, and any related restrictions, limitations or warnings in the label of any approved product candidates;
• regulatory developments in the United States and other countries;
• the performance of our third-party suppliers, manufacturers and contract research organizations and our ability to obtain alternative sources of raw materials; and
• our ability to attract and retain key personnel.

These and other risks and uncertainties are described in greater detail under the caption “Risk Factors” in Item 1A of Part I of this report and in other filings that we make with the Securities and Exchange Commission, or SEC. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. We caution you not to place undue reliance on any forward-looking statement.

In addition, any forward-looking statement in this Annual Report on Form 10-K represents our views only as of the date of this annual report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.
Item 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel bile acid modulators to treat orphan pediatric liver diseases and gastrointestinal, or GI, disorders where improper flow or absorption of bile causes serious medical conditions for which there is high unmet need. The initial target indication for our lead product candidate, A4250, is progressive familial intrahepatic cholestasis, or PFIC, a rare, life-threatening genetic disorder affecting young children for which there is currently no approved drug treatment. A4250 is currently being evaluated in a Phase 2 clinical trial in children with chronic cholestasis that is intended to support a planned Phase 3 clinical trial in patients with PFIC. In addition to PFIC and subject to obtaining additional capital, we plan to consider conducting future clinical development of A4250 as a treatment for other pediatric cholestatic liver diseases and disorders. Our clinical-stage product candidates in addition to A4250 include elobixibat, for which our licensee has filed a new drug application for approval in Japan to treat chronic constipation, and A3384, which is in development to treat bile acid malabsorption, or BAM. We also have a preclinical program in nonalcoholic steatohepatitis, or NASH.

Bile acids are a component of bile, a key digestive liquid made in the liver, that play a critical role in dietary absorption and the regulation of metabolic processes. Specifically, bile acids are recycled from the small intestine to the liver as part of a process known as enterohepatic circulation. When the flow of bile from the liver stops or is disrupted, a condition known as cholestasis, bile acids accumulate in the liver and in the serum, which is a component of blood. Elevated bile acids in the liver and serum often lead to severe liver damage and other consequences, including itching, or pruritus. A4250 partially inhibits a protein known as ileal sodium dependent bile acid transporter, or IBAT, which is responsible for initiating the recirculation of bile acids from the small intestine to the liver. As an IBAT inhibitor, A4250 acts to reduce bile acids in the liver and serum and to increase bile acids being excreted through the colon. Elobixibat is also an IBAT inhibitor.

A4250 — our lead product candidate for PFIC and potentially other orphan pediatric liver diseases. A4250 is a novel, minimally absorbed, orally administered IBAT inhibitor. Our initial target indication for A4250 is PFIC. A4250 is currently being evaluated in an open label, dose finding Phase 2 clinical trial in children with chronic cholestasis that is intended to support a planned Phase 3 clinical trial in patients with PFIC. The Phase 2 trial includes children with chronic cholestasis caused by any of a number of different liver conditions, including PFIC, biliary atresia, Alagille syndrome, or ALGS, and sclerosing cholangitis. Because it is an open label study, preliminary data are available as of March 27, 2017 from all cohorts. These data show a reduction in serum bile acids in a substantial majority of patients and improvement in pruritus that was significantly correlated with the reduction in serum bile acids. In addition, A4250 was generally well tolerated in the trial. We expect final data from the trial to become available in the first half of 2017.

PFIC. We plan to conduct a Phase 3 clinical trial of A4250 in patients with PFIC, as well as an extension study to evaluate long-term outcomes. We expect the PFIC trial to commence in the second half of 2017. We have chosen PFIC as the lead indication for A4250 because we believe there is an especially strong scientific rationale for the use of an IBAT inhibitor to prevent progressive liver disease caused by PFIC.

The precise prevalence of PFIC is unknown, but PFIC has been estimated to affect between one in every 50,000 to 100,000 children born worldwide. Based on the estimated incidence and need for liver transplant, published birth rates, and estimates of the effect of pediatric liver transplant on life expectancy, we estimate the prevalence of PFIC to be approximately 10,000 patients in major pharmaceutical markets, including approximately 3,200 in the United States and 5,000 in the European Union. There are currently no drugs approved for the treatment of PFIC. First-line treatment for PFIC is typically off-label ursodeoxycholic acid, or UDCA, which is approved in the United States and elsewhere for the treatment of primary biliary cholangitis, or PBC. However, many PFIC patients do not respond well to UDCA, undergo partial external bile diversion, or PEBD, surgery and often require liver transplantation. PEBD surgery is a life-altering and undesirable procedure in which bile is drained outside the body to a stoma bag that must be worn by the patient 24 hours a day. Of all PFIC patients, we believe A4250 will primarily benefit those who have not yet undergone PEBD surgery or liver transplant, as well as those who have had or may have surgery to reverse the PEBD procedure. Accordingly, we estimate the addressable PFIC patient population for A4250 to be approximately 1,200 patients in the United States and approximately 1,900 patients in the European Union.
Other Indications Under Consideration. We intend to consider conducting future clinical development of A4250 as a treatment for other pediatric cholestatic liver diseases and disorders in addition to PFIC. These indications may include any or all of ALGS, biliary atresia, sclerosing cholangitis and pediatric cholestatic pruritus.

ALGS is a genetic condition associated with liver, heart, eye and skeletal abnormalities. In particular, ALGS patients have fewer than normal bile ducts inside the liver, which leads to cholestasis and the accumulation of bile and causes scarring in the liver. The prevalence of ALGS has been estimated to be one in 70,000 newborns. There are currently no drugs approved for the treatment of ALGS. Current treatment for ALGS is generally in line with current treatments for PFIC as described above.

Biliary atresia is a partial or total blocking or absence of large bile ducts that causes cholestasis and resulting accumulation of bile that damages the liver. The estimated worldwide incidence of biliary atresia is one in every 18,500 births. There are currently no drugs approved for the treatment of biliary atresia. The current standard of care is a surgery known as the Kasai procedure, or hepatoportoenterostomy, in which the obstructed bile ducts are removed and a section of the small intestine is connected to the liver directly. However, only an estimated 25% of those initially undergoing the Kasai procedure will survive to their twenties without need for liver transplantation.

Sclerosing cholangitis refers to swelling (inflammation), scarring, and destruction of bile ducts inside and outside of the liver. The first symptoms are typically fatigue, itching and jaundice, and many patients with sclerosing cholangitis also suffer from irritable bowel syndrome with diarrhea. The estimated incidence of sclerosing cholangitis is 6.3 cases per 100,000 people. There are currently no drugs approved for the treatment of sclerosing cholangitis. First-line treatment is typically off-label UDCA, although UDCA has not been established to be safe and effective in patients with sclerosing cholangitis in well controlled clinical trials.

Pediatric cholestatic pruritus refers to pruritus symptoms in children suffering from any disease or condition characterized by chronic cholestasis. Severe pruritus is a debilitating symptom afflicting cholestatic patients and, although pruritus cannot reliably be relieved by scratching, patients often resort to destructive scratching behaviors that can cause bleeding and scarring. Cholestatic liver disease has been estimated to affect approximately one in 2,500 newborns worldwide, and, based on reported rates of pruritus across several different causes of pediatric cholestasis, we estimate pruritus to affect approximately 45% of all children with cholestatic liver disease. There are currently no drugs approved specifically for the treatment of pediatric cholestatic pruritus.

Other Clinical-Stage Product Candidates — Elobixibat and A3384.

Elobixibat. Elobixibat is a second novel, minimally absorbed, orally administered IBAT inhibitor. We have granted commercial rights to elobixibat for the treatment of chronic constipation and other GI diseases in Japan and other select markets in Asia to EA Pharma Co., Ltd., (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.), or EA Pharma, a company formed by a business combination between Ajinomoto Pharmaceuticals and the GI treatment business of Eisai Co., Ltd. Following positive results from a Phase 3 clinical trial conducted by EA Pharma in Japan, we announced in February 2017 that EA Pharma submitted a new drug application to the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, for elobixibat for the treatment of chronic constipation. If elobixibat receives marketing approval in Japan, EA Pharma plans to co-market elobixibat in Japan with another company, Mochida Pharmaceutical Co., Ltd, or Mochida.

We have commercial rights to elobixibat in the United States, Europe and otherwise outside of the territories licensed to EA Pharma. We are currently evaluating whether we will seek a license or other partnering transaction with a third party for elobixibat in the United States or Europe. Whether or not we elect to seek such a transaction, we do not currently anticipate that we will conduct future clinical trials of elobixibat independently.

A3384. A3384 is a proprietary formulation of cholestyramine that is designed to release cholestyramine directly in the colon. We are developing A3384 as a treatment for BAM. BAM, which is sometimes also called bile acid diarrhea, occurs when bile acids are not sufficiently reabsorbed in the small intestine, causing elevated levels of bile acids to instead reach the colon and leading to chronic watery diarrhea. Based on a reported estimate of the prevalence of irritable bowel syndrome with diarrhea, or IBS-D, and published third-party studies that suggest approximately one-third of IBS-D patients have BAM, we estimate the prevalence of BAM to be approximately 1.3 million people in the United States and approximately 2.2 million people in the European Union. There are currently no drugs approved for the treatment of BAM.

Cholestyramine, which is approved in some countries in Europe to treat diarrhea associated with certain GI conditions, is commonly prescribed off-label to treat BAM. Cholestyramine is a well characterized bile acid sequestrant, which is also known as a resin. The benefit of cholestyramine has historically been limited both because of poor tolerability and because of its negative effect on absorption of other medications and important fat soluble vitamins. We believe that a better tolerated formulation that is capable of delaying the activity of cholestyramine until it reaches the colon has potential to provide therapeutic benefit for patients with BAM.
Our Corporate History

Prior to November 3, 2016, we were a specialty biopharmaceutical company known as Biodel Inc. that historically had been focused on the development and commercialization of innovative treatments for diabetes. Biodel was originally incorporated in the State of Delaware in December 2003 under the name “Global Positioning Group, Ltd.” and subsequently changed its name to “Biodel Inc.” Albireo Limited was formed in connection with a spinout transaction from AstraZeneca AB in 2008 in which AstraZeneca assigned to Albireo AB all of its rights in and to its portfolio of IBAT inhibitors, including elobixibat and A4250, as well as other programs that are currently at a preclinical stage.

On November 3, 2016, we completed a share exchange transaction, or the Transaction, pursuant to an Amended and Restated Share Exchange Agreement dated July 13, 2016 that we entered into with Albireo Limited and the shareholders and noteholders of Albireo Limited. In the Transaction, each holder of Albireo Limited shares or notes convertible into Albireo Limited shares sold their shares of Albireo Limited for newly issued shares of our common stock. As a result, Albireo Limited became a wholly owned subsidiary of Biodel, Biodel’s corporate name was changed to Albireo Pharma, Inc. and the business of Albireo Limited became our business.

The Role of Bile Acids and IBAT

The liver is responsible for many vital body functions, including the regulation of bile acid synthesis and metabolism. The liver uses cholesterol to produce bile acids, which are then transported to, and stored in, the gall bladder. In response to food ingestion, the gall bladder contracts and releases bile acids into the small intestine where they promote digestion and absorption of dietary fats and fat soluble vitamins A, D, E and K.

After completing digestion, bile acids bind to IBAT, which is sometimes referred to as the apical sodium bile acid transporter, or ASBT, at a location at the end of the small intestine known as the terminal ileum. As depicted below, IBAT then initiates the transport of bile acids across the intestinal wall through the portal vein back to the liver in the enterohepatic circulation process.

In healthy persons, approximately 95% of bile acids recirculate back to the liver, with the remainder being excreted to the colon. The liver produces a small amount of new bile acids every day to make up for this loss.

In addition to their role in digestion, bile acids are important signaling molecules that help regulate a network of metabolic pathways throughout the GI system. Bile acids bind to receptors in the colon that promote the release of intestinal hormones, such as glucagon-like peptide-1, or GLP-1, that can stimulate insulin release from the pancreas and, over time, decrease levels of plasma hemoglobin A1c, or HbA1c, a measure of glucose. In the liver, bile acids bind to other receptors that regulate bile acid production from cholesterol. Under normal conditions, bile acids bind to these receptors and inhibit the synthesis of new bile acids. As bile acid levels are lowered, the liver produces needed bile acids from cholesterol, which requires increased uptake of cholesterol and results in the decrease of cholesterol levels in the liver and otherwise in circulation in the body.
Cholestatic liver disease results in the accumulation of elevated bile acids in the liver and in the serum. Elevated bile acid levels are linked with progressive liver disease. In addition, although a direct causative correlation has not been definitely established, there is substantial clinical support linking elevated serum bile acids to pruritus, a challenging symptom impacting patients with cholestatic liver disease.

Interruption of enterohepatic circulation in patients with PFIC or ALGS surgically via the PEBD procedure has been shown to lower serum bile acid levels, relieve pruritus, improve clinical outcomes and delay the progression of serious liver disease. A4250 is designed to treat PFIC and other cholestatic liver diseases pharmacologically by inhibiting IBAT to reduce bile acids in the liver and serum, while at the same time reducing pruritus. In addition to the beneficial effects that may be achievable through IBAT inhibition, A4250 is minimally absorbed into the bloodstream, resulting in minimal systemic exposure of the drug to the body.

Our Strategy

Our goal is to be a leader in the development and commercialization of novel therapeutics for orphan pediatric cholestatic liver diseases and disorders where there is high unmet medical need, while also leveraging our expertise in bile acid modulation to treat other liver and GI diseases and disorders. To achieve our goal, we intend to pursue the following strategies.

• Rapidly develop A4250 to regulatory approval to treat patients with PFIC. A4250 is currently being evaluated in a Phase 2 clinical trial in children with chronic cholestasis. It is our objective to conduct a single Phase 3 clinical trial in patients with PFIC that is sufficient to establish the efficacy of A4250 and support, together with safety data from a long-term extension study, applications for regulatory approval of A4250 in both the United States and European Union. We are currently seeking concurrence with our plan from regulatory authorities in the United States and Europe.

• Maximize the benefit and commercial potential of A4250 by expanding development to additional orphan pediatric cholestatic indications. Although we have chosen PFIC as our lead indication for A4250, we also believe A4250 can benefit children suffering from other cholestatic diseases and disorders. We intend to consider conducting future clinical development of A4250 as a treatment for one or more of these other pediatric cholestatic liver diseases and disorders in addition to PFIC to help address these unmet medical needs and to maximize the commercial potential of A4250.

• Develop the capability to commercialize A4250 to treat orphan pediatric liver diseases, if approved, through a targeted sales force in the United States and Europe and collaborate selectively to commercialize A4250 outside of these regions. If we receive regulatory approval in the United States or Europe for A4250 to treat PFIC or any other pediatric cholestatic liver disease or disorder, we plan to build the capabilities to effectively commercialize A4250 in the approved indication(s) in the applicable region. We believe that the required commercial organization would be modest in size and targeted to the relatively small number of specialists in the United States and Europe who treat children with cholestatic liver disease. If we receive regulatory approval outside of the United States and Europe for A4250 to treat PFIC or any other pediatric cholestatic liver disease or disorder, we plan to selectively utilize collaboration, distribution and other marketing arrangements with third parties to commercialize A4250 in the approved indication(s) in the regions outside the United States or Europe where we receive approval.

• Collaborate selectively to develop and commercialize product candidates targeting nonorphan indications, potentially including elobixibat, A3384 or any future product candidate to treat NASH. We intend to selectively seek alliances and collaborations to assist us in furthering the development or commercialization of product candidates targeting large primary care markets that must be served by large sales and marketing organizations. These product candidates may include any or all of elobixibat, A3384 and any potential future product candidate that arises from our preclinical program in NASH.
A4250

A4250 is currently being evaluated in a Phase 2 clinical trial in children with chronic cholestasis. Following completion of the trial, we plan to advance A4250 into a Phase 3 clinical trial in patients with PFIC and an extension study to evaluate long-term outcomes. We are currently designing our planned PFIC trial, including evaluating various potential endpoints to designate as the primary endpoint, whether alone or together with another primary endpoint. Subject to obtaining additional capital, we intend to consider conducting future clinical development of A4250 as a treatment for other pediatric cholestatic liver diseases and disorders in addition to PFIC.

A4250 is a highly potent and selective inhibitor of IBAT that is designed to reduce bile acid reabsorption from the small intestine to the liver, leading to reduced levels of bile acids in the serum and liver and increased excretion of bile acids via the colon. We believe that reducing liver and serum bile acid levels may reduce bile acid-related liver damage to improve liver function and alleviate symptoms of PFIC and other cholestatic liver diseases, including pruritus. Moreover, at therapeutic doses, A4250 has minimal systemic exposure, acts locally in the gut and, based on preclinical testing, appears to be excreted substantially intact in the feces, which may reduce the risk of systemic side effects and undesirable drug-drug interactions compared with drugs that have broad distribution in the body.

A4250 has been granted orphan drug designation for PFIC in the United States and the European Union.

Lead Indication for A4250

PFIC. PFIC is our lead indication for A4250. PFIC is a rare genetic disorder that causes progressive, life-threatening liver disease, which may start early after birth or at a young age and rapidly progress to end-stage liver disease. PFIC is commonly associated with elevated serum bile acids. Prominent symptoms of PFIC include pruritus, which is associated with severe sleep disturbance and diminished overall quality of life, and poor growth. First-line treatment in PFIC is typically off-label UDCA. UDCA is itself a type of bile acid that is thought to act by diluting the toxic effects in the liver and bile ducts of a different type of bile acids, known as hydrophobic bile acids, which are often elevated in cholestatic liver disease. Third-party retrospective analyses published in 2009 and 2010 indicate that, following treatment with UDCA, many PFIC patients require PEBD surgery and PFIC patients will often ultimately require liver transplantation. Although success rates vary, published third-party studies have shown that PEBD surgery can slow and, in some cases, stop the progression of liver disease and lead to reduced pruritus and improved sleep. We believe these outcomes validate our approach of reducing liver and serum bile acids with an IBAT inhibitor such as A4250 to treat PFIC.

The precise prevalence of PFIC is unknown, but PFIC has been estimated to affect between one in every 50,000 to 100,000 children born worldwide. Based on the estimated incidence, published birth rates and estimates of the effect of pediatric liver transplant on life expectancy, we estimate the prevalence of PFIC in 2016 to be approximately 10,000 patients in major pharmaceutical markets, including approximately 3,200 in the United States and 5,000 in the European Union. Of these people, those who have not yet received PEBD or liver transplant, as well as those who have had or may have PEBD reversal surgery, may benefit from treatment with A4250. Causes for reversal surgery include PEBD failure, complications or, particularly for patients entering their teenage years, dissatisfaction with the need to use a stoma bag for social or body image reasons. We estimate the addressable PFIC population for A4250 to be approximately 1,200 patients in the United States and approximately 1,900 patients in the European Union. In addition, we believe the addressable PFIC patient population for A4250 has potential to increase as more patients who are dissatisfied with PEBD consider reversal surgery if A4250 becomes a new treatment option.
Three alternative gene defects have been identified that correlate to three separate PFIC subtypes, known as types 1, 2 and 3.

- **PFIC, type 1**, which is sometimes referred to as “Byler disease” or “FIC1 deficiency,” is caused by impaired bile secretion due to mutations in the ATP8B1 gene that result in an imbalance of molecules known as phospholipids that is associated with cholestasis and elevated bile acids in the liver. Children affected by PFIC, type 1 usually develop cholestasis in the first months of life and, in the absence of surgical treatment, progress to cirrhosis and end-stage liver disease before the end of the first decade of life. PFIC, type 1 is especially common in the Old Order Amish population in the United States, as well as the Inuit population of Greenland.

- **PFIC, type 2**, which is sometimes referred to as “Byler syndrome” or “BSEP deficiency,” is caused by impaired bile salt secretion due to mutations in the ABCB11 gene that result in the buildup of bile salts in liver cells. Children with PFIC, type 2 often develop liver failure within the first few years of life and are at increased risk of developing hepatocellular carcinoma, the most common form of liver cancer.

- **PFIC, type 3**, which typically presents in the first years of childhood with progressive cholestasis, is caused by mutations in the ABCB4 gene. Mutations in the ABCB4 gene lead to a lack of phospholipids available to bind to bile acids, resulting in a buildup of bile acids that damages liver cells.

Recently, TJP2 gene, NR1H4 gene or Myo5b gene mutations have been proposed to be causes of PFIC. In addition, some patients with PFIC do not have a mutation in any of the ATP8B1, ABCB11, ABCB4, TJP2, NR1H4 or Myo5b genes. In these cases, the cause of the condition is unknown.

### Potential Additional Target Indications for A4250

**ALGS.** ALGS is a genetic condition associated with liver, heart, eye and skeletal abnormalities. In particular, ALGS patients have fewer than normal bile ducts inside the liver, which leads to cholestasis and the accumulation of bile and causes scarring in the liver. Symptoms include jaundice, pruritus, poor growth and specific facial features and typically develop in the first two years of life.

There are currently no drugs approved for the treatment of ALGS. Current treatments for ALGS are generally in line with current treatments for PFIC as described above, including off-label UDCA, PEBD surgery and, where liver disease is advanced, liver transplantation.

The prevalence of ALGS has been estimated to be one in 70,000 newborns. ALGS is predominately caused by mutations in a gene called Jagged1. In a small number of cases, ALGS results from mutations in a gene called Notch2.

**Biliary atresia.** Biliary atresia is a partial or total blocking or absence of large bile ducts that irreversibly prevents bile flow from the liver to the small intestine, causing cholestasis and resulting accumulation of bile that damages the liver. The damage leads to scarring, loss of liver tissue and cirrhosis, which makes it difficult for the liver to remove toxins from the blood and deteriorates the liver. Biliary atresia is life threatening.

There are currently no drugs approved for the treatment of biliary atresia. The current standard of care is the Kasai procedure. The chance of a successful Kasai procedure is highest if performed before a patient is two months of age. However, even with early intervention, scarring of the liver can continue, resulting in cirrhosis and eventually the need for transplantation. Only an estimated 25% of those initially undergoing the Kasai procedure will survive to their twenties without need for liver transplantation.

The estimated worldwide incidence of biliary atresia is one in every 18,500 births. Of all biliary atresia patients, we believe A4250 will primarily benefit those who have undergone a Kasai procedure that has been sufficiently successful to obviate the need for liver transplant within the first year of life. We estimate the addressable biliary atresia patient population for A4250 to be approximately 3,500 patients in the United States and approximately 5,500 patients in the European Union.

The exact cause of biliary atresia is unknown, but it is thought to result from an event in the womb or around the time of birth. Possible triggers may include viral or bacterial infection, an immune system malfunction, a genetic mutation, a problem during liver or bile duct development or exposure to toxic substances.

**Sclerosing cholangitis.** Sclerosing cholangitis refers to swelling (inflammation), scarring, and destruction of bile ducts inside and outside of the liver. The first symptoms are typically fatigue, itching and jaundice, and many patients with sclerosing cholangitis also suffer from irritable bowel syndrome with diarrhea. The estimated incidence of sclerosing cholangitis is 6.3 cases per 100,000 people. There are currently no drugs approved for the treatment of sclerosing cholangitis. First-line treatment is typically off-label UDCA, First-line treatment is typically off-label UDCA, although UDCA has not been established to be safe and effective in patients with sclerosing cholangitis in well controlled clinical trials.
Pediatric cholestatic pruritus. Pediatric cholestatic pruritus refers to debilitating pruritus symptoms in children suffering from any disease or condition characterized by chronic cholestasis, including among others PFIC, biliary atresia, ALGS, alpha-1 antitrypsin deficiency, cystic fibrosis and sclerosing cholangitis. Phrases such as “pins and needles,” “like having chronic poison ivy” or “crawling” have been used to describe the sensations of pruritus. Although pruritus cannot reliably be relieved by scratching, patients with pruritus often resort to destructive scratching behaviors that can cause bleeding and scarring. Pruritus can lead to a marked decrease in quality of life due, among other things, to impaired sleep and depression.

Based on reported rates of pruritus across several different causes of pediatric cholestasis and an estimated one in 2,500 newborns worldwide afflicted with cholestatic liver disease, we estimate pruritus to affect approximately 45% of all children with cholestatic liver disease, which projects to approximately 11,700 children with cholestatic pruritus in the United States and approximately 15,000 children with cholestatic pruritus in the European Union.

There are currently no drugs approved specifically for the treatment of pediatric cholestatic pruritus, and the standard of care varies based on the underlying liver disease. Medications such as cholestyramine, other bile acid resins, the antibiotic derivative rifampin, and the opioid antagonist naltrexone are sometimes used to treat patients suffering from pruritus, but these agents have been shown to have limited efficacy, poor tolerability or inadequate safety profiles. Of these medications, only cholestyramine has been approved in the United States for the treatment of pruritus (specifically, pruritus associated with partial biliary obstruction). However, cholestyramine is only modestly effective at lowering bile acid levels or slowing progressive liver disease because, in its immediate release form, it has significant side effects, including the reduction of absorption of vitamins A, D, E and K that can exacerbate vitamin deficiencies in children with cholestatic liver disease.

Development of A4250

Preclinical and Phase 1 Clinical Development

To assess the preclinical efficacy of A4250 to treat cholestasis, we studied A4250 in a mouse model in which select genes had been removed from the mice to induce cholestatic liver injury. In the model, A4250 significantly reduced serum levels of bile acids and normalized levels of alanine aminotransferase, or ALT, and alkaline phosphatase, or ALP, which are enzymes in the liver that are elevated in a diseased liver. A4250 also significantly inhibited the expression of proteins known to be associated with inflammation, including tumor necrosis factor alpha (Tnf-α), vascular cell adhesion molecule-1 (Vcam-1) and monocyte chemoattractant protein-1 (Mcp-1), and proteins known to be associated with fibrosis, including collagen, type 1 alpha1 (Col1a1) and collagen, type 1 alpha2 (Col1a2).

In addition, we completed a placebo controlled Phase 1 clinical trial of A4250 in healthy volunteers. The trial enrolled a total of 104 subjects and had three parts — a single ascending dose phase evaluating five different doses of A4250, a multiple ascending dose phase evaluating three different doses of A4250 (a 1 mg dose once daily, a 3 mg dose once daily and a 1.5 mg dose twice daily) over seven days, and a multiple ascending dose phase evaluating A4250 in combination with a bile acid sequestrant over seven days.

A4250 was generally well tolerated in all dose groups in the trial. In addition, A4250 was associated with a variety of biological effects, including a dose-related reduction in serum bile acids, decreased levels of the protein Fibroblast Growth Factor 19, or FGF19, and increased levels of the bile acid intermediate 7α-hydroxy-4-cholesten-3-one, or C4. The effects on FGF19 and C4 levels are consistent with the IBAT inhibition mechanism, as IBAT inhibition reduces levels of bile acids in cells in the distal small intestine, which leads to decreased FGF19 production. There were no treatment-related serious adverse events, or SAEs, and the most commonly reported adverse event was diarrhea. Based on the results of the trial, we determined to include doses up to 3 mg daily in our next clinical trials.

Concluded Phase 2 Clinical Trial in PBC

A4250 was previously evaluated in an investigator-initiated Phase 2 clinical trial for the treatment of PBC. We facilitated the trial, which was concluded in the fourth quarter of 2016, primarily to provide additional learning on the effects of A4250 in patients with cholestatic liver disease to guide future development and to address feedback received from the FDA at a pre-investigational new drug, or IND, meeting regarding the need to generate data in adults with cholestatic liver disease prior to initiating clinical development in children in the United States. PBC is a chronic disease of the liver in which the bile ducts become inflated and are slowly destroyed. When bile ducts are damaged, bile acids can build up in the liver, leading to irreversible cirrhosis. As cirrhosis progresses and the amount of scar tissue in the liver increases, the liver loses its ability to function. Cirrhosis also prevents blood from the intestines from returning to the heart.
The trial was an open label, crossover study designed to evaluate the safety and tolerability of A4250, the efficacy of A4250 in relieving pruritus and the effects of A4250 on liver biochemistry and bile acid metabolism in patients with PBC and cholestatic pruritus. The investigator conducted the trial at two sites in Sweden. The trial design provided for enrollment of adult patients who had not responded adequately to at least six months of treatment with UDCA and who met specified criteria for elevated serum levels of ALP and for itching.

In the trial, patients initially continued their existing regimen of either cholestyramine or colestipol for four weeks. After a two-week washout period, patients in the first cohort received a 1.5 mg once daily oral dose of A4250 for one week and a 3 mg once daily oral dose of A4250 for the succeeding three weeks. A4250 was administered in a powder formulation in a capsule, and patients who did not tolerate the higher dose could revert to the lower dose at the discretion of the investigator. After another two-week washout period beginning at the end of the four-week A4250 treatment period, patients again returned to their initial dosing regimen of either cholestyramine or colestipol for four weeks.

Following completion of the first cohort, the investigator began to enroll a second cohort of six patients into the trial to receive a lower daily dose of A4250 than patients in the first cohort received. However, the investigator experienced recruitment delays for the second cohort and determined to conclude the study prior to completion of the second cohort, citing GI side effects.

The primary endpoint of the trial was the incidence of treatment-emergent SAEs during the treatment period. The VAS-itch, a commonly used tool to assess pruritus based on a linear 10-point scale, was one of the exploratory efficacy endpoints in the trial.

Based on data from the trial that we received from the investigator, nine patients received A4250 and all of them reported a substantial reduction in pruritus, assessed by the VAS-itch scale, at the time of the first assessment (one week). The reduction in pruritus was sustained throughout the remaining period of participation in the trial with dosing with A4250, and pruritus levels returned to pre-A4250 levels when dosing was stopped.

Two of the five patients in the first cohort dropped out of the trial due to diarrhea, an effect consistent with the IBAT inhibition mechanism. Three of the four patients in the abbreviated second cohort of the trial dropped out prior to completion of the four-week dosing period due to GI side effects, including diarrhea, abdominal pain and, in one case, bleeding.

Ongoing Phase 2 Clinical Trial in Children with Chronic Cholestasis

Our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis is an open label, dose finding trial designed to evaluate the safety and efficacy of A4250. The chronic cholestasis may be caused by any of a number of different conditions, including PFIC, biliary atresia, ALGS or sclerosing cholangitis. We are conducting the trial at seven sites in Denmark, France, Germany, Sweden and the United Kingdom. We commenced enrollment in August 2015.

The trial is designed to enroll up to 24 patients between one and 18 years of age who meet specified criteria for elevated serum bile acids and itching. Following screening, patients receive a single oral dose of A4250 on the first day of the trial. If pharmacokinetic assessments meet objective criteria for minimal systemic exposure of A4250 and, at a follow-up visit between 10 and 14 days later, there are no safety concerns, patients then receive oral doses of A4250 once daily for four weeks. The term “pharmacokinetic” refers to how a drug moves within the body, including its absorption, distribution, metabolism and excretion. The trial design provides for six dose groups, ranging from 0.01 mg/kg to 0.2 mg/kg. An independent data safety and monitoring board, or DSMB, determines whether to initiate each successive dose group based on evaluation of safety, tolerability and pharmacokinetic data from the preceding dose group. A4250 is administered in the trial as pellets contained in a gelatin capsule that can be either swallowed whole or opened, enabling the pellets to be sprinkled on and mixed in food such as yogurt. This pellet formulation is different from the powder formulation used in the investigator-initiated clinical trial in PBC and prior clinical trials described above.

The primary efficacy endpoint of the trial is change from baseline in total serum bile acids at the end of the four-week treatment period. Secondary efficacy endpoints include change from baseline on various patient or caretaker-reported assessments of change in itching, including VAS-itch, the partial PO-SCORAD scale and the Whittington itching score, and evaluation of liver biochemistry. The PO-SCORAD is a 10-point scale that assesses itching and sleep disturbance. The Whittington itching score assesses the severity of itching based on specified alternative descriptions of effect on the skin. For each of the efficacy endpoints, “baseline” refers to the most recent assessment of the applicable measure taken prior to the beginning of the four-week treatment period, which varies among endpoints. The primary safety endpoint of the trial is the incidence of treatment-emergent SAEs during the treatment period.

Data from this dose-finding trial became available on a cohort-by-cohort basis, but will not become final until the database is locked. As of March 27, 2017, all cohorts have completed the trial, representing 10 patients with PFIC and a total of 20 patients overall. Four patients in the trial participated in two different cohorts.
The preliminary data show a reduction in serum bile acids in a substantial majority of patients. The mean reduction in serum bile acids among cohorts ranged from 31% +/- 23% (standard error of the mean, or SEM) to 63% +/- SEM 12%, with some patients experiencing reductions in excess of 90%. The subpopulation of PFIC patients (n = 10, including three patients who participated in two different cohorts) in the trial had a greater mean reduction in serum bile acids than patients in the trial with other cholestatic liver diseases. Overall, the reductions in serum bile acids exhibited high variability which is due to the wide range of doses and to the various diseases and disorders represented and variability in baseline serum bile acid levels within and across cohorts in the trial.

The preliminary data also showed improvement in pruritus across multiple assessment scales, with a significant correlation between reduction in serum bile acids and reduction in pruritus. In addition, a trend in the improvement of sleep disturbance was observed.

In addition, the various liver biochemistry measures assessed showed high patient variability, including both increases and decreases. In the trial’s fifth cohort (0.2 mg/kg A4250 dosing), a patient with ALGS whose ALT and aspartate aminotransferase, or AST, had begun increasing prior to enrollment in the trial showed elevated transaminases during the trial that had not come down at the trial’s follow-up visit two weeks following completion of dosing. These elevations were not accompanied by any increase in bilirubin levels, and there are reports in the medical literature of ALGS patients having increased ALT and AST levels after undergoing PEBD surgery, which, like A4250, is designed to reduce bile acids in the liver. After review and analysis, the independent DSMB approved continued dosing in the sixth and final cohort in the trial at an A4250 dose not to exceed 0.2 mg/kg.

There were no patient dropouts in the trial, and A4250 has exhibited a favorable overall tolerability profile. In particular, there was only one incidence of diarrhea, which occurred prior to the four-week treatment period and was characterized by the applicable clinical investigator as mild. There were two treatment-emergent SAEs reported in the trial, both of which were determined by the applicable clinical investigator to be not related to A4250. We expect final data from the trial to become available in the first half of 2017.

**Elobixibat**

Our product candidate elobixibat is licensed to EA Pharma in Japan and other select markets in Asia. EA Pharma has completed a Phase 3 clinical trial of elobixibat as a treatment for chronic constipation in Japan, and the trial achieved positive results. Subsequently, in February 2017, EA Pharma submitted a new drug application to the Japanese PMDA for elobixibat for the treatment of chronic constipation in Japan. A clinical trial designed to evaluate the long-term safety of elobixibat in Japanese patients with chronic constipation being conducted by EA Pharma remains ongoing. If elobixibat receives marketing approval in Japan, EA Pharma plans to co-market elobixibat in Japan with another company, Mochida.

We have commercial rights to elobixibat in the United States, Europe and all other territories not licensed to EA Pharma. We are currently evaluating alternative study designs for a potential future Phase 3 clinical development program for elobixibat for the treatment of chronic idiopathic constipation, or CIC, in the United States and Europe. We are also currently evaluating whether we will seek a license or other partnering transaction with a third party for elobixibat in the United States or Europe. Whether or not we elect to seek such a transaction, we do not currently anticipate that we will conduct future clinical trials of elobixibat independently.

CIC is a GI disorder characterized by infrequent bowel movements or difficult passage of stools that persists for three months or longer. In Japan, the target indication for elobixibat is chronic constipation, which we believe, based on discussions with EA Pharma, also includes patients that would in other jurisdictions be diagnosed with irritable bowel syndrome with constipation, or IBS-C. Accordingly, we believe that chronic constipation represents a broader patient population in Japan than CIC.

Elobixibat is, like A4250, an IBAT inhibitor. By inhibiting reabsorption of bile acids from the small intestine to the liver, elobixibat is expected to increase the flow of bile acid to the colon. Because elobixibat affects both secretion and motility in the colon, which is the site in the GI tract where constipation originates, we believe that elobixibat has potential to provide competitive advantages over currently available treatments for chronic constipation, which operate in the small bowel.

Third party studies have shown a correlation between increased bile acid levels in the colon, increased secretion of water and electrolytes in the colon and faster colonic transit. Conversely, slower colonic transit has been shown to result from introduction of a sequestrant that reduces bile acids in the colon. Colonic transit, or the time it takes for food to travel through the digestive system, is a function of motility. Motility refers to the ability to digest and propel intestinal contents. It is well established that bile acids in the colon stimulate motility, and scientific evidence suggests that this effect results from bile acid binding to TGR5 receptors. Because increasing bile acid levels in the colon has a positive effect on both colonic secretion and colonic motility, we believe elobixibat can benefit patients suffering from chronic constipation. Moreover, at therapeutic doses, elobixibat has minimal systemic exposure, acts locally in the gut and is excreted substantially intact in the feces, which may reduce the risk of systemic side effects and undesirable drug-drug interactions compared with drugs that have broad distribution in the body.
**Chronic (Idiopathic) Constipation**

Though occasional constipation is very common, some people experience chronic constipation that can interfere with their ability to go about their daily tasks. Pursuant to applicable Rome III diagnostic criteria, two or more of the following symptoms must be present: straining during at least 25% of defecations, lumpy or hard stools in at least 25% of defecations, sensation of incomplete evacuation for at least 25% of defecations, sensation of pelvic obstruction or blockage for at least 25% of defecations, use of fingers or other manual maneuvers to facilitate at least 25% of defecations, and passing fewer than three stools per week. In order to support a diagnosis of constipation, the patient must rarely have loose stools without the use of laxatives. Further, in order for constipation to be considered chronic, these criteria must be present for at least three months, with symptom onset at least six months prior to diagnosis. The Rome III diagnostic criteria are established diagnostic measures for various GI disorders set forth by the Rome Foundation, a not-for-profit organization based in the United States. The term “idiopathic” indicates that the cause of the chronic constipation is unknown and not due to any underlying illness or medication.

The current standard of care for constipation is over-the-counter, or OTC, laxatives, which may improve symptoms of constipation but often exacerbate pain and bloating. Marketed products in the United States that may be prescribed for chronic constipation include Linzess (linaclotide) and Amitiza (lubiprostone). However, the benefit of these treatment options is limited by tolerability issues, including in particular diarrhea for linaclotide and nausea for lubiprostone. Amitiza is also approved in Japan, among other countries, and, in December 2016, Linzess was approved in Japan for the treatment of IBS-C.

Although estimates of the prevalence of CIC vary, a third party retrospective analysis in 2011 of 100 published studies estimated the prevalence of CIC in adults to be approximately 14%, which represents over 36 million people in the United States, and over 61 million people in the European Union. We believe many people with CIC do not seek medical care and suffer in silence while unsuccessfully self-treating with fiber or OTC laxatives.

**Preclinical and Early Clinical Development of Elobixibat**

Prior to Albireo Limited’s inception in 2008, elobixibat was evaluated by its predecessor owner, AstraZeneca, in various preclinical studies and Phase 1 single ascending dose and multiple ascending dose clinical trials. In Phase 1 clinical development, elobixibat was generally well tolerated in healthy volunteers and showed minimal systemic exposure. Subsequently, we conducted a two-year nonclinical carcinogenicity toxicology study that did not result in any findings of concern and we or our former licensee conducted various additional Phase 1 and early Phase 2 clinical trials to assess the pharmacokinetics and various effects of elobixibat. Findings from these studies indicated, among other things, favorable effects of elobixibat on colonic transit and on low-density lipoprotein, or LDL or “bad” cholesterol.

**Completed Phase 2b Clinical Trial in the United States**

We completed a multicenter, double blind, placebo controlled Phase 2b clinical trial of elobixibat as a treatment for CIC in 2010. We conducted the trial at 45 sites in the United States. Enrollment criteria included a diagnosis of CIC and meeting specified thresholds for numbers of complete SBMs, or CSBMs, per week during the two weeks prior to randomization. An SBM was defined in the trial as a bowel movement occurring without a laxative, enema or suppository usage in the past 24 hours. A CSBM was defined in the trial as an SBM accompanied by a self-report of complete evacuation.

After a screening period during which patients were taken off laxatives and other excluded medications, patients in the trial entered a two-week baseline period. Following the baseline period, 190 patients were randomized to receive a once daily oral tablet dose of one of three doses of elobixibat (5, 10 or 15 mg), or placebo, for eight weeks. Of the randomized patients, 161 patients completed the trial.

The primary endpoint of the trial was change in number of weekly SBMs from baseline to the first treatment week for patients who received elobixibat compared with patients who received a placebo. The results demonstrated a dose response in favor of elobixibat among all three dose groups and were statistically significant in the 10 mg (p < 0.002) and 15 mg (p < 0.001) dose groups. A clinical trial result is statistically significant if it is unlikely to have occurred by chance. The statistical significance of a clinical trial result, such as an observed difference between two treatment groups or cohorts, is determined by a widely used statistical method that establishes the “p”-value of the result. A p-value of 0.05 (or less) indicates that there is a 1-in-20 (or less) statistical probability that the clinical trial result occurred by chance and typically represents statistical significance. If a p-value is above 0.05, the result is generally not considered statistically significant. The p-value of < 0.002 for the 10 mg elobixibat dose group indicates that there is a less than 1-in-500 statistical probability that the difference compared with placebo occurred by chance, and the p-value of < 0.001 for the 15 mg elobixibat dose group indicates that there is a less than 1-in-1,000 statistical probability that the difference compared with placebo occurred by chance.
Secondary efficacy endpoints of the trial included evaluations of changes in mean weekly number of SBMs and CSBMs, time to first SBM or CSBM, overall constipation response and reduction in C4 and LDL cholesterol levels. The 10 mg and 15 mg elobixibat doses met all of these secondary endpoints with statistical significance.

All doses of elobixibat were generally well tolerated in the clinical trial. The most frequently reported adverse events in the trial were abdominal pain and diarrhea, which occurred most often in the highest elobixibat dose group (abdominal pain: 10.4%, 5 mg elobixibat; 10.6%, 10 mg elobixibat; and 27.1%, 15 mg elobixibat; versus 0% placebo; and diarrhea: 8.3%, 5 mg elobixibat; 6.4%, 10 mg elobixibat; and 12.5%, 15 mg elobixibat; versus 2.2% placebo). None of the three SAEs reported in the trial (bleeding colonic diverticulum two weeks after the end of treatment in the 5 mg elobixibat dose group, breast carcinoma in the 10 mg elobixibat dose group, and shoulder pain in the placebo group) was considered by the applicable investigator to be related to study drug.

Completed Phase 2b Clinical Trial Conducted by EA Pharma in Japan

Our licensee, EA Pharma, completed a multicenter, double blind, placebo controlled Phase 2b clinical trial of elobixibat as a treatment for chronic constipation in 2015. Patients in the trial entered the two-week baseline period during which they were taken off excluded medications. Following the baseline period, patients were randomized to receive a once daily oral dose of either a low, mid or high dose of elobixibat for two weeks. During the baseline period and the treatment period, patients reported daily bowel and abdominal symptoms. Of the randomized patients, 154 patients completed the trial.

The primary endpoint of the trial was change in number of weekly SBMs from baseline to the first treatment week for patients who received elobixibat compared with patients who received a placebo. In the trial, both the mid and high dose groups of elobixibat showed a highly statistically significant advantage on change from baseline in weekly SBM frequency compared with placebo (p < 0.001). The findings in favor of elobixibat were substantially the same on a secondary endpoint of the trial assessing change from baseline in weekly CSBM frequency.

All doses of elobixibat were generally well tolerated in the trial, and no SAEs were reported. As in our completed Phase 2b clinical trial, the most frequently reported adverse events in the trial were abdominal pain and diarrhea, which were both assessed by EA Pharma to be typically mild.

Completed Phase 3 Clinical Trial Conducted by EA Pharma in Japan; Ongoing Long-Term Safety Trial

In October 2016, we announced positive results from a Phase 3 clinical trial of elobixibat as a treatment for chronic constipation conducted by EA Pharma in Japan. The trial was a multicenter, double blind, placebo controlled trial in which patients with chronic constipation received a fixed dose of elobixibat or placebo once daily for two weeks. In the trial, elobixibat met the primary endpoint, which was change in the number of weekly SBMs from baseline to the first treatment week compared with placebo, with high statistical significance. Elobixibat also met all secondary efficacy endpoints in the trial assessed statistically, including assessments of change in frequency of CSBMs, time to first SBM, severity of constipation and stool consistency, with high statistical significance.

There were no SAEs reported in the trial. Consistent with prior clinical trials of elobixibat, the most common adverse events were abdominal pain (18.8%) and diarrhea (13.0%), all of which were characterized as mild or, in one case, moderate in severity.

A clinical trial designed to evaluate the long-term safety of elobixibat in Japanese patients with chronic constipation over 52 weeks being conducted by EA Pharma remains ongoing. The long-term safety trial is a multicenter, open label trial in which patients with chronic constipation receive once daily dosing of elobixibat. An interim analysis of 340 patients dosed for 24 weeks showed a safety and tolerability profile of elobixibat consistent overall with prior clinical trials of elobixibat in Japan.

Phase 3 Clinical Trials Conducted by a Former Licensee

Two Phase 3 clinical trials conducted by a former licensee of ours to evaluate the efficacy and safety of elobixibat as a treatment for CIC, known as Echo 1 and Echo 2, ended in 2014. Our former licensee stopped Echo 1 and Echo 2 early due to an issue related to the distribution of study drug to study sites that was unrelated to the performance of elobixibat. Subsequent analysis by our former licensee determined the issue to have affected only Echo 2 and a small number of patients. As a result of the early termination of the trials, each of Echo 1 and Echo 2 enrolled substantially fewer than the number of patients contemplated by the trial’s statistical plan. A third Phase 3 clinical trial conducted by our former licensee to evaluate the long-term safety of elobixibat, known as Echo 3, ended in 2015.

Echo 1, Echo 2 were multicenter, double blind, placebo controlled Phase 3 clinical trial of elobixibat as a treatment for CIC conducted at 71 sites in the United States, Belgium, Canada, Czech Republic, Germany, Israel, the United Kingdom, Poland and South Africa. SBM and CSBM were defined in the trial in the same manner as our completed Phase 2b trial of elobixibat in CIC discussed above. The statistical plan for the trial contemplated that 840 patients would be enrolled.
After a screening period, patients in the trial entered a two-week baseline period. Following the baseline period, patients were randomized in a 1:1:1 ratio to receive a once daily oral dose of 5 mg of elobixibat, 10 mg of elobixibat or placebo, in tablet form, for 26 weeks. During the baseline period and the treatment period, patients reported daily bowel and abdominal symptoms. At the time the trial was stopped, 376 patients had been randomized into the trial, of which 312 patients had completed 12 weeks of treatment and 146 patients had completed 26 weeks of treatment.

The primary endpoint of the trial was the overall CSBM response. CSBM response refers to a patient having at least three CSBMs per week and an increase of at least one CSBM per week from baseline, in each case for at least nine of the first 12 weeks of the treatment period and at least three of the weeks from week 9 to week 12. The 5 mg elobixibat dose met the primary endpoint, and the result was statistically significant based on the study’s predefined statistical methodology (p = 0.029). There was a trend in favor of the 10 mg elobixibat dose on the primary endpoint, but the result did not achieve statistical significance using the same methodology. Subsequently, at a meeting with the FDA held in 2016, the FDA advised us that, based on the unplanned stopping of the study, the FDA would apply a different statistical methodology than had been predefined and utilized for the study. Using the FDA’s chosen statistical methodology, neither the 5 mg nor the 10 mg dose of elobixibat achieved statistical significance on the primary endpoint in Echo 1.

All doses of elobixibat were generally well tolerated in the trial. The rate of discontinuation due to adverse events was dose related (7%, 5 mg elobixibat and 9%, 10 mg elobixibat, versus 2% placebo). There were dose-related incidences of treatment-emergent abdominal pain and diarrhea considered a reasonable possibility to be treated related (abdominal pain: 4%, 5 mg elobixibat and 12%, 10 mg elobixibat, versus 2% placebo; diarrhea: 6%, 5 mg elobixibat and 6%, 10 mg elobixibat, versus 2% placebo). None of the three SAEs reported in the 5 mg elobixibat dose group, two SAEs reported in the 10 mg elobixibat dose group and one SAE reported in the placebo group were considered by the applicable investigator to be related to study drug. The reported SAEs were: in the 5 mg elobixibat dose group, inflammation of the gallbladder, developmental bone growth disease and carpal tunnel syndrome; in the 10 mg elobixibat dose group, glaucoma and back pain worsening; and in the placebo group, hemorrhoids.

Echo 2. Echo 2 was a multicenter, double blind, placebo controlled Phase 3 clinical trial of elobixibat as a treatment for CIC. The trial was conducted at 79 sites in the United States, Canada, Czech Republic, Germany, Hungary, Poland, Slovakia, Sweden, South Africa and the United Kingdom. Enrollment criteria, primary and key secondary endpoints and trial design were substantially the same as for Echo 1, except that Echo 2 from the outset provided for a 12-week treatment period and included a four-week post-treatment withdrawal period. The statistical plan for the trial contemplated that 840 patients would be enrolled.

Following the screening and baseline periods, patients were randomized in a 1:1:1 ratio to receive a once daily oral dose of 5 mg of elobixibat, 10 mg of elobixibat or placebo, in tablet form. During the baseline period and the treatment period, patients reported daily bowel and abdominal symptoms. At the time the trial was stopped, 314 patients had been randomized into the trial, of which 219 patients completed the trial including the withdrawal period.

In the trial, there were trends in favor of both the 5 mg and 10 mg elobixibat doses compared with placebo on the primary endpoint, but the result did not reach statistical significance. There were no signs of rebound during the four-week withdrawal period after the treatment period.

All doses of elobixibat were generally well tolerated in the trial. The rate of discontinuation due to adverse events was the same in the 5 mg elobixibat and placebo dose groups (2%) and greater in the 10 mg elobixibat dose group (6%). There were dose-related incidences of abdominal pain and diarrhea considered a reasonable possibility to be treatment related (abdominal pain: 2%, 5 mg elobixibat and 8%, 10 mg elobixibat, versus 2% placebo; diarrhea (7%, 5 mg elobixibat and 9%, 10 mg elobixibat, versus <1% placebo). There was one SAE reported in the 5 mg elobixibat dose group compared with five SAEs in the placebo group. The reported SAE in the 5 mg elobixibat dose group (basal cell carcinoma on the lip) occurred during the withdrawal period and was not considered by the applicable investigator to be related to study drug. The SAEs reported in the placebo group were tonsillitis, abnormal uterine bleeding, noncancerous uterine tumor, hysterectomy and exacerbation of hypertension.

Long-Term Safety. The long-term safety trial was a multicenter, open label, Phase 3 extension clinical trial of elobixibat as a treatment for CIC. The trial was conducted at 62 sites in the United States, Belgium, Canada, Czech Republic, Hungary, Poland, Slovakia, South Africa, Sweden and the United Kingdom. Enrollment criteria included completion of at least 12 weeks of double blind treatment in either Echo 1 or Echo 2. The trial enrolled 411 patients. Patients received a 10 mg dose of elobixibat in tablet form once daily, subject to reduction to 5 mg in the discretion of the applicable investigator, for up to 52 weeks. Of these patients, 282 patients completed 52 weeks of treatment with elobixibat and 316 patients completed at least 24 weeks of treatment with elobixibat.

There were several co-primary endpoints in the trial, all related to safety. In the trial, elobixibat was generally well tolerated, with a safety profile similar to Echo 1 and Echo 2. In particular, there was only one treatment-emergent SAE reported (constipation) that was considered by the applicable investigator to be related to study drug. Treatment-emergent adverse events leading to discontinuation occurred in 6.1% of patients, and the majority of treatment-emergent adverse events overall were classified as mild or moderate. Most adverse events were classified as GI.
A3384

A3384 is a proprietary formulation of cholestyramine that is designed to release cholestyramine directly in the colon. We are developing A3384 as a treatment for BAM. BAM, which is sometimes also called bile acid diarrhea, occurs when bile acids are not sufficiently reabsorbed in the small intestine, causing elevated levels of bile acids to instead reach the colon and leading to chronic watery diarrhea.

There are no drugs currently approved for the treatment of BAM. Cholestyramine, which is approved in some countries in Europe to treat diarrhea associated with certain GI conditions, is commonly prescribed off label to treat BAM. However, cholestyramine is typically taken as a powder that does not dissolve in water and has been described as “drinking sand.” Because of poor tolerability and because of its negative effect on absorption of other medications and important fat soluble vitamins, the benefit of cholestyramine in the treatment of BAM has been limited. We believe that a formulation that has a more favorable tolerability profile than immediate release cholestyramine can benefit patients with BAM.

We have completed a Phase 2 clinical trial of a prior formulation of A3384 in BAM and we are in the late stages of a subsequent pharmaceutical development program designed to identify an optimized formulation of A3384 capable of selectively delivering a greater amount of cholestyramine to the colon. The pharmaceutical development program has to date resulted in two alternative formulations of A3384, each constituting a coating surrounding pellets of cholestyramine that travel through the body intact until the coating is dissolved in the colon to permit bile acids to bind to the cholestyramine. We are continuing to optimize these alternative formulations and, when our optimization is complete, plan to evaluate one or both of them in a potential future Phase 2 clinical trial in BAM. We do not anticipate conducting future clinical development of A3384 unless we obtain additional capital, whether from our license agreement with EA Pharma for elobixibat, from a future offering of debt or equity securities or otherwise.

Bile Acid Malabsorption

BAM is a common cause of chronic watery diarrhea, with affected individuals having their bowels open several times a day. When bile acids are secreted into the colon, bacteria in the colon acts to convert the bile acids into different bile acids known as deoxycholate and lithocholate. These secondary bile acids play a key role in stimulating electrolyte and water secretion, which increases colonic motility and shortens colonic transit time. Highly elevated levels of these secondary bile acids can produce watery diarrhea, as well as other GI symptoms such as bloating, urgency and fecal incontinence.

We estimate the prevalence of BAM to be approximately 1.3 million people in the United States and approximately 2.2 million people in the European Union. The approach to treating BAM currently depends on binding excess bile acids to reduce their secretory actions, using a bile acid sequestrant such as cholestyramine or a variant such as colestipol or coleveselam. However, many patients cannot tolerate these medications because of the texture or taste, because they worsen the diarrhea, cause intolerable nausea, heartburn, wind or bloating or because they negatively impact the absorption of important fat soluble vitamins or other medications. A third-party analysis of patients given a bile acid sequestrant to lower cholesterol showed that over half discontinued treatment within one year, and similar discontinuation was seen in a separate published study that followed treated patients with BAM.

Completed Phase 2 Clinical Trial of a Prior Formulation of A3384 in BAM

We completed a multicenter, double blind, placebo controlled Phase 2 clinical trial of a prior formulation of A3384 as a treatment for BAM in 2014. The discussion of the completed clinical trial that follows refers to the prior formulation as A3384. There were 19 patients enrolled in the trial based on a diagnosis of BAM or bile acid diarrhea and meeting specified criteria for numbers of bowel movements and liquid or soft stools per day. We had initially planned to enroll 36 patients in the trial. However, due to slower than expected patient enrollment and the fact that subjects in a Phase 1 clinical trial of A4250 in combination with A3384 that we were conducting in parallel had experienced diarrhea, we elected to discontinue enrollment in our BAM trial. As a result, the trial was not sufficiently powered to be able to detect statistically significant superiority of A3384 compared with placebo.

Patients in the trial continued their current treatment with immediate release cholestyramine or another conventional bile acid resin for one week (referred to as baseline period 1), following which the bile acid resin was withdrawn for two weeks (referred to as baseline period 2). At that point, patients were randomized to receive twice daily oral doses of 250 mg of A3384, 1000 mg of A3384 or placebo for two weeks. The primary efficacy endpoint of the trial was change in mean daily number of bowel movements from baseline period 2 to the second treatment week for patients who received A3384 compared with patients who received a placebo.

In the trial, patients who received either dose of A3384 showed a numerically greater mean reduction in the number of mean daily bowel movements compared with placebo, but the result did not reach statistical significance. A secondary endpoint comparing mean daily episodes of diarrhea from baseline period 2 to the second treatment week showed a strong trend in favor of each dose of A3384 evaluated compared with placebo and reached statistical significance in the 250 mg A3384 dataset (p < 0.05) and combined
A3384 dose dataset (p < 0.01). Another secondary endpoint comparing mean daily stool consistency from baseline period 2 to the second treatment week showed a strong trend in favor of 250 mg A3384 and the combined A3384 dose groups, but the results did not reach statistical significance. There were some numerical advantages in favor of one or both A3384 dose groups or in the combined A3384 dose dataset on other secondary endpoints, including assessments of abdominal discomfort, bloating and global symptom relief, but none approached statistical significance.

Both doses of A3384 were generally well tolerated in the clinical trial, with no adverse events leading to discontinuation in either A3384 dose group. The only SAE reported in the trial, metastasis with unknown primary tumor, was considered by the investigator to be not related to study drug.

Preclinical Program in NASH

We have an ongoing preclinical program directed towards discovering and advancing to the clinic a novel compound that modulates bile acid levels to treat NASH. NASH is a common, serious and sometimes fatal chronic liver disease that resembles alcoholic liver disease, but occurs in people who drink little or no alcohol. Based on multiple epidemiological studies published by third parties in 2014 and 2015, we estimate that NASH affects 2 to 3.5% of adults, representing over 9 million people in the United States and 10 million people in the European Union. There are currently no drugs approved for the treatment of NASH. Lifestyle changes, including modification of diet and exercise to reduce body weight, as well as treatment of concomitant diabetes and dyslipidemia, are commonly accepted as the standard of care for NASH, but have not conclusively been shown to prevent disease progression.

Some of the principal characteristics of NASH include high LDL levels, resistance to insulin in the body, chronic inflammation in the liver and progressive scarring of tissue, known as fibrosis. We have generated favorable clinical or preclinical data on each of these measures with our IBAT inhibitors, either A4250 or elobixibat, supporting the potential of bile acid modulators generally, and IBAT inhibitors specifically, to become a new treatment option for NASH.

In particular, the reduction in the reuptake of bile acids triggered by IBAT inhibition signals to the liver to make more bile acids to ensure the presence of a sufficient supply. The liver makes these bile acids from cholesterol, which has the effect of reducing levels of LDL levels in the plasma. Also, increased bile acids in the colon resulting from IBAT inhibition stimulates the secretion of GLP-1 (glucagon-like peptide-1), which regulates insulin release from the pancreas and has been shown to decrease insulin resistance. Data from our clinical trials of elobixibat in patients with CIC or abnormal lipid levels demonstrated both of these effects. In addition, as discussed above under “A4250 — Development of A4250 — Preclinical and Phase 1 Clinical Development,” in a preclinical mouse model of cholestatic liver injury, A4250 significantly inhibited the expression of different proteins known to be associated with inflammation and fibrosis. Moreover, in preclinical studies conducted by us or third parties, compounds that inhibit the IBAT have been reported to reduce liver concentrations of certain bile acids and cholesterol believed to play a role in the progression of NASH.

The results of a nonclinical study of A4250 conducted in an established model of NASH in mice known as the STAM™ model provide further support for the promise of IBAT inhibition mechanism to treat NASH. In the study, NASH conditions were simulated by injecting the mice with the drug streptozotocin soon after birth and providing a high fat diet beginning at four weeks. Baseline was established at week six, following which three cohorts of mice received 0.5 mg/kg of A4250, 10 mg/kg of A4250 or vehicle only once daily for 21 days. In the study, compared with the vehicle group, the 10 mg/kg A4250 dose group showed significant improvement (p < 0.05) on the nonalcoholic fatty liver disease activity score, or NAS, near significant improvement on a fibrosis measure (p = 0.06) and numerical improvement on plasma ALT levels and triglycerides. The 0.5 mg/kg A4250 dose group showed incremental advantages on some of these measures. We believe that NAS results with 10 mg/kg A4250 are competitive with NAS results previously presented from the same model for obeticholic acid, which is marketed as Ocaliva in combination with UDCA, or as a monotherapy for patients unable to tolerate UDCA, to treat PBC by Intercept Pharmaceuticals, Inc., or Intercept, and is currently in Phase 3 development as a treatment for NASH.

License Agreements

Agreement with EA Pharma

Albireo AB, a wholly owned indirect subsidiary of ours, entered into a license agreement with EA Pharma (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.) for the development and commercialization of elobixibat in specified countries in Asia in April 2012. Albireo AB subsequently transferred the agreement to its wholly owned subsidiary, Elobix AB, and the agreement was amended in January 2015 and April 2016. For the remainder of this discussion of the agreement, “we” and the like refer to either or both of Albireo AB or Elobix AB, as the context requires.
Pursuant to the agreement, we granted EA Pharma an exclusive license under patents and other technology owned or licensed by us to develop and commercialize elobixibat in Japan, Indonesia, Korea, Taiwan, Thailand and Vietnam for all prophylactic or therapeutic uses of a pharmaceutical product for specified GI diseases and disorders, symptoms of constipation of all causes, or postoperative ileus or for use in colonoscopy cleansing procedures. The agreement also provides that the scope of the license may be expanded to include specified liver diseases, if we or an affiliate or licensee takes specified development actions outside of EA Pharma’s licensed territory with elobixibat in that specified liver disease, or files an application for regulatory approval of elobixibat outside of EA Pharma’s licensed territory for that specified liver disease, or otherwise approves that EA Pharma conduct a clinical trial in that specified liver disease.

**Payment Terms.** As of March 1, 2017, we have received approximately $34.2 million in upfront and milestone payments from EA Pharma under the agreement. We are eligible to receive additional payments of up to €13.3 million if specified regulatory events are achieved for elobixibat and up to 3.5 billion Japanese Yen if specified sales milestones are achieved for elobixibat. We are also eligible for stepped royalties beginning in the high single digits on any future net sales of elobixibat.

EA Pharma’s obligation to pay royalties to us for elobixibat expires on a country-by-country basis on the later of expiration of the patent rights in a country that have a specified scope and that we either licensed to EA Pharma or, subject to a specified term limit, are developed by EA Pharma, alone or together with us, in the course of its activities under the agreement or expiration of regulatory exclusivity for elobixibat in that country. The Japanese patent rights with respect to elobixibat that we licensed to EA Pharma expire between 2021 and 2024, subject to patent term extension that may be available in Japan. In addition, we have two pending patent applications on specific crystal polymorphs of elobixibat that, if issued in Japan, will expire in 2034 and 2035, respectively. Royalty rates are subject to reduction under the agreement in specified circumstances, including in any country if elobixibat is subject to generic competition that exceeds a specified level, if the bulk price for unformulated elobixibat purchased from us for use in Japan exceeds a specified threshold or if EA Pharma licenses patent rights from any third party under circumstances where it is legally required to do so to commercialize elobixibat in its licensed field in a particular country in its licensed territory.

**Development and Commercialization.** EA Pharma is responsible for funding and using commercially reasonable efforts to execute the development and commercialization of elobixibat in its licensed field and licensed territory pursuant to agreed territory development and commercialization plans that are updated from time to time. In Japan, EA Pharma is developing and plans to commercialize elobixibat jointly with Mochida pursuant to a sublicense agreement. A joint development committee and a joint commercialization committee, each comprising representatives of each company, oversees activities under the agreement. We are responsible for the development and commercialization of elobixibat outside of EA Pharma’s licensed territory.

We have historically procured unformulated elobixibat for EA Pharma’s development activities under the agreement pursuant to a complementary supply agreement. EA Pharma is responsible for commercial manufacture and supply of elobixibat in its licensed territory.

**Restrictions.** EA Pharma is not permitted to conduct clinical development or commercialize elobixibat outside of its licensed field of use or licensed territory. We are not permitted to commercialize elobixibat for any field of use in EA Pharma’s licensed territory. In addition, if we determine to develop elobixibat in a liver disease outside of EA Pharma’s licensed territory, our development is subject to specified restrictions on clinical trial design. After the first commercial sale of elobixibat in any country in EA Pharma’s licensed field, neither we nor EA Pharma may commercialize a different product for the treatment of chronic constipation or IBS-C in that country, subject to specified exceptions.

**Term and Termination.** Either we or EA Pharma can terminate the agreement in its entirety or on a country-by-country basis if the other party materially breaches the agreement and the breach is not cured within a specified period. Also, either we or EA Pharma can terminate the agreement in its entirety if a specified bankruptcy-related event with regard to the other party occurs. EA Pharma also has the right to terminate the agreement in its entirety or on a country-by-country basis (except for Japan) for any reason upon 180 days’ notice. The rights and obligations of the parties that survive termination of the agreement vary depending on the basis for the termination.

**Terminated Agreement with Ferring International Center S.A.**

We entered into a license agreement with Ferring International Center S.A., or Ferring, for the development and commercialization of elobixibat outside of the territories licensed to EA Pharma in July 2012, following completion of our Phase 2b clinical trial of elobixibat to treat CIC. Pursuant to the agreement, Ferring commenced a Phase 3 clinical program of elobixibat to treat CIC. In May 2014, Ferring stopped two Phase 3 clinical trials of elobixibat that Ferring had been conducting due to an issue related to the distribution of study drug to study sites that was unrelated to the performance of elobixibat. Subsequently, in March 2015, Ferring terminated the agreement, effective in September 2015. As a result of the termination of the agreement, all licenses that we granted to Ferring under the license agreement terminated and commercial rights to elobixibat in Ferring’s licensed territory reverted to us. In
addition, Ferring was required, among other things, to assign to us all rights to all regulatory submissions and approvals controlled by Ferring pertaining to elobixibat in the licensed territory and to grant to us an exclusive right of reference to data, and specified licenses to data and technology, related to elobixibat for the development and commercialization of elobixibat in its licensed field. Notwithstanding the termination of the license agreement, Ferring may be entitled to low single-digit royalty payments on net sales of elobixibat on a country-by-country and product-by-product basis in specified circumstances.

Patents and Proprietary Rights

We actively seek to protect the proprietary technology that we consider important to our business, including compositions and forms and their methods of use in the United States, Europe and other jurisdictions internationally that we consider key pharmaceutical markets. We also rely upon trade secrets and contracts to protect our proprietary information.

As of March 1, 2017, our patent estate included 16 issued patents and six pending patent applications in the United States and approximately 425 counterpart patents and patent applications in other jurisdictions, including 16 European regional issued patents and approximately four Patent Cooperation Treaty, or PCT, applications which allow us to seek corresponding patent protection worldwide. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular jurisdiction.

We consider the following United States, European (EP) and, in the case of elobixibat, Japanese (JP) patents to be particularly important to the protection of our clinical-stage product candidates.

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Summary Description</th>
<th>Expiration Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4250</td>
<td>Composition of matter of A4250</td>
<td>September 2022</td>
</tr>
<tr>
<td></td>
<td>Method of using an inhibitor of the ileal bile acid transporter to treat liver disease</td>
<td>November 2031 (EP) (pending in US)</td>
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<tr>
<td></td>
<td>Method of using an inhibitor of the ileal bile acid transporter in combination with a bile acid binder to treat liver disease</td>
<td>November 2031 (EP) (pending in US)</td>
</tr>
<tr>
<td>Elobixibat</td>
<td>Composition of matter of elobixibat</td>
<td>December 2021 (EP, JP); August 2022 (US)</td>
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<tr>
<td></td>
<td>Method of using an inhibitor of the ileal bile acid transporter to treat Chronic Idiopathic Constipation or Irritable Bowel Syndrome</td>
<td>April 2024</td>
</tr>
<tr>
<td></td>
<td>Crystal modifications of elobixibat</td>
<td>April 2034 (issued, US, EP; pending JP)</td>
</tr>
<tr>
<td></td>
<td>Crystal modifications of elobixibat</td>
<td>October 2035 (PCT pending)</td>
</tr>
<tr>
<td>A3384</td>
<td>Pharmaceutical formulations comprising cholestyramine</td>
<td>February 2037 (PCT pending)</td>
</tr>
</tbody>
</table>

We also have issued patents and pending patent applications with equivalent or substantially comparable protection for our product candidates in jurisdictions internationally that we consider key pharmaceutical markets.

The patent expiration dates referenced above do not reflect any potential patent term extension that we may receive for the United States under The United States Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, or similar patent term extension legislation in Europe and Japan. The Hatch-Waxman Act generally permits a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of FDA approval. The patent term restoration period is generally one-half of the time between the effective date of an investigational new drug application, or IND, and the submission date of a new drug application, or NDA, plus the time between the submission date and approval date of an NDA. Only one patent applicable to an approved drug is eligible for an extension, and, with limited exceptions, the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for patent term extension.
In Japan, the Japanese Pharmaceutical Affairs Law generally permits the extension of the patent term for a drug as compensation for patent term lost during the regulatory review process by the Japanese PMDA. The patent term extension corresponds to the period from the date of the start of clinical trials or the date of patent registration, whichever is later, until one day prior to the date of approval for the drug. The term of a patent can be extended for up to five years, irrespective of the remaining natural term of the patent as of the date of approval. Each patent that covers the active ingredient in the approved drug, or a method of using the approved drug in the approved indication, is eligible for the extension, which means that, for any particular drug, multiple patents may be extended. The extension must be applied for prior to expiration of the patent and within three months from the date of approval. The Japanese Patent Office reviews and approves applications for patent term extension.

Sales and Marketing

We currently do not have a commercial organization for the marketing, sales and distribution of pharmaceutical products. We intend to build the commercial infrastructure necessary to effectively support the commercialization of A4250 in the United States and Europe, if A4250 is approved for PFIC or any other pediatric cholestatic liver disease or disorder. We believe that our commercial organization can be modest in size and targeted to the relatively small number of specialists in the United States and Europe who treat children with orphan cholestatic liver disease.

The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, internal sales support, an internal marketing group and distribution support. Additional capabilities important to the marketplace include the management of key accounts such as managed care organizations, group purchasing organizations, specialty pharmacies, government accounts and reimbursement support. Based on the number of physicians that treat orphan pediatric cholestatic liver diseases and disorders, we believe that we can effectively target the physician audience for A4250 in the United States and Europe by establishing a sales force either internally or by contract. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which may be committed prior to any confirmation that A4250 will be approved.

Outside of the United States and Europe, we plan to selectively utilize collaborations, distribution or other marketing arrangements with third parties to commercialize A4250 in any approved indication(s). Likewise, we intend to selectively seek alliances and collaborations to assist us in furthering the development or commercialization of product candidates, such as A3384 and, potentially, elobixibat, targeting large primary care markets that must be served by large sales and marketing organizations.

Manufacturing

We do not own or operate, and currently have no plans to establish, manufacturing facilities for the production of clinical or commercial quantities of A4250, elobixibat, A3384 or any of our other product candidates. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop.

We currently engage a single third-party manufacturer to provide the active pharmaceutical ingredient, or API, for A4250 and elobixibat. We also currently engage single third-party manufacturers to provide fill and finish services for the final drug product formulation of each of A4250, elobixibat and A3384 for use in our clinical trials.

We obtain the supplies of our API and drug products from these manufacturers pursuant to agreements that include specific supply timelines, quality and volume expectations. We obtain the supplies of our product candidates from these manufacturers under master services contracts and specific work orders. However, we do not have long-term supply arrangements in place. We do not currently have arrangements in place for redundant supply or a second source for API for any of A4250, elobixibat or A3384. If any of our current manufacturers becomes unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

A4250 and elobixibat are organic compounds of low molecular weight, and are referred to as “small molecules.” A3384 is a specialized formulation of cholestyramine, which is a polymer. A polymer is a chemical compound made up of small molecules arranged in a repeating structure to form a larger molecule. We have selected these compounds based on their potential efficacy and safety, although they are also associated with reasonable cost of goods, ready availability of starting materials and ease of synthesis. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.
Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with larger or more established companies.

Our commercial opportunity could be reduced or eliminated if our 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. Our competitors also may obtain marketing approvals for their products more rapidly than we obtain approval for our products. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, tolerability, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

We are aware of other companies that are developing product candidates that, like A4250 and elobixibat, act via IBAT inhibition. Shire plc’s SHP625, also known as maralixibat and formerly known as LUM001, is currently being studied in a Phase 2 clinical trial in PFIC, and we believe that Shire plans to conduct Phase 2/3 clinical development of SHP625 as a treatment for PFIC. We also believe that SHP625 is additionally in Phase 2 development as a treatment for ALGS, that GlaxoSmithKline’s GSK2330672 is in Phase 2 clinical development as a treatment for patients with PBC and that Shire’s SHP626 is in Phase 2 development as a treatment for NASH. In June 2016, Shire announced that the FDA has granted breakthrough therapy designation for SHP625 for PFIC, type 2.

The competition in our target indications includes the following.

**PFIC and other pediatric cholestatic liver diseases and disorders.** For many cholestatic liver diseases and disorders, including in particular PFIC, there are no approved therapies. With regard to the pruritus that is characteristic of these diseases, symptomatic off-label treatment with bile acid sequestrants, such as cholestyramine (marketed as Questran in the United States and as Colestyr, Efensol, Ipocol, Kolestran, Lipocol, Olestry, Prevalite or Quantalan in various other countries), typically provides only modest relief. Bristol Myers Squibb has discontinued manufacture of Questran, but generic versions of the drug are marketed by Upsher-Smith Laboratories, Inc., Par Pharmaceutical Companies, Inc. and Sandoz, the generic pharmaceuticals division of Novartis AG.

A number of other drugs, including UDCA, a bile acid, rifampin, an antibiotic derivative, and naltrexone, an opioid antagonist, are used off-label for patients suffering from cholestatic liver disease. Additionally, surgical interventions, such as PEBD surgery, and external liver filtering procedures are also employed as an attempt to lower bile acid levels, manage pruritus and improve measures of liver function.

As noted above, we believe that Shire plans to conduct Phase 2/3 clinical development of SHP625 as a treatment for PFIC. In addition, we believe Intercept’s obeticholic acid, which is approved in the United States in combination with UDCA, or as a monotherapy for patients unable to tolerate UDCA, to treat PBC, is in Phase 2 development as a treatment for biliary atresia.

**CIC.** Linaclotide, marketed as Linzess by Ironwood Pharmaceuticals, Inc. and Allergan plc, is approved in the United States for the treatment of CIC and IBS-C. Linaclotide is marketed in Europe as Constella by Ironwood and Allergan for the treatment of IBS-C and has also been approved in Japan for the treatment of IBS-C. Linaclotide targets guanylate cyclase C in the intestines and, by doing so, induces intestinal chloride secretion, which results in the outpouring of water into the intestine. The primary side effect of linaclotide is diarrhea. In addition, lubiprostone, which is marketed in the United States as Amitiza by Takeda Pharmaceutical Company Limited, is approved in the United States for the treatment of CIC, IBS-C and opioid-induced constipation. Amitiza is also approved for the treatment of CIC in the United Kingdom and Switzerland, and for the treatment of chronic constipation in Japan, where it is marketed by Mylan, N.V. Amitiza binds selectively to and activates the type-2 chloride channel in the intestine releasing chloride and water into the intestine. The primary side effect of Amitiza is nausea. Prucalopride, marketed by Shire as Resolor, is a motility agent approved in the European Union for the treatment of CIC, but it is not approved in the United States. Resolor is associated with a high rate of headaches. In addition, Resolor belongs to a class of drugs known as 5-HT receptor drugs that has been linked to cardiovascular safety issues.

Numerous OTC products are available for constipation. These include psyllium husk (such as Metamucil), methylcellulose (such as Citrucel), calcium polycarbophil (such as FiberCon), lactulose (such as Cephulac), polyethylene glycol (such as MiraLax), sennosides (such as Exlax), bisacodyl (such as Ducolax), docusate sodium (such as Colace), magnesium hydroxide (such as Milk of Magnesia), saline enemas (such as Fleet) and sorbitol. Given the low barriers to access, many CIC sufferers first try OTC fiber and laxatives, but these options are not sufficiently effective for many people.
In addition, Synergy Pharmaceuticals, Inc. has a product candidate known as plecanatide, to be marketed as Trulance, that is approved in the United States to treat CIC and for which it has completed two Phase 3 clinical trials in IBS-C. Plecanatide is, like linaclotide, a guanylate cyclase-C agonist. Ardelyx, Inc. has a product candidate, tenapanor, that is in Phase 3 clinical development in IBS-C. Tenapanor inhibits the sodium transporter NHE3 and reduces sodium uptake from the gut to increase the secretion of water in the intestines.

**BAM.** There are no approved drugs in the United States or Europe for the treatment of BAM. The most commonly used off-label treatment has been a bile acid sequestrant/resin, such as immediate release cholestyramine (which is approved in some countries in Europe to treat diarrhea associated with certain GI conditions) or colestipol, to keep bile acids from stimulating secretion in the colon. However, the benefits of immediate release cholestyramine and colestipol are limited because many patients cannot tolerate these medications because of the texture and taste or because they worsen the diarrhea or cause intolerable nausea, heartburn, wind or bloating. Another bile acid sequestrant sometimes used off label to treat to BAM is colesvelam, a cholesterol-lowering medicine marketed by Daiichi Sankyo Inc. as Welchol in the United States and by Genzyme Europe B.V. as Cholestagel in the European Union. Colesevelam is marketed in a tablet form that has fewer tolerability issues than other bile acid sequestrants, but its utility may be limited because it prevents absorption of other medications and important fat soluble vitamins. In addition, obeticholic acid has previously been studied by Intercept in a Phase 2 clinical trial as a treatment for BAM.

Patients with BAM following ileal resection surgery may also have a more generalized fat malabsorption as part of a short-bowel syndrome. In these patients, a low-fat diet supplemented with medium-chain triglycerides or cholylsarcosine, a synthetic cholic acid conjugate, may be used. Patients with BAM secondary to Crohn’s ileitis may be treated with glucocorticoid, a steroid hormone. Microscopic colitis patients may be given budesonide, a glucocorticoid steroid. Patients with BAM secondary to small intestinal bacterial overgrowth may require antibiotic therapy.

**Government Regulation**

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

### Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process, the approval process or after approval may subject an applicant or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOI, or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- preparation and submission to the FDA of an NDA;
• review of the product by an FDA advisory committee, where appropriate or if applicable;
• satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity;
• payment of user fees and securing FDA approval of the NDA; and
• compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA, if applicable.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or API and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can be initiated or restarted (in cases when the trial is placed on clinical hold after it has already begun).

In addition, an IRB representing each institution that is participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to clinical trial subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials, including details of the protocol and eventually study results, also must be submitted within specific timeframes to the National Institutes of Health for public dissemination on the federal ClinicalTrials.gov data registry.

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

• Phase 1. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition, in order to be tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
• Phase 2. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, in order to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
• Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in one or more well-controlled clinical trials in order to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the drug, and to provide adequate information for the labeling of the drug.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at
all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product’s chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA, which requests approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.0 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $98,000 per product and $512,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA’s receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. After the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date the NDA is accepted for filing, and most applications for “priority review” products are meant to be reviewed within six months from the date the NDA is accepted for filing. The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the drug product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS are tailored to the specific risk/benefit profile of a drug and can include requirements such as medication guides for patients, detailed communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, restricted distribution, and the use of patient registries. The FDA may require a REMS as a condition of approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS and the specific components that are involved can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making final approval decisions about a particular new drug application.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may grant a product the fast track designation if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and
the FDA may initiate review of sections of a fast track product’s NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA’s time period goal for reviewing a fast track product application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process.

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory program for products designated as “breakthrough therapies.” A product may be designated as a breakthrough therapy if it is intended, either 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 the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to designated breakthrough therapies, including: holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Finally, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA’s goal for taking action on a marketing application from ten months to six months.

**Accelerated Approval Pathway**

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that generally provides a meaningful therapeutic advantage to patients over existing treatments and based upon a demonstration that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. As part of the process of designing our planned clinical trial of A4250 in patients with PFIC, we are considering whether we will pursue the accelerated approval process for A4250.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor’s agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug’s clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.
The FDA’s Decision on an NDA

On the basis of the FDA’s evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue either an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information and for specific indications. A complete response letter (CRL) generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in response to the CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product; require that contraindications, warnings or precautions be included in the product labeling; require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug’s safety after approval; require testing and surveillance programs to monitor the product after commercialization; or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.
In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act, or DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023.

**Abbreviated New Drug Applications for Generic Drugs**

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD. Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug . . .”

Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of nonpatent exclusivity for the RLD has expired. The FDCA provides a period of five years of nonpatent data exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years after the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

**Hatch-Waxman Patent Certification and the 30-Month Stay**

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant’s product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Specifically, the applicant for a follow-on drug product must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product’s listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).
If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA in question has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA applicant.

**Pediatric Clinical Trials and Exclusivity**

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric trial plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric trial or trials the applicant plans to conduct, including trial objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA’s internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

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

**Orphan Drug Designation and Exclusivity**

The FDA has granted orphan drug designation to A4250 for the treatment of PFIC, as well as for PBC. Under the Orphan Drug Act, the FDA may designate a drug 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 drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the designation request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. 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 or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

**Patent Term Restoration and Extension**

The term of a U.S. patent that covers a drug, biological product or approved medical device may also be eligible for patent term extension when FDA approval is granted, provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. For drugs, the Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension, and only those claims reading on the approved drug may be extended. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug, provided that statutory and regulatory requirements are met. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.
**Regulation Outside the United States**

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

**Regulation and Marketing Authorization in the European Union**

The process governing approval of medicinal products in the European Union follows essentially the same lines as in the United States and, likewise, generally involves satisfactorily completing each of the following:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the applicable E.U. Good Laboratory Practice regulations;
- submission to the relevant national authorities of a clinical trial application, or CTA, which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication;
- submission to the relevant competent authorities of a marketing authorization application, or MAA, which includes the data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labelling;
- satisfactory completion of an inspection by the relevant national authorities of the manufacturing facility or facilities, including those of third parties, at which the product is produced to assess compliance with strictly enforced current cGMP;
- potential audits of the nonclinical and clinical trial sites that generated the data in support of the MAA; and
- review and approval by the relevant competent authority of the MAA before any commercial marketing, sale or shipment of the product.

**Preclinical Studies**

Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animal studies, in order to assess the potential safety and efficacy of the potential product. The conduct of the preclinical tests and formulation of potential product for testing must comply with the relevant E.U. regulations and requirements. The results of the preclinical tests, together with relevant manufacturing information and analytical data, are submitted as part of the CTA.

**Clinical Trial Approval**

Requirements for the conduct of clinical trials in the European Union including Good Clinical Practice, or GCP, are implemented in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of an E.U. member state in which a trial is planned to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the European Commission passed the new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new E.U. clinical trials legislation was passed as a regulation that is directly applicable in all E.U. member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable.
The new Regulation (EU) No 536/2014 aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include:

- a streamlined application procedure via a single entry point, the E.U. portal;
- a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states;
- a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I is assessed jointly by all member states concerned and Part II is assessed separately by each member state concerned);
- strictly defined deadlines for the assessment of clinical trial application; and
- the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Regulation (EU) No 536/2014.

**PRIME Designation**

The EMA grants access to the Priority Medicines, or PRIME, program to investigational medicines for which it determines there to be preliminary data available showing the potential to address an unmet medical need and bring a major therapeutic advantage to patients. As part of the program, EMA provides early and enhanced dialogue and support to optimize the development of eligible medicines and speed up their evaluation, aiming to bring promising treatments to patients sooner. In the fourth quarter of 2016, the EMA granted access to the PRIME program for A4250 to treat PFIC.

**Marketing Authorization**

Authorization to market a product in the member states of the European Union proceeds under one of four procedures: a centralized authorization procedure, a mutual recognition procedure, a decentralized procedure or a national procedure.

**Centralized Authorization Procedure**

The centralized procedure enables applicants to obtain a marketing authorization that is valid in all E.U. member states based on a single application. Certain medicinal products, including products developed by means of biotechnological processes, must undergo the centralized authorization procedure for marketing authorization, which, if granted by the European Commission, is automatically valid in all 28 E.U. member states. The European Medicines Agency, or EMA, and the European Commission administer this centralized authorization procedure pursuant to Regulation (EC) No 726/2004.

Pursuant to Regulation (EC) No 726/2004, this procedure is mandatory for various types of products, including, among others, products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.

The centralized authorization procedure is optional for other medicinal products if they contain a new active substance or if the applicant shows that the medicinal product concerned constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization is in the interest of patients in the European Union.

**Administrative Procedure**

Under the centralized authorization procedure, the EMA’s Committee for Human Medicinal Products, or CHMP, serves as the scientific committee that renders opinions about the safety, efficacy and quality of medicinal products for human use on behalf of the EMA. The CHMP is composed of experts nominated by each member state’s national authority for medicinal products, with an expert appointed to act as Rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a Co-Rapporteur. After approval, the Rapporteur(s) continue to monitor the product throughout its life cycle. The CHMP has 210 days to adopt an opinion as to whether a marketing authorization should be granted. The process usually takes longer in case additional information is requested, which triggers clock-stops in the procedural timelines. The process is complex and involves extensive consultation with the regulatory authorities of member states and a number of experts. When an application is submitted for a marketing authorization in respect of a drug that is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may pursuant to Article 14(9) Regulation (EC) No 726/2004 request an accelerated assessment procedure. If the CHMP accepts such request, the time-limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time-limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. Once the procedure is completed, a European Public Assessment Report, or EPAR, is produced. If the opinion is negative, information is given as to the grounds on which this conclusion was reached. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the E.U. member states, which in total can take more than 60 days.
**Conditional Approval**

In specific circumstances, E.U. legislation (Article 14(7) Regulation (EC) No 726/2004 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the risk-benefit balance of the product candidate is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

**Marketing Authorization under Exceptional Circumstances**

Under Article 14(8) Regulation (EC) No 726/2004, products for which the applicant can demonstrate that comprehensive data (in line with the requirements laid down in Annex I of Directive 2001/83/EC, as amended) cannot be provided (due to specific reasons foreseen in the legislation) might be eligible for marketing authorization under exceptional circumstances. This type of authorization is reviewed annually to reassess the risk-benefit balance. The fulfillment of any specific procedures/obligations imposed as part of the marketing authorization under exceptional circumstances is aimed at the provision of information on the safe and effective use of the product and will normally not lead to the completion of a full dossier/approval.

**Market Authorizations Granted by Authorities of E.U. Member States**

In general, if the centralized procedure is not followed, there are three alternative procedures as prescribed in Directive 2001/83/EC:

- The decentralized procedure allows applicants to file identical applications to several E.U. member states and receive simultaneous national approvals based on the recognition by E.U. member states of an assessment by a reference member state.
- The national procedure is only available for products intended to be authorized in a single E.U. member state.
- A mutual recognition procedure similar to the decentralized procedure is available when a marketing authorization has already been obtained in at least one E.U. member state.

A marketing authorization may be granted only to an applicant established in the European Union.

**Pediatric Studies**

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.
**Periods of Authorization and Renewals**

A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

**Orphan Drug Designation and Exclusivity**

The European Commission, following an evaluation by the EMA’s Committee for Orphan Medicinal Products, has designated A4250 as an orphan medicinal product for the treatment of PFIC, as well as for the treatment of PBC and ALGS. Pursuant to Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000, the European Commission can grant such orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Union, or a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized E.U. marketing authorization, as well as ten years of market exclusivity following marketing authorization of the designated orphan drug. During this market exclusivity period, neither the EMA, the European Commission nor the member states can accept an application or grant a marketing authorization for a similar medicinal product. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as those contained in an authorized orphan medicinal product and that is intended for the same therapeutic indication. A “similar active substance” is defined as an active substance that is identical or has the same principal molecular structural features (but not necessarily all of the same molecular features) and acts via the same mechanism as the authorized orphan medicinal product. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the already approved orphan drug. Furthermore, a product can lose orphan designation and the related benefits, prior to us having obtained a marketing authorization, if it is demonstrated that the orphan designation criteria are no longer met.

**Regulatory Data Protection**

E.U. legislation also provides for a system of regulatory data and market exclusivity. According to Article 14(11) of Regulation (EC) No 726/2004, as amended, and Article 10(1) of Directive 2001/83/EC, as amended, upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator’s data to assess a generic (abbreviated) application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator’s data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder, or MAH, 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 version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, preclinical tests and clinical trials. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of ten years of orphan market exclusivity—see also Orphan Drug Designation and Exclusivity. Depending upon the timing and duration of the E.U. marketing authorization process, products may be eligible for up to five years’ supplementary protection certificates, or SPCs, pursuant to Regulation (EC) No 469/2009. Such SPCs extend the rights under the basic patent for the drug.
Regulatory Requirements After a Marketing Authorization has been Obtained

If we obtain authorization for a medicinal product in the European Union, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products:

Pharmacovigilance and other requirements

We will, for example, have to comply with the E.U.’s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. Other requirements relate, for example, to the manufacturing of products and APIs in accordance with good manufacturing practice standards. E.U. regulators may conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Noncompliance with E.U. requirements regarding safety monitoring or pharmacovigilance, or requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the European Union. Similarly, failure to comply with the E.U.’s requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual E.U. member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

Manufacturing

The manufacturing of authorized drugs, for which a separate manufacturer’s license is mandatory, must be conducted in strict compliance with the EMA’s cGMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. The EMA enforces its cGMP requirements through mandatory registration of facilities and inspections of those facilities. The EMA may have a coordinating role for these inspections although the responsibility for carrying them out rests with the member states’ competent authority under whose responsibility the manufacturer falls. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and could subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Marketing and Promotion

The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs or the general public, are strictly regulated in the European Union under Directive 2001/83/EC. The applicable regulations aim to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the competent authority of the authorizing member state. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Patent Term Extension

In order to compensate the patentee for delays in obtaining a marketing authorization for a patented product, an SPC may be granted extending the exclusivity period for that specific product by up to five years. Applications for SPCs must be made to the relevant patent office in each E.U. member state and the granted certificates are valid only in the member state of grant. An application has to be made by the patent owner within six months of the first marketing authorization being granted in the European Union (assuming the patent in question has not expired, lapsed or been revoked) or within six months of the grant of the patent (if the marketing authorization is granted first). In the context of SPCs, the term “product” means the active ingredient or combination of active ingredients for a medicinal product and the term “patent” means a patent protecting such a product or a new manufacturing process or application for it. The duration of an SPC is calculated as the difference between the patent’s filing date and the date of the first marketing authorization, minus five years, subject to a maximum term of five years.

A six month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the European Union.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health
In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of our product candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. member states, and parallel distribution (arbitrage between low-priced and high-priced member states), can further reduce prices. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or 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, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; the federal transparency requirements under the Physician Payments Sunshine Act require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers.
Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Employees

As of March 1, 2017, we employed 13 full-time employees, of whom five hold Ph.D. or M.D. degrees, or the foreign equivalent. Of these employees seven were engaged in research and development and six were engaged in general and administrative functions. Of these employees, seven were located in Sweden and six were located in the United States. Our employees in Sweden are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

Our internet address is http://www.albireopharma.com. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investors section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.
An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10-K, including our consolidated financial statements and related notes thereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to continue to incur losses and may never generate profits from operations or maintain profitability.

Since inception, we have incurred significant operating losses. Without regard to the historical operating results of our predecessor, Biodel Inc., or Biodel, our net loss was approximately $16.3 million for the year ended December 31, 2016 and $6.8 million for the year ended December 31, 2015, and we had an accumulated deficit of $25.9 million as of December 31, 2016. To date, we have financed our operations primarily through issuances of preference shares or convertible loan notes, upfront fees paid upon entering into or amending license agreements, payments received upon the achievement of specified milestone events under the license agreements, grants and venture debt borrowings. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed the development of any drugs. We expect to continue to incur significant expenses and increasing operating losses for at least the next few years as we continue our development of, and seek marketing approvals for, our product candidates, prepare for and begin the commercialization of any approved products, and add infrastructure and personnel to support our product development efforts and operations as a public company in the United States. The net losses we incur may fluctuate significantly from quarter to quarter and year to year.

Our ability to generate profits from operations and thereafter to remain profitable depends heavily on:

- the scope, number, progress, duration, endpoints, cost, results and timing of clinical trials and nonclinical studies of our current or potential future product candidates, including in particular the scope, progress, duration, endpoints, cost, results and timing for initiation and completion of our planned Phase 3 clinical trial of A4250 in patients with progressive familial intrahepatic cholestasis, or PFIC;
- our ability to raise sufficient funds to support the development and potential commercialization of our product candidates;
- the outcomes and timing of regulatory reviews, approvals or other actions;
- our ability to obtain marketing approval for our product candidates;
- whether and to what extent milestone events are achieved under our license agreement with EA Pharma Co., Ltd. (formerly Ajinomoto Pharmaceuticals Co., Ltd.), or EA Pharma, or any potential future licensee or collaborator;
- our ability to establish and maintain additional licensing, collaboration or similar arrangements on favorable terms and whether and to what extent we retain development or commercialization responsibilities under any new licensing, collaboration or similar arrangement;
- the success of any other business, product or technology that we acquire or in which we invest;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio;
- our ability to manufacture any approved products on commercially reasonable terms;
- our ability to establish a sales and marketing organization or suitable third-party alternatives for any approved product; and
- the number and characteristics of product candidates and programs that we pursue.

Based on our current plans, we do not expect to generate significant revenue unless and until we or a current or potential future licensee or collaborator obtains marketing approval for, and commercializes, one or more of our product candidates, which we do not expect to occur until at least 2018. Neither we nor a licensee may ever succeed in obtaining marketing approval for, or commercializing, our product candidates and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations and remain profitable would decrease our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decline in our value could also cause you to lose all or part of your investment.
Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organization and staffing, developing and securing our technology, entering into licensing arrangements for elobixibat, raising capital and undertaking preclinical studies and clinical trials of our product candidates. We have not yet demonstrated our ability to successfully complete development of any product candidate, obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Assuming we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

We will need substantial additional funding and, in particular, may not have sufficient cash to fund a planned Phase 3 clinical trial of A4250 in patients with PFIC to completion. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our research and development expenses to increase substantially in future periods, particularly as we advance A4250 into planned clinical development for the treatment of patients with PFIC. We expect that our research and development expenses would increase even further if we conduct clinical trials of any or all of A4250 for the treatment of additional pediatric cholestatic liver diseases and disorders, elobixibat for the treatment of chronic idiopathic constipation, or CIC, or A3384 for the treatment of bile acid malabsorption, or BAM, advance our preclinical program in nonalcoholic steatohepatitis, or NASH, into later stages of development or initiate additional preclinical programs for potential future product candidates. In addition, if we obtain marketing approval for any of our product candidates that are not then subject to licensing, collaboration or similar arrangements with third parties, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we expect to incur additional costs associated with operating as a public company in the United States. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Based on current plans, we expect to initiate our planned Phase 3 clinical trial of A4250 in patients with PFIC in the second half of 2017. Whether our current cash resources, together with the projected receipt of a contingent milestone payment under our agreement with EA Pharma for elobixibat, will be sufficient to enable us to fund the trial to completion without additional financing is uncertain, and, in the absence of additional financing, we will not in any case have sufficient resources to complete the trial unless we receive the EA Pharma milestone payment. Our ability to fund the planned trial of A4250 for the treatment of patients with PFIC through its completion, and our future capital requirements generally, will depend on many factors, including:

- the costs, design, duration and any potential delays of the planned clinical trial of A4250 that may result from, among other things, the factors described below under “— The likelihood that our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis will be sufficient to enable a single Phase 3 trial to support, together with additional long-term safety data, an application for marketing approval of A4250 is uncertain. If the FDA or EMA determines that a longer or more expansive clinical program is required to support approval than we anticipate, it would materially harm our business.” and “If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates, or entry into licensing, collaboration or similar arrangements, could be delayed or prevented.”;
- whether we will be required to conduct additional activities beyond those currently contemplated to establish the characteristics of a positive response on the patient-reported and caregiver-reported outcome instruments to assess pruritus that we are developing for potential use in the planned PFIC trial, which could delay initiation of the planned PFIC trial;
- the same factors that our ability to generate profits from operations and thereafter to remain profitable depend heavily on, as described above under “— We have incurred significant losses since our inception. We expect to continue to incur losses and may never generate profits from operations or maintain profitability.”;
- the outcomes and timing of regulatory reviews, approvals or other actions;
- the costs of acquiring, licensing or investing in businesses, product candidates and technologies;
- the costs to maintain, expand and defend the scope of our intellectual property portfolio;
the costs to secure or establish sales, marketing and commercial manufacturing capabilities or arrangements with third parties;
our need and ability to hire additional management and scientific and medical personnel;
the costs to operate as a public company in the United States, including the need to implement additional financial and reporting systems and other internal systems and infrastructure for our business;
market acceptance of our product candidates, to the extent any are approved for commercial sale; and
the effect of competing technological and market developments.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that will not be commercially available for sale by us for at least the next few years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. In particular, if we do not have sufficient funds to complete the planned Phase 3 clinical trial of A4250 in patients with PFIC, we will be required to obtain additional financing in order to complete that trial. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms, or at all. The unavailability of additional financing on acceptable terms, or at all, would have an adverse effect on your investment.

Raising additional capital may cause dilution to our investors, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, licensing, collaboration or similar arrangements, grants and debt financings. We do not have any committed external source of funds. We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on January 10, 2017 and pursuant to which we registered for sale up to $100 million of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. We may seek to raise additional capital at any time. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions.

If we raise additional funds through licensing, collaboration or similar arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research and development programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Development and Commercialization of Our Product Candidates

We depend heavily on the success of our lead product candidate, A4250, which we are developing initially for the treatment of patients with PFIC and potentially also for other pediatric cholestatic liver diseases and disorders. We also depend on the success in Japan of our product candidate elobixibat, which our licensee EA Pharma is developing in Japan for the treatment of chronic constipation. If we are unable to commercialize A4250 or experience significant delays in doing so, or if EA Pharma is unable to commercialize elobixibat in Japan or experiences significant delays in doing so, our business will be materially harmed.

A4250 is in Phase 2 clinical development. Our licensee EA Pharma has completed a Phase 3 clinical trial of elobixibat and submitted a new drug application to the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, for elobixibat for the treatment of chronic constipation in Japan. We are currently evaluating whether we will seek to identify and enter into a license or other partnering transaction with a third party for elobixibat in the United States or Europe. Whether or not we elect to seek such a transaction, and whether or not we identify and successfully enter into a suitable licensing, collaboration or similar arrangement with a third party for a particular region, we do not currently anticipate that we will conduct future clinical trials of elobixibat independently. Our other clinical-stage product candidate, A3384, is in Phase 2 development. However, we do not anticipate conducting future clinical trials of A3384 unless and until we obtain additional capital, whether from our license agreement with EA Pharma for elobixibat, from potential future licensing, collaboration or similar arrangements or from any future offering of our debt or equity securities.
Our ability to generate product revenues, which may not occur until at least 2018 with respect to elobixibat in Japan and otherwise for at least the next few years, if at all, will depend heavily on the successful development and commercialization of A4250 as a treatment for patients with PFIC and the ability of EA Pharma to obtain marketing approval for, and successfully commercialize, elobixibat in Japan as a treatment for chronic constipation. Our ability to generate product revenues may also depend on the successful development and commercialization of A3384 to treat BAM or of elobixibat in the United States or Europe to treat CIC. The success of each of these product candidates will depend on a number of factors, including the following:

- our ability to obtain additional capital, whether from our license agreement with EA Pharma for elobixibat, from potential future licensing, collaboration or similar arrangements or from any future offering of our debt or equity securities;
- our ability to identify and enter into potential future licenses or other collaboration arrangements with third parties and the terms of the arrangements;
- successful completion of clinical development;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio;
- establishing sales, marketing and distribution capabilities;
- generating commercial sales of A4250, elobixibat or A3384, as applicable, if and when approved, whether alone or in collaboration with others;
- acceptance of A4250, elobixibat or A3384, as applicable, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies; and
- maintaining an acceptable safety profile of A4250, elobixibat or A3384, as applicable, following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize A4250, elobixibat or A3384, which would materially harm our business.

If clinical trials of A4250 or any of our other product candidates fail to demonstrate safety and efficacy to the satisfaction of the U.S. Food and Drug Administration, or the FDA, or the European Medicines Agency, or the EMA, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of the applicable product candidate.

In connection with obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials. In particular, the small number of subjects and patients in our early clinical trials may make the results of these clinical trials less predictive of the outcome of later clinical trials. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. There is no assurance that we will be able to design and execute a clinical trial to support marketing approval. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

If we are required to conduct additional or longer clinical trials or other testing of A4250 or any of our other product candidates beyond those that we currently contemplate, if we are unable to successfully complete our clinical trials or other testing, or if the results of these clinical trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as we intended or desired;
The clinical trial designs, endpoints and outcomes that will be required to obtain marketing approval of A4250 to treat PFIC patients are uncertain and, in any case, may vary among the FDA, EMA and other regulatory authorities outside of the United States and European Union. As a result, there is increased risk that we will not be able to gain concurrence with regulatory authorities regarding an acceptable coordinated development plan for A4250, that the outcome of any clinical trial of A4250 will not be favorable or that, even if favorable, regulatory authorities may not find the results of any clinical trial of A4250 to be sufficient to support marketing approval. We may never receive marketing approval for A4250 as a treatment for patients with PFIC or any other indication. Similar risks also apply for A3384, which we are developing as a treatment for BAM.

No product is currently approved for the treatment of either of PFIC or BAM in the United States, European Union or, to our knowledge, any other jurisdiction, and there is limited clinical experience in PFIC and in BAM. Accordingly, there is not a well-established development path that, with positive outcomes in clinical trials, would be reasonably assured of receiving marketing approval for these indications.

To support marketing approval of a drug, the FDA requires a demonstration of efficacy based on an endpoint reflecting clinical benefit. However, under Subpart H regulations, the FDA can grant accelerated approval based on a surrogate endpoint that is reasonably likely to predict clinical benefit. We are currently evaluating whether we will design our planned Phase 3 clinical trial of A4250 in patients with PFIC with an objective of seeking accelerated approval under Subpart H or with the objective of seeking full approval and we have not definitively determined the primary endpoint or endpoints for the planned trial. If we elect to use a surrogate endpoint and seek accelerated approval under Subpart H, the FDA or EMA may determine that the surrogate endpoint, or that the outcome shown in the planned trial on the surrogate endpoint, does not establish a reasonable likelihood of predicting clinical benefit or otherwise is not sufficient to support approval, even if the surrogate endpoint is met with statistical significance. If this occurs, our business would be materially harmed.

In addition, if we pursue an accelerated approval under Subpart H for A4250, we will be required to conduct a post-approval clinical outcomes trial to confirm its clinical benefit in PFIC. There can be no assurance that any post-approval trial that we conduct will confirm that the surrogate endpoint used for accelerated approval will eventually show an adequate correlation with clinical outcomes. If a clinical outcomes confirmatory trial that we conduct fails to show such adequate correlation, we may not be able to maintain any previously granted marketing approval for A4250 in PFIC that we may obtain. Likewise, it is possible that any marketing authorization we may receive in the future from the EMA for A4250 for the treatment of PFIC could be conditional on post-authorization studies and not be considered a full authorization. Our ability to obtain and maintain conditional marketing authorization in the European Union will be limited to specific circumstances and subject to several conditions and obligations, if obtained at all, including the completion of a clinical outcomes trial to confirm the clinical benefit of A4250 in PFIC. Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under European Union law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions.

If we elect to design our planned Phase 3 clinical trial of A4250 in patients with PFIC with the objective of seeking accelerated approval in the United States under Subpart H or conditional marketing authorization in Europe, it is possible that we will select the reduction of serum bile acids, a surrogate endpoint, as a co-primary endpoint for the trial. To support the clinical utility of reduction in serum bile acids in the treatment of patients with PFIC, we have sponsored an independent study pooling and analyzing long-term PFIC patient data from a number of leading PFIC academic centers, which we refer to as the PFIC Study Group. However, even if the analysis conducted by the PFIC Study Group provides favorable data that we believe supports the predictive clinical benefit of reducing serum bile acids in PFIC patients, the likelihood that the FDA or EMA will accept reduction of serum bile acids to support marketing approval of A4250 is uncertain and the likelihood of acceptance to support marketing approval of A4250 for the treatment of PFIC itself, rather than for the treatment of pruritus associated with PFIC, is even more uncertain.
It is also possible that we will select reduction of pruritus as a primary endpoint for our planned trial in PFIC patients. Because the assessment of pruritus relies on subjective patient or caregiver feedback, it is inherently difficult to evaluate and measure consistently. The measure of pruritus can be influenced by factors outside of our control and can vary widely from measurement point to measurement point for a particular patient, from patient to patient and from site to site within a clinical trial. Moreover, patients given an inactive comparator, or placebo, in a clinical trial may perceive a change in pruritus that is greater than we anticipated when designing the trial or that is comparable to the change experienced by patients given A4250, which could obscure the effect of A4250 in the planned trial and reduce the likelihood that the trial will be successful.

In addition, it is our objective that the data from our planned Phase 3 clinical trial of A4250 in patients with PFIC be sufficient to support, together with safety data from an extension study to evaluate long-term outcomes, an application for marketing approval for A4250. The FDA and EMA generally require two pivotal clinical trials to support marketing approval of a drug. If the FDA or EMA requires us to conduct additional clinical trials beyond the ones that we currently contemplate in order to support marketing approval of A4250 to treat patients with PFIC in the United States or European Union, or if the FDA requires one or more different clinical trial designs or endpoints to support marketing approval in the United States than the EMA requires to support marketing approval in the European Union, it would result in a more expensive and potentially longer development program for A4250 than we currently contemplate, which could delay our ability to generate product revenues with A4250, interfere with our ability to enter into any potential licensing or collaboration arrangements with respect to this program, cause our value to decline, and limit our ability to obtain additional financing that may be necessary to complete the planned pivotal program. Even if the FDA and EMA support our objective to conduct a single Phase 3 trial of A4250 as the basis, together with safety data from an extension study to evaluate long-term outcomes, an application for marketing approval for A4250 in PFIC, either regulatory authority may require that we meet the primary endpoint or endpoints in the trial at a higher level of statistical significance than would otherwise be required for a trial to be successful, which would reduce the likelihood of a positive trial.

Likewise, if we conduct any future clinical trial designed to support marketing approval of A3384 as a treatment for BAM, the FDA, EMA or any regulatory authority outside of the United States or the European Union may determine that the designs or endpoints of the trial, or that the outcomes shown on any particular endpoints in the trial, are not sufficient to establish a clinically meaningful benefit for A3384 in the treatment of BAM or otherwise to support marketing approval, even if the primary endpoint or endpoints of the trial is met with statistical significance.

There is limited clinical experience in PFIC. Our planned Phase 3 clinical trial of A4250 in patients with PFIC is likely to utilize novel endpoints and measurement methodologies with which the FDA, EMA and other regulatory authorities have little experience. A regulatory authority may ultimately determine that an outcome instrument that we use in the planned trial is not adequately reliable or valid for use with PFIC patients, which would delay and potentially prevent our receipt of marketing approval for A4250.

We are developing A4250 initially as a treatment for patients with PFIC, and there is limited clinical experience in PFIC. We may also conduct future development of A4250 for other pediatric cholestatic liver diseases and disorders for which there is likewise limited clinical experience. Our planned PFIC trial, as well as potential future clinical trials of A4250 in patients with PFIC or other pediatric cholestatic liver diseases, are likely to use novel endpoints and measurement methodologies with which the FDA, EMA and other regulatory authorities have limited or no experience. The degree of novelty or other limitations of these endpoints and methodologies may impact the likelihood that our planned PFIC clinical trial, or any other future clinical trial of A4250, will be successful or otherwise delay or prevent marketing approval of A4250. For example, it is possible that we will select reduction of pruritus as a primary endpoint for our planned Phase 3 clinical trial of A4250 in patients with PFIC. Change in pruritus is assessed using patient-reported or, in the case of young children, caregiver-reported outcome instrument. We are currently working with a contract research organization to develop patient-reported and caregiver-reported outcome instruments to assess pruritus in the planned PFIC trial. We plan to establish the reliability and validity of the outcome instruments that we develop to meet applicable regulatory standards within, but not before, the planned trial. The FDA or EMA may ultimately determine that the outcome instrument that we use to assess pruritus is not adequately reliable or valid for use with PFIC patients, whether because it was not applied by clinical investigators sufficiently consistently, was not sufficiently sensitive to detect varying degrees of pruritus, or for any other reason. If this were to occur, our ability to obtain marketing approval for A4250 would be delayed and we may never receive marketing approval for A4250.

Favorable results seen to date in clinical trials of A4250 may not be predictive of favorable results in our planned Phase 3 clinical trial of A4250 in patients with PFIC, which is expected to involve different doses, dosing regimen and duration, number of patients and outcome measures and may have other differences in design or execution.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials, even after promising results in earlier trials or in preclinical studies. Similarly, companies have experienced disappointing outcomes in later phases of a multiphase clinical trial, even after promising results in an early phase of the trial. A4250
has been evaluated in an investigator-initiated Phase 2 clinical trial for the treatment of PBC and in an ongoing, open label Phase 2 trial in children with chronic cholestasis. Based on data from the PBC trial that we received from the investigator, nine patients received A4250 and all of them reported a substantial reduction in pruritus. In addition, preliminary data from our ongoing Phase 2 trial in children with chronic cholestasis show a reduction in serum bile acids in a substantial majority of patients and improvement in pruritus that was significantly correlated with the reduction in serum bile acids.

Our planned Phase 3 trial of A4250 in patients with PFIC is expected to involve a greater number of patients, different outcome measures, doses, dosing regimen and duration and may have other differences in trial design, in addition to the difference in patient population, compared with either the PBC trial or the pediatric chronic cholestasis trial. If the favorable findings on pruritus and serum bile acids seen in these two Phase 2 trials are not replicated in the final data from our ongoing chronic cholestasis trial, in our planned trial of A4250 in patients with PFIC or in any other future trial of A4250 in patients PFIC or other pediatric cholestatic liver disease or disorder, we may not obtain marketing approval for A4250 to treat any indication, in which case our business would be materially and adversely affected.

We are currently designing our planned Phase 3 trial of A4250 in patients with PFIC, including evaluating various potential endpoints to designate as the primary endpoint, whether alone or together with another primary endpoint. It is possible that change in pruritus will be the primary endpoint in the planned trial. It is customary to use a patient-reported or caregiver-reported outcome instrument to qualify and assess pruritus in clinical trials, but the specific measures can vary from trial to trial. For example, the pruritus scales that were used in the PBC trial are not the same as the scales used in our trial in children with chronic cholestasis, except that the visual analogue scale of itching, known as VAS-itch, is common to both trials. If we decide to use change in pruritus as a primary endpoint in our planned trial of A4250 in patients with PFIC, we plan to use patient-reported and caregiver-reported outcome instruments that we are currently developing that employ or rely on different questions or assessments, require a different outcome to establish a positive response or are otherwise different from the outcome instruments used in our ongoing trial in children with chronic cholestasis. The differences in these instruments may reduce the likelihood that the preliminary data from our ongoing trial of A4250 in children with chronic cholestasis or the results of the concluded PBC trial of A4250 will be predictive of favorable results in the planned PFIC trial.

In addition, we are currently considering doses of A4250 for our planned Phase 3 trial that for some PFIC patients may not be precisely the same as the weight-based doses that we are evaluating in our ongoing Phase 2 trial of A4250 in children with chronic cholestasis. Although we expect that patients in the planned trial of approximately the same weight will receive the same total dose of A4250, any difference in relative weights between particular patients will result in a difference in weight-based doses between those patients. This may reduce the likelihood that weight-based data from the Phase 2 trial will be predictive of favorable results in our planned PFIC trial.

The likelihood that our ongoing Phase 2 clinical trial of A4250 in children with chronic cholestasis will be sufficient to enable a single Phase 3 trial to support, together with additional long-term safety data, an application for marketing approval of A4250 is uncertain. If the FDA or EMA determines that a longer or more expensive clinical program is required to support approval than we anticipate, it would materially harm our business.

We plan to seek concurrence from the FDA and EMA that a single Phase 3 clinical trial in patients with PFIC will be sufficient to establish the efficacy of A4250 to support, together with additional long-term safety data, an application for regulatory approval as a treatment for patients with PFIC in the United States and European Union. The likelihood that the FDA and EMA will concur with our plan is uncertain. The FDA or EMA may instead determine that multiple Phase 3 clinical trials are required to establish the efficacy of A4250 in patients with PFIC or that a single trial must have a longer treatment duration than we currently anticipate to be potentially sufficient. If the FDA or EMA takes this position, it would result in a longer or more expensive and potentially longer development program for A4250 than we currently contemplate, which could delay our ability to generate product revenues with A4250, interfere with our ability to enter into any potential licensing or collaboration arrangements with respect to this program, cause our value to decline, and limit our ability to obtain additional financing that may be necessary to complete the planned pivotal program.

In addition, we are enrolling in our ongoing study children with chronic cholestasis caused by any of a number of different liver conditions, including PFIC, biliary atresia, Alagille syndrome, or ALGS, and sclerosing cholangitis. As a result of these enrollment criteria, the number of different PFIC patients participating in the trial is 10. If the FDA, EMA or any regulatory authority outside of the United States or European Union determines that 10 PFIC patients is insufficient, or that the number of patients with PFIC in any particular age range is insufficient, it is more likely that the applicable regulatory authority will require that we conduct more than our planned single Phase 3 trial in patients with PFIC to establish the efficacy of A4250 to support marketing approval.
If we experience delays or difficulties in the enrollment of patients in our planned Phase 3 clinical trial of A4250 in patients with PFIC, our receipt of marketing approval for A4250 could be delayed or prevented.

Recruiting patients for orphan pediatric liver diseases is challenging. We have previously experienced enrollment delays in our clinical trials of A4250 and are aware of at least one third-party clinical trial in PFIC patients that may be ongoing at the time of our planned Phase 3 trial of A4250 in patients with PFIC. If we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials of our product candidates, we may not be able to initiate or continue the clinical trials. In particular, if we experience enrollment delays in our planned Phase 3 trial of A4250 in patients with PFIC, our cash resources may not be sufficient to enable us to fund the trial to completion, which could cause our value to decline and limit our ability to obtain additional financing.

Potential clinical trial participants may not be adequately diagnosed or identified with the diseases that we are targeting and may not meet the inclusion criteria for our trials. PFIC and other pediatric cholestatic liver diseases or disorders for which we may develop A4250 is a rare disease or disorder with a limited patient population, which could result in slow enrollment of clinical trial participants. Further, there are only a limited number of specialist physicians that treat these diseases and disorders, and major clinical centers that treat these diseases and disorders are concentrated in a few geographic regions.

Patient enrollment is affected by many factors, including:

- size of the target patient population;
- severity of the disease or disorder under investigation;
- eligibility criteria for the clinical trial in question;
- other clinical trials being conducted at the same time involving patients who have the disease or disorder under investigation;
- perceived risks and benefits of the product candidate under study;
- approval and availability of other therapies to treat the disease or disorder that is being investigated in the clinical trial;
- willingness or unwillingness to participate in a placebo controlled clinical trial;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients in our ongoing or planned clinical trials of A4250, or any of our other product candidates, would result in significant delays or may require us to abandon one or more clinical trials altogether.

If the commercial opportunity in PFIC is smaller than we anticipate, or if A4250 receives approval to treat only a specific subpopulation of patients with PFIC or only a specific symptom of PFIC, our future revenue from A4250 will be adversely affected and our business will suffer.

If the size of the commercial opportunities in any of our target indications is smaller than we anticipate, we may not be able to achieve profitability and growth. We are developing A4250 initially as a treatment for patients with PFIC and potentially also as a treatment for patients with other pediatric cholestatic liver diseases and disorders. PFIC and these other diseases and disorders are each rare, with a limited patient population. Moreover, we expect that the addressable PFIC patient population for A4250 is only a subset of the overall patient population, specifically patients who have not yet received partial external bile diversion, or PEBD, surgery or liver transplant surgery or patients who have had PEBD reversal surgery. In addition, there are different subtypes of PFIC and the beneficial effects of A4250 may vary among patients with different subtypes or among children of different ages. We expect that the inclusion criteria for our planned Phase 3 clinical trial will include some, but not all, PFIC subtypes. A4250 may ultimately receive regulatory approval, if at all, as a treatment for some but not all of the subtypes, or for children of some ages but not others. Moreover, it is possible that we will select reduction of pruritus as the sole primary endpoint for our planned PFIC trial. In that event, regulatory authorities may deem the trial to support approval for the treatment of pruritus associated with PFIC but not for the treatment of PFIC itself. If A4250 ultimately receives marketing approval for only certain PFIC subtypes, or for only PFIC patients of certain ages, or for only pruritus associated with PFIC, the commercial opportunity for A4250 may be smaller than we anticipate and our business may be harmed.
It is critical to our ability to grow and become profitable that we successfully identify patients with these rare cholestatic liver diseases and disorders. Our projections of the number of people who have PFIC or our other target cholestatic liver diseases and disorders, as well as the subset who have the potential to benefit from treatment with A4250, are based on a variety of sources, including third-party estimates and analyses in the scientific literature, and may prove to be incorrect. Further, new information may emerge that changes our estimate of the prevalence of these diseases or the number of patient candidates for A4250. The effort to identify patients with PFIC or our other potential target indications is at an early stage, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the addressable patient population for A4250 may be limited or may not be amenable to treatment with A4250, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for A4250, we may never achieve profitability because the potential target patient population for A4250 is small.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates, or entry into licensing, collaboration or similar arrangements, could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may be unable to recruit and enroll a sufficient number of patients in our clinical trials to ensure adequate statistical power to detect any statistically significant treatment effects;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks or undesirable side effects;
- regulators, institutional review boards or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the clinical trials.

For example, in March 2015, Ferring International Center S.A., or Ferring, stopped early two Phase 3 clinical trials of elobixibat that Ferring had been conducting pursuant to a now-terminated license agreement with us due to an issue related to the distribution of study drug to study sites that was unrelated to the performance of elobixibat. We were unable as a result of the stopping of the trials to obtain data for the total number of patients for which the trials were designed, and the abbreviated trials are not sufficient to support an application for marketing approval.

Our product development costs will increase if we experience delays in testing or marketing approvals. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or 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 and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations.
The benefit of IBAT inhibition in the treatment for patients with PFIC or any of our other target indications is unproven, and we do not know whether we will be able to develop any products of commercial value for these indications.

A4250 is an ileal bile acid transporter, or IBAT, inhibitor. There is no marketed drug that relies on IBAT inhibition for the treatment of PFIC or any other indication for which we plan to develop A4250. Shire plc, or Shire, reported in 2015 and 2016 that its product candidate for the treatment of PFIC and other rare liver diseases, SHP625, which has been reported to be an IBAT inhibitor, failed to meet the respective primary endpoints of Phase 2 clinical trials in multiple adult and pediatric indications. We cannot assure you that we will be able to replicate or improve upon our findings from preclinical studies and early clinical trials in later-stage clinical trials of A4250 for the treatment of patients with PFIC or any of our other target indications or that our focus on IBAT inhibition as a medically useful mechanism of action will result in the development of a commercially viable drug that safely and effectively treats PFIC or any of our other target indications.

If the FDA concludes that more clinical or nonclinical data than we currently anticipate is required to support the approval of A3384 for the treatment of BAM under Section 505(b)(2) of the Federal Food Drug and Cosmetics Act, or Section 505(b)(2), or if the requirements for A3384 under Section 505(b)(2) are not as we expect, the approval pathway for A3384 will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We expect that we may seek FDA approval for A3384 for the treatment of BAM through the Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act. Section 505(b)(2) permits the filing of a new drug application, or NDA, where at least some of the information required for approval comes from studies that were not conducted by or for the applicant, and for which the applicant has not received a right of reference, which could expedite the development program for A3384 by potentially decreasing the amount of clinical and preclinical data that we would need to generate in order to obtain FDA approval. However, the 505(b) (2) regulatory pathway does not preclude the possibility that additional clinical trials or nonclinical studies may be required; for example, for new indications where the applicant cannot rely on published literature or the FDA’s finding of safety and effectiveness. If the FDA requires more data to support the approval of A3384 to treat BAM than we currently anticipate, the time and financial resources required to obtain FDA approval for A3384, and complications and risks associated with A3384, would likely substantially increase. Moreover, if we are unable to pursue the Section 505(b)(2) regulatory pathway for any reason, new competitive products could reach the market more quickly than A3384, which would likely harm our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that A3384 will receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain competitors and others have objected to the FDA’s interpretation of Section 505(b)(2). If the FDA’s interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b) (2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our 505(b)(2) NDA for up to 30 months depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to faster product development or earlier approval. Moreover, even if A3384 is approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which A3384 may be marketed or to other conditions of approval, or may contain requirements for costly post marketing testing and surveillance to monitor the safety or efficacy of the products.

BAM is not easily diagnosed and the number of patients suffering from BAM has not been established with precision. If the actual number of patients is smaller than we estimate, we may not be able to recruit patients into our clinical trial in this indication in a timely manner or at all, and we may not be able to obtain regulatory approval for A3384 to treat this condition.

BAM is not easily diagnosed. There is no patient registry or other method of establishing with precision the actual number of patients with BAM in any geography. The best diagnostic method currently, the 75Se-Homocholic Acid Taurine test, is not available in many countries and evaluation of bile acid synthesis markers, such as FGF19, and the bile acid intermediate C4 is not a routine diagnostic test. We estimate the prevalence of BAM to be approximately 1.3 million people in the United States and approximately 2.2 million people in the European Union. We derive our estimated prevalence from a reported estimate of the prevalence of irritable bowel syndrome with diarrhea, or IBS-D, and published third-party studies that suggest approximately one-third of IBS-D patients
have BAM. If the estimates on which we have relied are not accurate or if the results of studies on which we have relied are outdated, our estimate of the number of patients with BAM may be inaccurate, we may not be able to recruit patients into any future clinical trial of A3384 in BAM in a timely manner, or at all, and the commercial opportunity for A3384 may be smaller than we anticipate.

**If serious or unacceptable side effects are identified during the development of A4250, elobixibat or A3384 or any other product candidate, we may need to abandon or limit our development of that product candidate.**

All of our product candidates are in clinical or preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have other unexpected, unacceptable characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many investigational products that initially showed promise in clinical or earlier stage testing have later been found to cause side effects or other safety issues that prevented further development.

For example, the investigator for the investigator-initiated Phase 2 clinical trial of A4250 in PBC determined to conclude the trial prior to its intended completion, citing gastrointestinal (GI) side effects. If the GI side effects cited by the investigator in the PBC trial are predictive of an inadequate tolerability profile of A4250, the overall commercial opportunity for A4250 may be lower than we expect. Even if we receive regulatory approval for A4250, if the approved dose of A4250 is not well tolerated, A4250 may not achieve market acceptance by physicians, patients, third-party payors or others in the medical community, which would materially and adversely affect our business.

**Even if A4250, elobixibat or A3384 or any potential future product candidate of ours receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.**

If A4250, elobixibat, A3384 or any potential future product candidate of ours receives marketing approval, the approved product may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If an approved product does not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments or competitive products;
- the prevalence and severity of any side effects;
- whether physicians will be willing to prescribe A4250 to patients with PFIC if the primary endpoint in our clinical trial or trials of A4250 in patients with PFIC is the reduction of pruritus or a surrogate measure, as opposed to a direct measure of reducing or eliminating progressive liver disease;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the adequacy of supply of our product candidates;
- the availability of third-party coverage and adequate reimbursement;
- the timing of any such marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on concomitant use of other medications.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement for our product candidates may be affected by political, economic and regulatory developments in the United States, the European Union and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of A4250, elobixibat or A3384 or any potential future product candidate of ours that receives marketing approval.
If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell A4250 or any of our other current or potential future product candidates, we may not be successful in commercializing the applicable product candidate if it receives marketing approval.

We do not have a sales or marketing infrastructure and have no experience as a company in the sale or marketing of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If we receive marketing approval in the United States or Europe for A4250 to treat PFIC or any other pediatric cholestatic liver disease or disorder, we plan to build the capabilities to commercialize A4250 in the approved indication(s) in the applicable region with our own focused, specialized sales force. Outside of the United States and Europe, we plan to selectively utilize collaboration, distribution or other marketing arrangements with third parties to commercialize A4250. Also, we intend to selectively seek licensing, collaboration or similar arrangements to assist us in furthering the development or commercialization of product candidates, such as A3384, targeting large primary care markets that must be served by large sales and marketing organizations. There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establishes marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

• our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
• the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
• the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
• unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues or the profitability of these product revenues are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products to treat our target indications or markets before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Competitors may also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approvals from regulatory authorities and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies that may be complementary to or necessary for our programs.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are approved for broader indications or patient populations, or are more convenient or less expensive than any products that we develop and commercialize. Our competitors may also obtain marketing approval for their products more rapidly than we may obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market.
In particular, we are aware of other companies that are developing product candidates that, like our product candidates A4250 and elobixibat, act via IBAT inhibition. Shire’s SHP625, also known as maralixibat and formerly known as LUM001, is currently being studied in a Phase 2 clinical trial in PFIC, and we believe that Shire plans to conduct Phase 2/3 clinical development of SHP625 as a treatment for PFIC. We also believe that SHP625 is additionally in Phase 2 development as a treatment for ALGS. In June 2016, Shire announced that the FDA has granted breakthrough therapy designation for SHP625 for PFIC, type 2. We also believe that GlaxoSmithKline’s GSK2330672 is in Phase 2 clinical development as a treatment for patients with PBC and that Shire’s SHP626 is in Phase 2 development as a treatment for biliary atresia.

If approved, our product candidates will compete for a share of the existing market with numerous other products. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include the following.

• For PFIC and many other cholestatic liver diseases, there are no approved drug treatments. First-line treatment for PFIC is typically off-label ursodeoxycholic acid, or UDCA, which is approved in the United States and elsewhere for the treatment of PBC. PFIC patients often require surgical intervention such as PEBD surgery or liver transplant. As noted above, we believe Shire plans to conduct Phase 2/3 clinical development of SHP625 in PFIC. In addition, we believe that Intercept Pharmaceuticals’ obeticholic acid, which is approved in the United States in combination with UDCA, or as a monotherapy for patients unable to tolerate UDCA, to treat PFIC, is in Phase 2 development as a treatment for biliary atresia.

• For the pruritus that is characteristic of many cholestatic liver diseases, symptomatic off-label treatment with: UDCA; bile acid sequestrants, such as generic cholestyramine (as Questran in the United States and as Colestyr, Efensol, Ipocol, Kolestran, Lipocol, Olestryr, Prevalite or Quantalan in various other countries), marketed by Upsher-Smith Laboratories, Inc., Par Pharmaceutical Companies, Inc. and Sandoz, the generic pharmaceuticals division of Novartis AG; rifampin, an antibiotic derivative; or naltrexone, an opioid antagonist.

• For CIC: linaclotide, a guanylate cyclase-C agonist marketed by Ironwood Pharmaceuticals, Inc. and Allergan plc in the United States as Linzess and in Europe (for a related condition, irritable bowel syndrome with constipation, or IBS-C) as Constella and for which a marketing application filed by Astellas Pharma Inc. has been approved in Japan for IBS-C; lubiprostone, a type-2 chloride channel marketed as Amitiza by Takeda Pharmaceutical Company Limited in the United States and select countries in Europe and by Mylan N.V. in Japan; prucalopride, a motility agent marketed by Shire in the European Union as Resolor; and numerous OTC products, including psyllium husk (such as Metamucil), methylcellulose (such as Citrucel), calcium polycarbophil (such as FiberCon), lactulose (such as Cephulac), polyethylene glycol (such as MiraLax), sennosides (such as Exlax), bisacodyl (such as Ducolax), docusate sodium (such as Colace), magnesium hydroxide (such as Milk of Magnesia), saline enemas (such as Fleet) and sorbitol.

• In addition, Synergy Pharmaceuticals, Inc. has a product candidate known as plecanatide, a guanylate cyclase-C agonist to be marketed as Trulance, which is approved in the United States to treat CIC and for which it has completed two Phase 3 clinical trials in IBS-C. Ardelyx, Inc. has a product candidate, tenapanor, a sodium transporter NHE3 inhibitor that is in Phase 3 clinical development to treat IBS-C.

• For BAM, there is no approved drug treatment. Off-label treatments include: bile acid sequestrants, such as immediate release cholestyramine (which is approved in some countries in Europe to treat diarrhea associated with certain GI conditions), colestipol and colesevelam, a cholesterol-lowering medicine marketed by Daiichi Sankyo Inc. as Welchol in the United States and by Genzyme Europe B.V. as Cholestagel in the European Union. In addition, obeticholic acid has previously been studied by Intercept in a Phase 2 clinical trial as a treatment for BAM.

Patients with BAM following ileal resection surgery may be treated with a low-fat diet supplemented with medium-chain triglycerides or choleylsarcosine, a synthetic cholic acid conjugate. Patients with BAM secondary to Crohn’s ileitis may be treated with glucocorticoid, a steroid hormone. Microscopic colitis patients may be given budesonide, a glucocorticoid steroid. Patients with BAM secondary to small intestinal bacterial overgrowth may require antibiotic therapy.

Even if we are able to commercialize A4250, elobixibat, A3384 or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and, in some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted.
As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize A4250, elobixibat, A3384 or any other product candidate successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. and E.U. healthcare industries and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for A4250, elobixibat, A3384 or any other product that we commercialize and, if coverage and reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for A4250 may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug, and any launch of a competitive product is likely to create downward pressure on the price initially charged. If reimbursement is not available or is available only to a limited degree, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacturing, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

**Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.**

In some countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.
We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to clinical trial participants or patients;
- loss of revenue;
- increased insurance costs; and
- the inability to commercialize any products that we may develop.

We have separate liability insurance policies that cover each of our clinical trials. These policies provide coverage in varying amounts, up to a maximum of €5.0 million in the aggregate for the applicable clinical trial. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin conducting more expansive clinical development of, or commercializing, A4250, elobixibat, A3384 or any potential future product candidate of ours. 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.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates. Currently, we are focusing our resources predominantly on A4250. As a result, we may forego or delay pursuit of opportunities with elobixibat, A3384 or potential future product candidates that later could prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates may not yield any commercially viable products.

We have historically based our research and development efforts on IBAT inhibitors, including A4250 and elobixibat, to treat cholestatic liver diseases and CIC and on our proprietary formulations of an established bile acid sequestrant, A3384, to treat BAM. Notwithstanding our investment to date and anticipated future investment, we have not yet developed, and may never successfully develop, any marketed drugs using these approaches. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through licensing, collaboration or other royalty or similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to Our Dependence on Third Parties

We rely on EA Pharma for the successful development and commercialization of elobixibat to treat chronic constipation in Japan and other select markets in Asia.

We entered into a license agreement with EA Pharma (formerly known as Ajinomoto Pharmaceuticals) for elobixibat in April 2012. We cannot predict the ultimate success of the arrangement. The agreement provides for milestone payments to us if specified regulatory and commercial milestone events are achieved and provides us with royalty-based revenue if elobixibat is successfully...
commercialized. EA Pharma has submitted a new drug application to the Japanese PMDA for elobixibat for the treatment of chronic constipation in Japan. If elobixibat receives marketing approval in Japan, EA Pharma plans to co-market elobixibat in Japan with another company, Mochida Pharmaceutical Co., Ltd, or Mochida.

EA Pharma is responsible for all future development and potential commercialization of elobixibat in its licensed field (namely, all prophylactic or therapeutic uses of a pharmaceutical product for gastrointestinal diseases and disorders, symptoms of constipation of all causes or postoperative ileus, in colonoscopy cleansing procedures and, in specified circumstances, select liver diseases) in Japan, Indonesia, Korea, Taiwan, Thailand and Vietnam, and has substantial control over the conduct and timing of development efforts with respect to elobixibat in these countries. We have little control over the amount and timing of resources that EA Pharma devotes, or Mochida devotes, to the development of elobixibat. If EA Pharma or Mochida fails to devote sufficient financial and other resources, the development and potential commercialization of elobixibat in Japan and otherwise in EA Pharma’s licensed territory would be adversely affected. This would result in a delay in milestone payments to us and, if marketing approval for elobixibat in EA Pharma’s licensed territory is obtained, royalties that we could receive on any future elobixibat product sales.

EA Pharma has the right to terminate the elobixibat agreement on a country-by-country basis or in its entirety for an uncured material breach by us or in specified bankruptcy or similar events. EA Pharma also has the right, with 180 days’ notice, to terminate the agreement in its entirety or on a country-by-country basis (except for Japan) for any reason.

If EA Pharma terminates the elobixibat agreement at any time, for any reason, it would negatively impact our development of elobixibat in Japan and otherwise in EA Pharma’s licensed territory, would materially harm our business and could accelerate our need for additional capital. In particular, we would not receive future milestone or royalty payments from EA Pharma and would have to fund any further clinical development and commercialization of elobixibat in Japan on our own, seek another licensee or collaborator for clinical development and commercialization or abandon the development and commercialization of elobixibat in Japan.

If we do not pursue the development and potential commercialization of elobixibat for the treatment of CIC in the United States or Europe, whether through a licensing, collaboration or similar arrangement or otherwise, the revenue that we will generate based on elobixibat may be lower.

In addition to our agreement with EA Pharma for elobixibat in Japan and other select markets in Asia, we are currently evaluating whether we will seek a license or other partnering transaction with a third party for elobixibat in the United States or Europe. The cost and duration of the additional clinical trial or trials that would be required by the FDA and EMA to support marketing approval of elobixibat to treat CIC is currently uncertain. Even if we were to seek to establish licensing, collaboration or similar arrangement with a third party for the United States or Europe, the uncertain regulatory requirements may interfere with our ability to do so on acceptable terms, or at all. We do not currently anticipate that we will conduct future clinical trials of elobixibat for the United States or Europe independently, whether or not we elect to seek a suitable third-party arrangement. If we do not enter into suitable third-party arrangements and do not ourselves conduct clinical trials of elobixibat for the United States or Europe, the revenue that we will generate based on elobixibat will be limited to payments that we receive under our agreement with EA Pharma, which will reduce the overall commercial potential of elobixibat and may harm our business.

We rely on third parties to conduct our clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such clinical trials.

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions, clinical investigators and government agencies, to perform this function. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. Moreover, the FDA and foreign regulatory authorities require us to comply with standards, commonly referred to as Good Clinical Practice, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity of data and confidentiality of clinical trial participants are protected. We are also required to register clinical trials subject to FDA regulation and, with some exceptions, post the results of completed clinical trials on a government-sponsored database, www.ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. The National Institutes of Health also has announced plans to require sponsors to post results of clinical trials for unapproved products, including unfavorable results in clinical trials for unapproved uses of approved products.
Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of our product candidates. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients, or API, in our product candidates. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We do not currently have any agreements with third-party manufacturers for the long-term clinical or commercial supply of any of our product candidates. We currently engage a single third-party manufacturer to provide API for A4250 and elobixibat. We also currently engage single third-party manufacturers to provide fill and finish services for the final drug product formulation of A4250 used in our ongoing Phase 2 clinical trial and, in the case of elobixibat, clinical trials conducted by our licensee. We may in the future be unable to conclude agreements for commercial supply with third-party manufacturers on acceptable terms, or at all.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may encounter difficulties in achieving volume production, laboratory testing, quality control or quality assurance or suffer shortages of qualified personnel, any of which could result in our inability to manufacture sufficient quantities to meet clinical timelines for a particular product candidate, to obtain marketing approval for the product candidate or to commercialize the product candidate. In addition, third-party manufacturers may not be able to comply with current good manufacturing practice, or GMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

If the third parties that we engage to manufacture product for our preclinical tests and clinical trials cease to continue to do so for any reason, we likely would experience delays in advancing these clinical trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.
Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

We may depend on additional collaborations, licenses or similar arrangements with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have licensed rights to develop and commercialize elobixibat for CIC and other gastrointestinal diseases and disorders to EA Pharma in Japan and other select markets in Asia. We may in the future enter into other licensing, collaboration or similar arrangements for the development and commercialization of A4250, elobixibat, A3384 or any potential future product candidate of ours for any or all indications and for any or all territories, except for the rights currently subject to EA Pharma’s license with respect to elobixibat.

Our likely counterparties for any licensing, collaboration or similar arrangement include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Except for our agreement with EA Pharma, we are not currently party to any such arrangement for A4250, elobixibat or A3384. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of the applicable product candidate. Our ability to generate revenues from these arrangements will depend on our collaborators’ abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Any licensing, collaboration or similar arrangement involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators’ strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, 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;
- collaborators may independently develop, or develop with third parties, products that compete directly or indirectly with our products or 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;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- 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;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between us and a collaborator as to the ownership of intellectual property arising during the collaboration;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others or make us a less attractive collaboration partner by narrowing the scope of potential collaborations into which we may enter;
• disputes may arise between us and a collaborator that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and

• collaborations may be terminated and, if terminated, may result in a need to identify and enter into a new licensing, collaboration or similar arrangement or obtain additional capital to pursue further development or commercialization of the applicable product candidates.

For example, in March 2015, Ferring terminated a 2012 license agreement with us for the development and commercialization of elobixibat worldwide, excluding the territory licensed to EA Pharma. Ferring’s termination of the license agreement followed its stopping early two Phase 3 clinical trials of elobixibat that Ferring had been conducting due to an issue related to the distribution of study drug to study sites that was unrelated to the performance of elobixibat. As a result, to exploit the potential of elobixibat in the United States, Europe and otherwise outside of EA Pharma’s licensed territory, we would need to either identify and enter into additional licensing, collaboration or similar arrangements or expend our own resources to conduct further development of elobixibat. We are currently evaluating whether we will seek to identify and enter into a license or other partnering transaction with a third party for elobixibat in the United States or Europe. Whether or not we elect to seek such a transaction, we do not currently anticipate that we will conduct future clinical trials of elobixibat independently.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

*If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.*

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration 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 a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. For example, any Phase 3 program of elobixibat in the United States or Europe will depend on whether we elect to seek, and successfully enter into, a licensing, collaboration or similar arrangement under which that Phase 3 program would be conducted. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.
The terms of our loan facility agreement and the associated security agreements may restrict our ability to engage in certain transactions and adversely affect our operating flexibility.

In December 2014, we entered into a loan facility agreement with Kreos Capital IV (UK) Limited, or Kreos, which was revised in February 2016 and further amended and restated pursuant to a supplemental deed entered into in May 2016. We have also entered into certain guaranties and security agreements with Kreos. Pursuant to the terms of the loan facility agreement and the associated security agreements, subject to certain exceptions, we cannot engage in specified transactions unless certain conditions are met or we receive the prior approval of Kreos. These transactions include:

- disposing of our business or certain assets;
- entering into licensing arrangements regarding our intellectual property, other than on an arm’s length basis in the ordinary course of business where the proceeds of an arrangement are used for our business;
- certain changes to our business or ownership;
- incurring additional debt or liens or making payments on other debt;
- making certain investments and declaring dividends;
- being acquired by or merging with another entity;
- engaging in some transactions with affiliates; or
- encumbering intellectual property.

If Kreos does not provide its consent to such actions, we could be prohibited from engaging in transactions that could be beneficial to our business and our stockholders unless we repay the loan, which may not be desirable or possible. The obligations under the loan facility agreement are secured by substantially all of our assets. If we default under the loan facility agreement or the associated security agreements, including for an inability to repay amounts as they become due, and we are unable to obtain a waiver for such a default, Kreos would have a right to accelerate our obligation to repay the entire loan, obtain control of our cash accounts and foreclose on the secured assets in order to satisfy our obligations under the loan facility agreement. Any such action on the part of Kreos against us could have a materially adverse impact on our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products 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 technology and products. We seek to protect our proprietary position by filing patent applications in the United States, in Europe and in certain additional jurisdictions related to our novel technologies and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. 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. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering the licensed technology or product candidates. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted or enforced in a manner consistent with the best interests of our business.

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 products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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, narrow the scope of our patent protection or make enforcement more difficult or uncertain.
The laws of other countries may not protect our patent rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. For this or other reasons, we may not pursue or obtain patent protection in all major markets or may not obtain protection that enables us to prevent the entry of third parties onto the market.

Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind 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 know with certainty whether we were the first to make the inventions claimed in our U.S. patents or pending U.S. patent applications filed prior to March 16, 2013.

Moreover, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, reissue, inter partes review, post grant review, interference proceedings or other patent office proceedings, court litigation or International Trade Commission proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation concerning our patent rights could reduce the scope of or prevent the enforceability of, or invalidate, our patent rights, allowing third parties to commercialize our technology or products, or equivalent or similar technology or products, and so to compete directly with us, without payment to us, or, where such proceedings involve third-party patents, result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened or narrowed by operation of any of the foregoing, such an event could dissuade companies from collaborating with us to license, develop or commercialize current or potential future product candidates of ours.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors from competing with us or otherwise to provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar, improved or alternative technologies or products in a noninfringing manner. For example, although A3384 is the subject matter of pending patent applications that claim pharmaceutical formulations, patent protection is not available for composition-of-matter claims that only recite the API for A3384 without limitation to its formulation. Because A3384 lacks composition-of-matter protection for its API, competitors will, subject to obtaining marketing approval, be able to offer and sell products with the same API so long as these competitors do not infringe any of our issued patents. Moreover, method-of-treatment patent claims are more difficult to enforce than composition-of-matter claims for reasons including off-label sale, potential divided infringement issues and use of the subject compound in noninfringing manners. Physicians are permitted to prescribe an approved product for uses that are not described in the product’s labeling. Although off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. Off-label sales would limit our ability to generate revenue from the sale of our product candidates, if approved for commercial sale. In addition, if a third party were able to design around our dosage-form and formulation patents and create a different formulation and dosage form that is not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing our product.

In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, such as orphan drug exclusivity in the United States, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of a marketing authorization application becoming publicly available. Such developments could enable other companies to use our clinical trial data to assist in their own product development and to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States, Europe and elsewhere. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, 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 products. Future changes in U.S. statutory or case law beyond our control could affect some or all of the foregoing possibilities. 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. This could be the case even after giving effect to patent term extensions and data exclusivity provisions preventing third parties from relying on clinical trial data filed by us for marketing approval in support of their own applications for such approval. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.
In addition, we have pledged certain of our patent rights related to A4250 and elobixibat as collateral under our loan agreement with Kreos.

We may become involved in lawsuits or other enforcement proceedings to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and potentially unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property or that our patent and other intellectual property rights are invalid or unenforceable, including for antitrust reasons. As a result, in a patent infringement proceeding, a court or administrative body may decide that a patent of ours is invalid or unenforceable, in whole or in part, or may construe the patent’s claims narrowly and so refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the competitor technology in question. Even if we are successful in a patent infringement action, the unsuccessful party may subsequently raise antitrust issues and bring a follow-on action. Antitrust issues may also provide a bar to settlement or constrain the permissible settlement terms. Further, settlement agreements in the pharmaceutical sector are the subject of ongoing review by the antitrust authorities in the European Union.

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 current or potential future licensees or collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, inter partes review, reexamination, reissue or post-grant review proceedings before the USPTO. The risks of being involved in such litigation and office proceedings may also increase as our product candidates approach commercialization, and as our business gains greater visibility operating as a publicly traded company in the United States. Third parties may assert infringement claims against us based on existing or future intellectual property rights and so restrict our freedom to operate. Third parties may also seek injunctive relief against us, whereby they would attempt to prevent us from practicing our technologies altogether pending outcome of any litigation against us. We may not be aware of all such intellectual property rights potentially relating to our product candidates prior to their assertion against us. For example, we have not conducted an in depth freedom-to-operate search or analysis for A4250 or for A3384. Any freedom-to-operate search or analysis previously conducted may not have uncovered all relevant patents and pending patent applications, and there may be pending or future patent applications that, if issued, would block us from commercializing A4250, elobixibat or A3384. Thus, we do not know with certainty whether A4250, elobixibat, A3384 or any other product candidate, or our commercialization of any such product candidate, does not and will not infringe any third party’s intellectual property.

If we are found to infringe a third party’s intellectual property rights, or in order to avoid or settle litigation, we could be required to obtain a license to enable us to continue developing and marketing our products 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 nonexclusive, thereby giving our competitors access to the same technologies that we have then licensed, and could require us to make substantial payments. Absent a license, we could be forced, including by court order, to cease commercializing the infringing technology or product. 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 commercializing our 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, or claims that we derived inventions from another, could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies. Although we try to ensure that our employees do not use the proprietary or otherwise confidential information or know-how of others in their work for us, we may be subject to claims that we or these employees have without authorization used or disclosed intellectual property, including trade secrets or other proprietary or confidential information, of any such employee’s former employer. Litigation may be necessary to defend against these claims.

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

If we fail in prosecuting or 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 prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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. 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, 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. Accordingly, costs and lost management time, as well as 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.

**If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.**

Depending upon the timing, duration and specifics of FDA marketing approval of A4250, elobixibat, A3384 or potential future product candidates of ours, if any, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension if, for example, we fail to apply within applicable deadlines, we fail to apply prior to expiration of relevant patents or if we otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our products will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. In the event that we are unable to obtain any patent term extension, the issued U.S. composition of matter patent for A4250 is expected to expire in 2022 assuming it withstands any challenge. In the event that the other U.S. patents and patent applications for A4250 and elobixibat, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2031 to 2035. We also expect that our patent applications for A3384, which to date have been filed as priority applications in the U.S., for development, 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. Accordingly, costs and lost management time, as well as 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.

**If EA Pharma does not obtain protection under applicable law in Japan by extending the patent terms for elobixibat, the period during which we may receive royalties will be shorter than it could otherwise be and our business may be materially harmed.**

Depending upon the timing, duration and specifics of Japanese PMDA marketing approval of elobixibat, if any, one or more of our patents in Japan may be eligible for limited patent term restoration. The Japanese Pharmaceutical Affairs Law generally permits the extension of the patent term for a drug as compensation for patent term lost during the regulatory review process by the Japanese PMDA. However, we may not be granted an extension if, for example, we fail to apply within applicable deadlines, we fail to apply prior to expiration of relevant patents or if we otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which EA Pharma will have the right to exclusively market elobixibat in Japan will be shortened, competitors may obtain approval of competing products following our patent expiration and our
royalty revenue could be reduced, possibly materially. In the event that we are unable to obtain any patent term extension, the issued composition of matter patent for elobixibat in Japan is expected to expire in 2021 and the issued patent for a method of using an IBAT inhibitor to treat CIC or IBS in Japan is expected to expire in 2024, in each case assuming it withstands any challenge. We expect that the other Japanese patents and patent applications for elobixibat, if issued and the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2034 to 2035. Additionally, under the Japanese Pharmaceutical Affairs Law, an application for approval of a generic version of an approved drug cannot be filed during a specified post-approval reexamination period. Currently, the reexamination period is eight years for drugs with new active ingredients.

**A3384 could be subject to competition arising from off-label use from immediate release cholestyramine.**

We have pending PCT patent applications covering pharmaceutical formulations of A3384. Even if these patents ultimately issue in the United States or elsewhere, we do not have patent rights covering the composition of matter of cholestyramine. As a result, we may be limited in our ability to prevent others from exploiting cholestyramine, which could have a negative impact on the commercial potential of A3384. In addition, cholestyramine is currently approved in the United States and some countries in Europe for various indications, including in some countries in Europe for diarrhea associated with certain GI conditions. Physicians currently prescribe cholestyramine for other indications that are not approved by the FDA or regulatory authorities outside of the United States, such as BAM. If we are unable to establish that A3384 is a superior drug to immediate release cholestyramine in the treatment of BAM, physicians may be likely to continue to prescribe immediate release cholestyramine and our potential future revenue from sales of A3384 would likely be materially and adversely affected.

**If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.**

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary and confidential information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into nondisclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary or confidential information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate the trade secret, from using that technology or information to compete with us. If any of our trade secrets, particularly unpatented know-how, were to be obtained or independently developed by a competitor, our competitive position would be harmed.

**Risks Related to Regulatory Approval and Marketing of Our Product Candidates**

**A rare pediatric disease designation may not lead to the receipt of a Priority Review Voucher, even if A4250 is approved.**

The FDA has awarded rare pediatric disease Priority Review Vouchers to sponsors of drug products intended to treat rare pediatric disease products if the treatment and product application meet certain criteria. Under this program, upon the approval of a qualifying NDA or biologics license application, BLA, for the treatment or prevention of a rare pediatric disease, the sponsor of the application may be eligible for a rare pediatric disease Priority Review Voucher that can be used to obtain priority review for a subsequent NDA or BLA. The Priority Review Voucher may be sold or transferred an unlimited number of times. We anticipate that we will request rare pediatric disease designation for A4250 for PFIC. For purposes of this program, the FDA defines a “rare pediatric disease” as a disease that affects fewer than 200,000 individuals in the U.S. and more than 50% of those patients are under the age of 18 years old. There can be no assurance, however, that the FDA will agree with our position that PFIC meets the criteria for a “rare pediatric disease.” If we submit a voluntary request for a rare pediatric disease designation and the request is granted by FDA, the FDA’s rare pediatric disease designation would give us the potential to receive a Priority Review Voucher if A4250 is approved for marketing. The rare pediatric disease Priority Review Voucher program is now set to expire at the end of September 2020, although a drug that has been designated under the program as of September 30, 2020 may still receive the Priority Review Voucher if it is approved for marketing before October 1, 2022. Therefore, there is no guarantee that we will receive a Priority Review Voucher for A4250 even if it is approved by the FDA to treat a rare pediatric disease.
If prior to any marketing approval in the European Union of A4250 to treat PFIC, Shire’s SHP625 is approved in the European Union to treat PFIC and at the time of approval maintains its designation as an orphan medicinal product, and if A4250 is deemed to be a similar medicinal product, within the meaning of E.U. law, to SHP625, we may not be able to obtain marketing approval of A4250 in the European Union for a significant period of time. In addition, A4250 may not be entitled to orphan drug exclusivity for A4250 in the United States or European Union notwithstanding its orphan designation.

Regulatory authorities in some jurisdictions, including the United States and European Union, may designate drugs for relatively small patient populations as orphan drugs. The FDA has granted orphan drug designation to A4250, which is an IBAT inhibitor, for the treatment of PFIC, as well as PBC, and the EMA has designated A4250 as an orphan medicinal product for the treatment of PFIC, as well as PBC and ALGS. Shire’s SHP625, which has also been reported to be an IBAT inhibitor, has also been granted orphan drug designation by the FDA and as an orphan medicinal product by the EMA.

Generally, if a designated orphan medicinal product receives the first marketing approval in the European Union for the orphan indication for which it has been designated and maintains at the time of approval its designation as an orphan medicinal product under applicable criteria, the product is entitled to a period of market exclusivity in the European Union. Subject to certain exceptions, this market exclusivity precludes the EMA from accepting another marketing application for a “similar medicinal product” for the same indication for 10 years, which can be reduced to six years if a drug no longer meets the criteria for orphan drug designation (including if the drug is sufficiently profitable so that market exclusivity is no longer justified). Under E.U. law, a “similar medicinal product” is a medicinal product that contains a similar active substance or substances as contained in the authorized orphan medicinal product and that is intended for the same therapeutic indication and a “similar active substance” is an active substance that is identical or has the same principal molecular structural features (but not necessarily all of the same molecular features) and acts via the same mechanism as the authorized orphan medicinal product.

SHP625 has been evaluated to date in a greater number of PFIC patients than has A4250. If (1) prior to marketing approval, if any, of A4250 to treat PFIC in the European Union, SHP625 is approved in the European Union to treat PFIC and at the time of approval maintains its designation as an orphan medicinal product, (2) A4250 is deemed to be a similar medicinal product to SHP625 and (3) we are not able to establish that A4250 provides a significant benefit to patients compared with SHP625, we may not be able to obtain marketing approval of A4250 in the European Union for at least several years.

Moreover, we may not be able to obtain orphan drug exclusivity in the United States or the European Union for A4250 for PFIC or any other indication, notwithstanding the fact that A4250 has been designated as an orphan drug in the United States or an orphan medicinal product in the European Union. For example, if a competitive product that is the same drug as A4250 is shown to be clinically superior, any orphan drug exclusivity that we have obtained in the United States will not block the approval of such competitive product. In addition, orphan drug exclusivity will not prevent the approval in the United States of a product that is the same drug as our product candidate if the FDA finds that we cannot assure the availability of sufficient quantities of the drug to meet the needs of the persons with the disease or condition for which the drug was designated. Moreover, if prior to marketing approval, if any, of A4250 to treat PFIC in the European Union, SHP625 or any other product is approved in the European Union to treat PFIC, A4250 may not be entitled to orphan drug exclusivity if we are not able to establish that it provides a significant benefit to patients compared with SHP625. Finally, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drug products can be approved for the same condition.

Even if we complete the necessary clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required marketing approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including A4250, elobixibat and A3384, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market A4250, elobixibat, A3384 or any other product candidate from regulatory authorities in any jurisdiction.

We have only limited experience in filing and supporting the applications necessary to obtain marketing approvals for product candidates and expect to rely on third-party contract research organizations to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and effectiveness. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that A4250, elobixibat, A3384 or any potential future product candidate of ours is not effective, is only moderately effective or has undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.
The process of obtaining marketing approvals is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies, clinical trials or other trials. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

**Our failure to obtain marketing approval in jurisdictions other than the United States and Europe would prevent our product candidates from being marketed in these other jurisdictions, and EA Pharma’s failure to obtain marketing approval of elobixibat in Japan would prevent elobixibat from being marketed in Japan. Any approval that we are granted for our product candidates in the United States or Europe would not assure approval of product candidates in the other or in any other jurisdiction.**

In order to market and sell A4250, elobixibat, A3384 or any potential future product candidate of ours in jurisdictions other than the United States or Europe, we or a current or potential future licensee or collaborator must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA or EMA approval. The regulatory approval process outside the United States and Europe generally includes all of the risks associated with obtaining FDA and EMA approval. In addition, some countries outside the United States and Europe require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We or a current or potential future licensee or collaborator may not obtain marketing, pricing or reimbursement approvals outside the United States and Europe on a timely basis, if at all. In particular, EA Pharma may not obtain marketing, pricing or reimbursement approvals for elobixibat in Japan on a timely basis, if at all.

Approval by the FDA does not ensure approval by the EMA, approval by the EMA does not assure approval by the FDA, and approval of either or both of the FDA and EMA does not assure approval by regulatory authorities in other countries or jurisdictions. Likewise, approval by any regulatory authority in any country or jurisdiction outside the United States or Europe, such as Japan, does not assure approval by regulatory authorities in other countries or jurisdictions or by the FDA or EMA. We and any current or potential future licensee or collaborator may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in any market. Marketing approvals in countries outside the United States and Europe do not ensure pricing approvals in those countries or in any other countries, and marketing approvals and pricing approvals do not ensure that reimbursement will be obtained.

**Our ability to obtain and maintain conditional marketing authorizations in the European Union is limited to specific circumstances and subject to several conditions and obligations. A failure to renew any conditional approval that we obtain prior to full approval for the applicable indication would prevent us from continuing to market our products.**

Conditional marketing authorizations in the European Union based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under E.U. law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies or trials, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions. Even if we obtain conditional approval for A4250 for the treatment of PFIC or any other pediatric cholestatic liver disease or disorder, we may not be able to renew such conditional approval.

**Even if we obtain marketing approval for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture or market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate profit.**

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the possible requirement to implement a risk evaluation and mitigation strategy or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We must
also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product’s approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers’ facilities are required to ensure that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMP.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have marketing approval for any of our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our products from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice and state attorneys general, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
• product seizure; or
• injunctions or the imposition of civil or criminal penalties.

Our noncompliance, or noncompliance by any future licensee or collaborator, with regulatory requirements relating to safety monitoring or pharmacovigilance, to the development of products for the pediatric population or to the protection of personal information can lead to significant penalties and sanctions.

*Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.*

If a drug is intended for the treatment of a serious or life threatening condition and the drug demonstrates the potential to address unmet medical needs for the condition, the drug sponsor may apply for FDA fast track designation. The designation offers the sponsor opportunities for interactions with the FDA review team and the possibility of a rolling review for certain portions of the marketing application. We believe that A4250 may meet the criteria to be designated as a fast track product. However, even if we seek and are granted a fast track designation for A4250, there is no assurance that A4250 will receive marketing approval from the FDA or that approval will be granted within any particular timeframe. We may also seek fast track designation for other current or potential future product candidates of ours. Even if the FDA grants fast track designation to one or more of these product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation that may in the future be granted to any of our product candidates if it believes that the designation is no longer supported by data from our clinical development program for that product candidate. Fast track designation alone does not guarantee qualification for the FDA’s priority review procedures.

*Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval.*

If the FDA determines that a product candidate intended to treat a serious disease, if approved, would provide a significant improvement in safety or effectiveness of the treatment of the disease, the FDA may designate the drug application for that product candidate for priority review. A priority review designation means that the goal for the FDA to review the marketing application is six months from the date of NDA acceptance for filing, rather than the standard review period of ten months from the date of NDA acceptance for filing. We may request priority review for A4250 or other current or potential future product candidates of ours at the time that the marketing application is submitted. The FDA has broad discretion with respect to whether or not to grant priority review status to an individual marketing application. As a result, even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving a priority review designation from the FDA does not guarantee approval of the drug application within the six-month review cycle or any time thereafter.

*Our relationships with customers, healthcare providers and professionals and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.*

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidate, including A4250, elobixibat or A3384, for which we obtain marketing approval. Our future arrangements with customers, healthcare providers and professionals, and third-party payors may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell or distribute any product candidate for which we obtain marketing approval.

The federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and pharmacy benefit managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback laws and regulations.

The federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Both the government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government.
The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

The federal Physician Payments Sunshine Act requirements under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report to the Department of Health and Human Services information related to payments and other transfers of value made to or at the request of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Among other payments, the law requires payments made to physicians and teaching hospitals for clinical trials be disclosed.

Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Violation of certain of these laws could also result in exclusion, suspension and debarment from government funded healthcare programs. Exclusion, suspension or debarment would significantly impact our ability to commercialize, sell or distribute any product candidate for which we obtain regulatory approval. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

**Legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any product that receives marketing approval.**

In the United States and in some other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of A4250, elobixibat, A3384 or any potential future product candidates of ours, restrict or regulate post-approval activities, or affect our ability to profitably sell any product candidates, including A4250, elobixibat or A3384, for which we obtain marketing approval. In addition, increased scrutiny by the U.S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, the Affordable Care Act became law in the United States. The Affordable Care Act is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health
industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revised the definition of “average manufacturer price” for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. As implementation of the Affordable Care Act is ongoing, the law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. In addition, there have been judicial and congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future, particularly in the light of the change in administration following the 2016 U.S. presidential election. Similarly, there are a number of state and local legislative and regulatory efforts related to drug pricing, including a drug price transparency law in Vermont that applies to pharmaceutical manufacturers, that may have an impact on our business.

In addition, the Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are unsure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or whether such changes will have any impact on our business.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or E.U. member state level may result in significant additional requirements or obstacles that may increase our operating costs.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms could result in reduced demand for our product candidates or additional pricing pressures, and may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

**We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.**

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or the FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA violations and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the government of the United States and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or Trade Control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.
We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

In connection with the preparation of our consolidated financial statements as of and for the years ended December 31, 2016, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting. If we are not able to remediate the material weakness and otherwise to maintain an effective system of internal control over financial reporting, the reliability of our financial reporting, investor confidence in us and the value of our common stock could be materially and adversely affected.

Under standards established by the United States Public Company Accounting Oversight Board, a material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected and corrected on a timely basis.

In connection with the audit of our 2016 financial statements, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting, specifically a lack of controls over the identification and review of complex accounting issues involving significant judgment or estimates in the financial statement closing process resulting from our limited in-house accounting and finance team. We currently rely on consultants and external advisors to provide assistance with financial reporting in accordance with the requirements of generally accepted accounting principles in the United States, or U.S. GAAP, and the rules and regulations of the Securities and Exchange Commission, or SEC, and these consultants and external advisors may not have direct knowledge of all of our business, transactions and contracts. Specifically, we and our independent registered public accounting firm determined that we did not have sufficient resources with U.S. GAAP and SEC financial reporting knowledge to ensure a timely and sufficient financial statement close process that includes resolution of complex accounting issues involving significant judgment and estimates.

We are working to remediate the material weakness. In particular, we hired a full-time chief financial officer in July 2016 and a controller in March 2017 and plan to develop and implement formal policies, processes and documentation procedures relating to our financial reporting. We estimate that we will remediate the material weakness prior to filing our annual report on Form 10-K for the year ending December 31, 2017, but we may not ever be able to remediate the material weakness. If we are unable to successfully remediate the material weakness and otherwise to establish and maintain an effective system of internal control over financial reporting, the reliability of our financial reporting, investor confidence in us and the value of our common stock could be materially and adversely affected.

If we fail to establish and maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.
Pursuant to Section 404, we are required to furnish a report by our management on the effectiveness of our internal control over financial reporting and, if and at such time as we cease to qualify as a “smaller reporting company” under applicable securities regulations, 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 we will not 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 consolidated financial statements. In addition, because we currently qualify as a “smaller reporting company” under applicable securities regulations, an attestation report on internal control over financial reporting issued by our independent registered public accounting will not be required. An independent assessment of our internal control over financial reporting might detect deficiencies that management’s assessment does not.

**Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.**

We are highly dependent on Ron Cooper, our President and Chief Executive Officer, and other principal members of our management and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance on any of our executive officers. The unplanned loss of the services of any of these persons could materially impact the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel, including in the United States and Sweden, will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous biotechnology and pharmaceutical companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

**We expect to expand our capabilities and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.**

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, finance and administration and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

**We incur significant costs and demands as a result of operating as a public company.**

We incur significant legal, accounting and other expenses to meet our obligations as a publicly traded company. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Act, the listing requirements of the NASDAQ Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways that are not currently anticipated. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations may make it difficult and expensive for us to maintain director and officer liability insurance coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers, which may adversely affect investor confidence in us and could cause our business or stock price to suffer.
We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations outside of the United States. Because our consolidated financial statements are presented in U.S. dollars, changes in currency exchange rates have had and could have in the future a significant effect on our operating results when our operating results are translated into U.S. dollars. Exchange rate fluctuations between local currencies and the dollar create risk in several ways, including the following: weakening of the dollar may increase the cost of overseas research and development expenses and the cost of sourced product components outside the United States; strengthening of the dollar may decrease the value of our revenues denominated in other currencies; the exchange rates on nondollar transactions and cash deposits can distort our financial results; and commercial pricing and profit margins may be affected.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and collaborators, including intentional failures to comply with FDA or Office of Inspector General regulations or similar regulations of comparable non-U.S. regulatory authorities, or noncompliance with regulatory standards and requirements and insider trading. Noncompliance with these laws and regulations could result in regulatory sanctions and serious harm to our reputation. 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 governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards 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 and results of operations, including the imposition of significant fines or other sanctions.

The vote by the United Kingdom electorate in favor of the United Kingdom’s exit from the European Union could adversely impact our business, results of operations and financial condition.

The passage of the referendum on the United Kingdom’s membership in the European Union, referred to as “Brexit,” in favor of the exit of the United Kingdom from the European Union, could cause disruption to and create uncertainty surrounding our business, which could have an adverse effect on our business, financial results and operations. Over the next few months, negotiations are expected to commence to determine the terms of the United Kingdom’s relationship with the European Union in the future, including trade terms between the United Kingdom and countries comprising the European Union. The effects of Brexit will depend on any agreements the United Kingdom makes to retain access to markets in the European Union, either during a transitional period or more permanently.

Assuming its implementation, Brexit would result in the United Kingdom no longer being a European Union Member State and a member of the European Union single market, which may result in increased trade barriers. Increased trade barriers could impact our results of operations. As we have a subsidiary registered in England and Wales and operating subsidiaries in Sweden, Brexit could result in restrictions on the movement of capital within our organization, the mobility of our personnel and the potential future commercialization of our product candidates and could change our tax benefits or liabilities, any of which could have a material adverse effect on our business, results of operations or financial condition.

Risks Related to Our Common Stock

Our stock price is expected to be volatile, and the market price of our common stock may drop.

The market price of our common stock could be subject to significant fluctuations. Market prices for securities of clinical-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;
- issues in manufacturing our approved products, if any, or product candidates;
- the results of our current and any future clinical trials of our product candidates;
- the entry into, or termination of, key agreements, including key commercial partner agreements;
• the initiation of, material developments in, or conclusion of litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
• announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments;
• adverse publicity relating to the markets in which we compete, including with respect to other products and potential products in such markets;
• the introduction of technological innovations or new therapies that compete with our product candidates or products, if any;
• the loss of key employees;
• changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
• general and industry-specific economic conditions that may affect our research and development expenditures;
• changes in the structure of health care payment systems;
• failure to maintain compliance with listing requirements of The NASDAQ Capital Market; and
• period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company’s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

Our stock price may be especially volatile because of, and investor interest in our common stock may be negatively affected by, unauthorized trading of our common stock on stock exchanges in Germany.

We are aware that our common stock may be trading on multiple stock exchanges in Germany, which we have not authorized. These German exchanges have been rumored to allow short selling of stock without assurance that shares sufficient to cover the trade are available, also known as “naked” short selling, or otherwise not comply with exchange requirements that are customary in the United States. The trading of our common stock on these German stock exchanges may make the market price of our common stock more volatile than it would otherwise be. This increased volatility, or the potential for this increased volatility, could have a negative impact on investor interest in our common stock, which could depress the market price of our common stock.

Our executive officers and directors and their affiliates have the ability to control or significantly influence all matters submitted to our stockholders for approval.

As of March 1, 2017, our executive officers and directors, and their affiliates, beneficially own or control approximately 39.4% of our outstanding shares of common stock (after giving effect to the exercise of all outstanding vested and unvested options to purchase shares of our common stock). Accordingly, these executive officers, directors and their affiliates, acting as a group, will have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may cause the price of our common stock to decline if investors perceive that conflicts of interest may exist or arise.

We are a smaller reporting company. We cannot be certain if the reduced disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors or otherwise limit our ability to raise additional funds.

We are currently a “smaller reporting company” under applicable securities regulations. A smaller reporting company is a company that has an aggregate market value of its voting stock held by non-affiliates, or public float, of less than $75 million as of the last business day of its most recently completed second fiscal quarter and does not meet certain exceptions. A smaller reporting company is able to provide simplified executive compensation disclosures in its filings, is exempt from the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that an independent registered public accounting firm provide an attestation report.
on the effectiveness of internal control over financial reporting, and has certain other reduced disclosure obligations in their SEC filings, including, among other things, only being required to provide two years of audited financial statements in annual reports. Reduced disclosure in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects.

In addition, we filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on January 10, 2017 and pursuant to which we registered for sale up to $100 million of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. Under SEC rules and regulations, we must meet certain requirements to use our Form S-3 registration statement to sell up to the full amount of $100 million of securities registered for sale under the Form S-3 registration statement. One such requirement is that the market value of our outstanding common stock held by non-affiliates, or public float, be at least $75 million as of a date within 60 days prior to the date on which the Form S-3 is filed (and within 60 days prior to the date of any Form 10-K filing thereafter by us, which is deemed a re-evaluation date). If we do not meet that requirement, then the aggregate market value of securities sold by us in a primary offering under our Form S-3 in any 12-month period is limited to an aggregate of one-third of our public float. SEC rules and regulations require that we periodically re-evaluate the value of our public float, and if, during the 60-day period prior the applicable re-evaluation date, our public float has not been equal to or greater than $75 million, we would become subject to the one-third of public float limitation described above. During the 60-day period prior to the date this Form 10-K is filed, which is our most recent re-evaluation date, our public float was greater than $75 million, and we are therefore not subject to the one-third of public float limitation, at least until our next re-evaluation date.

If our ability to utilize a Form S-3 registration statement becomes restricted under these rules, we could elect to raise capital pursuant to an exemption from registration under the Securities Act, or under a Form S-1 registration statement, but either of these alternatives would likely increase the cost of raising additional capital compared with the use of a Form S-3 registration statement. Furthermore, because of these limitations on primary securities offerings under a Form S-3 and the increased likelihood of greater costs and potential delays associated with the alternatives to using a Form S-3, the terms of any financing transaction that we are able to conduct may be less favorable or may cause us to be unable to obtain capital in a timely manner.

In addition, under current SEC rules and regulations, our common stock must be listed on a national securities exchange in order to utilize a Form S-3 registration statement (i) for a primary offering, if our public float is not at least $75 million as of a date within 60 days prior to the date on which the securities are sold under the Form S-3, or a re-evaluation date, whichever is later, and (ii) to register the resale of our securities by persons other than us. While our common stock is listed on The NASDAQ Capital Market, there can be no assurance that we will be able to maintain such listing.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

We currently expect to retain our future earnings to fund the development and growth of our business. In addition, we are prohibited from making any dividend payments under the terms of our loan facility. As a result, capital appreciation, if any, of our common stock will be your sole source of gain, if any, for the foreseeable future.

Future sales of shares by existing stockholders could cause our stock price to decline.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after applicable lock-up and other legal restrictions on resale discussed in this proxy statement lapse, the trading price of our common stock could decline. As of March 1, 2017, we had outstanding a total of approximately 6.3 million shares of common stock. Of these shares, only approximately 2.1 million shares of common stock are freely tradable, without restriction, in the public market as of March 1, 2017.

Prior to November 3, 2016, we were a specialty biopharmaceutical company known as Biotrol Inc. On November 3, 2016, we completed a share exchange transaction. Upon the completion of the share exchange transaction, we changed our name to “Albireo Pharma, Inc.” and the business of Albireo Limited became our business. The lock-up agreements entered into by the former directors and officers of Biotrol and the lock-up restrictions in the agreement for the share exchange provide that the shares subject to the lock-up restrictions will be released from such restrictions 180 days from November 3, 2016, the closing date of the share exchange. In addition, the shares of our common stock that were issued in the share exchange are restricted securities under the Securities Act and any sale of such shares without registration will be subject to the requirements of Rule 144 promulgated under the Securities Act. Based on shares outstanding as of March 1, 2017, up to an additional approximately 4.2 million shares of common stock will be eligible for sale in the public market, approximately 2.1 million of which are held by our directors, our executive officers and other affiliates and are subject to volume limitations under Rule 144 under the Securities Act, and various vesting agreements. In addition, approximately 855,923 shares of common stock that are subject to outstanding stock options as of March 1, 2017 will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and the lock-up agreements and to the extent the shares are registered for sale under the Securities Act or permitted for sale in the public market by Rules 144 and 701 under the Securities Act. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.
Because the share exchange completed pursuant to the Exchange Agreement resulted in an ownership change under Section 382 of the Internal Revenue Code of 1986, as amended, the pre-exchange net operating loss carryforwards and certain other tax attributes of Biodel will be subject to limitations. Our net operating loss carryforwards and other tax attributes may also be subject to additional limitations as a result of ownership changes.

If a corporation undergoes an “ownership change” within the meaning of Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, the corporation’s net operating loss carryforwards and certain other tax attributes arising from before the ownership change are subject to limitations on use after the ownership change. In general, an ownership change occurs if there is a cumulative change in the corporation’s equity ownership by certain stockholders that exceeds fifty percentage points over a rolling three-year period. Similar rules may apply under state tax laws. The share exchange resulted in an ownership change for Biodel and, accordingly, the ability to use the net operating loss carryforwards and certain other tax attributes of Biodel will be limited. Our net operating loss carryforwards may also be subject to limitation as a result of shifts in equity ownership or the completed share exchange. Additional ownership changes in the future could result in additional limitations on our net operating loss carryforwards. Consequently, even if we achieve profitability, we may not be able to utilize a material portion of these net operating loss carryforwards and other tax attributes, which could have a material adverse effect on our cash flow and results of operations.

We may become involved in securities class action litigation that could divert management’s attention and harm our business and insurance coverage may not be sufficient to cover all costs and damages.

In the past, securities class action or shareholder derivative litigation often follows certain significant business transactions, such as the sale of a business division or announcement of a merger. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management’s attention and resources, which could adversely affect our business.

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 certificate of incorporation and 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 you might otherwise receive a premium for your shares. These provisions could also 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, 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. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team.

Among others, 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 of directors;
• 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 stockholder rights plan or “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 of our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a person who owns 15% or more 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 15% or more of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.
Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

We lease approximately 5,116 square feet of office space in the building located at 10 Post Office Square, Boston, Massachusetts, which serves as our corporate headquarters. The lease expires on April 30, 2022, and we have the option to extend the term one time for an additional 5-year period. The current base monthly payment on the lease is $20,997, which is subject to specified annual increases of approximately 2% during the term of the lease and does not include operating expenses, utilities, taxes and insurance for which we are responsible. In addition, we lease approximately 5,100 square feet of office space in Gothenburg, Sweden under a lease that expires in November 2019. The current quarterly payment under the lease is 318,197 Swedish Kronor (approximately $34,939, based on the Swedish Kronor to U.S. Dollar exchange rate at December 31, 2016), subject to change based on applicable taxes and otherwise to increase based on changes in the Swedish Consumer Price Index. The lease renews automatically for consecutive three-year terms, unless notice of nonrenewal is given by either party at least nine months prior to the end of the current term and subject to our right to terminate the lease at any time upon six months’ notice. We believe that our existing facilities are adequate to meet our current needs and that suitable alternative spaces will be available in the future on commercially reasonable terms.

Item 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.
Prior to the closing of the Transaction on November 3, 2016, Biodel’s common stock was traded on The NASDAQ Capital Market under the symbol “BIOD.” On November 3, 2016, following the closing of the Transaction, we changed our name to “Albireo Pharma, Inc.” On November 4, 2016, our common stock began trading on The NASDAQ Capital Market under the symbol “ALBO.” The high and low sales prices per share of our common stock as reported by NASDAQ in each of the quarters within our two most recent fiscal years are set forth below. In connection with the closing of the Transaction, on November 3, 2016, we effected a 1-for-30 reverse stock split of our common stock. All of the prices in the table below have been adjusted to reflect the effect of the reverse stock split.

<table>
<thead>
<tr>
<th>Fiscal Quarter Ended</th>
<th>High</th>
<th>Low</th>
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<tbody>
<tr>
<td>March 31, 2015</td>
<td>$60.00</td>
<td>$34.20</td>
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<tr>
<td>June 30, 2015</td>
<td>$40.20</td>
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<td>September 30, 2015</td>
<td>$33.76</td>
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<tr>
<td>December 31, 2015</td>
<td>$15.00</td>
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</tr>
<tr>
<td>March 31, 2016</td>
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<tr>
<td>June 30, 2016</td>
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<tr>
<td>September 30, 2016</td>
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</tr>
<tr>
<td>December 31, 2016</td>
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<td>$13.20</td>
</tr>
</tbody>
</table>

On March 1, 2017, the closing price of our common stock was $25.90 per share.

Stockholders

As of March 1, 2017, we had 6,292,644 outstanding shares of common stock and no outstanding shares of preferred stock. As of March 1, 2017, there were approximately 45 holders of record of our common stock.

Dividends

Except for a single dividend paid by Albireo Limited in 2012, we have never paid or declared any cash dividends on our common stock. We currently intend to retain earnings, if any, to finance the growth and development of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, we are currently prohibited from making any dividend payments under the terms of our loan facility with our lender.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the quarter ended December 31, 2016.

Item 6. SELECTED FINANCIAL DATA

Not required for smaller reporting companies.
Overview

Prior to November 3, 2016, we were a specialty biopharmaceutical company known as Biodel Inc. that historically had been focused on the development and commercialization of innovative treatments for diabetes. On November 3, 2016, we completed a share exchange transaction, or the Transaction, pursuant to an Amended and Restated Share Exchange Agreement dated July 13, 2016 that we entered into with Albireo Limited and the shareholders and noteholders of Albireo Limited. Upon the completion of the Transaction, we changed our name to “Albireo Pharma, Inc.,” the business of Albireo Limited became our business and we became a biopharmaceutical company focused on the development and commercialization of novel bile acid modulators to treat orphan pediatric liver diseases and gastrointestinal disorders where improper flow or absorption of bile causes serious medical conditions for which there is high unmet need. The initial target indication for our lead product candidate, A4250, is progressive familial intrahepatic cholestasis, or PFIC, a rare, life-threatening genetic disorder affecting young children for which there is currently no approved drug treatment. A4250 is currently being evaluated in a Phase 2 clinical trial in children with chronic cholestasis that is intended to support a planned Phase 3 clinical trial in patients with PFIC. In addition to PFIC and subject to obtaining additional capital, we plan to consider conducting future clinical development of A4250 as a treatment for other pediatric cholestatic liver diseases and disorders. Our clinical-stage product candidates in addition to A4250 include elobixibat, for which our licensee has filed a new drug application for approval in Japan to treat chronic constipation, and A3384, which is in development to treat bile acid malabsorption. We also have a preclinical program in nonalcoholic steatohepatitis, or NASH.

For accounting purposes, the Transaction was treated as a “reverse acquisition” and Albireo Limited was considered the accounting acquirer. Accordingly, the discussion and analysis in this Item 7 reflect the historical results of Albireo Limited and its direct and indirect subsidiaries prior to completion of the Transaction and do not include the historical results of Biodel prior to completion of the Transaction.

Biodel Inc. was incorporated in December 2003 and commenced active operations in January 2004. Albireo Limited’s business began when Albireo Limited was spun out of AstraZeneca AB in 2008.

Since inception, we have incurred significant operating losses. As of December 31, 2016, we had an accumulated deficit of $25.9 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next few years as we continue our development of, and seek marketing approvals for, our product candidates, prepare for and begin the commercialization of any approved products, and add infrastructure and personnel to support our product development efforts and operations as a public company in the United States.

As a clinical-stage company, our revenues, expenses and results of operations are likely to fluctuate significantly from quarter to quarter and year to year. We believe that period-to-period comparisons of our results of operations should not be relied upon as indicative of our future performance.

As of December 31, 2016, we had approximately $29.9 million in cash and cash equivalents.

All common stock share and per share amounts in this Management’s Discussion and Analysis of Financial Condition and Results of Operations have been retroactively adjusted to reflect the exchange of shares in the Transaction based on an exchange ratio of 0.06999 and, where applicable, a 1-for-30 reverse stock split effected by Biodel Inc. on November 3, 2016 prior to completion of the Transaction.

Financial Operations Overview

The following discussion sets forth certain components of our consolidated statements of operations as well as factors that impact those items.
Revenue
We generate revenue primarily from the receipt of upfront or license fees, milestone payments and payment for procurement services that are made pursuant to license agreements or related supply agreements. License agreements with commercial partners generally include nonrefundable upfront fees and milestone payments, the receipt of which is dependent upon the achievement of certain development, regulatory or commercial milestones, as well as royalties on product sales of licensed products, if and when such product sales occur, and payments for procuring pharmaceutical ingredients. For these agreements, management applies judgment in the allocation of total agreement consideration to the separately identifiable components on a reliable basis that reasonably reflects the selling prices that might be expected to be achieved in stand-alone transactions.

For the years ended December 31, 2016 and 2015, we recognized into revenue $11.4 million and $5.1 million, respectively, in payments under our license agreements. For the year ended December 31, 2016, we recognized into revenue nonrefundable payments received from our licensee for elobixibat in Japan and other specified countries in Asia, EA Pharma Co., Ltd. (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.), or EA Pharma, of $8.0 million in connection with a renegotiated payment stream and $3.6 million triggered by the decision of EA Pharma to proceed with the preparation of a new drug application for elobixibat in Japan. We expect that any future revenue recognized under our license agreement with EA Pharma will fluctuate from quarter to quarter and year to year as a result of the uncertain timing of future milestone payments, if any.

Operating Expenses
Research and Development Expenses
Research and development expenses consist primarily of personnel costs (including salaries, benefits and other staff-related costs) for employees in research and development functions, costs associated with preclinical and clinical development services, including clinical trials and related manufacturing costs, third-party contract research organizations, or CROs, and related services and other outside costs, including fees for third-party professional services such as consultants. Our preclinical studies and clinical studies are performed by CROs. We expect to continue to focus our research and development efforts on preclinical studies and clinical trials of our product candidates. As a result, we expect our research and development expenses to continue to increase for the foreseeable future.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs such as fees paid to CROs and others in connection with our preclinical and clinical development activities and related manufacturing. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified.

Successful development of our current and potential future product candidates is highly uncertain. Completion dates and costs for our programs can vary significantly by product candidate and are difficult to predict. As a result, we cannot estimate with any degree of certainty the costs we will incur in connection with development of any of our product candidates. We anticipate we will make determinations as to which programs and product candidates to pursue and how much funding to direct to each program and product candidate on an ongoing basis in response to the results of ongoing and future clinical trials, our ability to enter into licensing, collaboration and similar arrangements with respect to current or potential future product candidates, success of research and development programs and assessments of commercial potential.

General and Administrative Expenses
General and administrative expenses consist primarily of personnel costs (including salaries and benefits) for our executive, finance and other administrative employees. In addition, general and administrative expenses include fees for third-party professional services, including consulting, information technology, legal and accounting services and other corporate expenses and allocated overhead.

Critical Accounting Policies and Estimates
Our management’s discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses. We base our estimates and assumptions on historical experience and on various assumptions that we believe are reasonable under the circumstances, and we evaluate them on an ongoing basis. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of revenues and expenses that are not readily apparent from other sources. Actual results and experiences may differ materially from these estimates and judgments. In addition, our reported financial condition and results of operations could vary if new accounting standards are enacted that are applicable to our business.
Our significant accounting policies are described in Note 1 to our audited consolidated financial statements for the year ended December 31, 2016 in this Annual Report on Form 10-K. We believe that our accounting policies relating to revenue recognition, research and development expenses, stock-based compensation and fair value of financial instruments are the most critical to understanding and evaluating our reported financial results. We have identified these policies as critical because they both are important to the presentation of our financial condition and results of operations and require us to make judgments and estimates on matters that are inherently uncertain and may change in future periods. For more information regarding these policies, you should refer to Note 1 of our audited consolidated financial statements included in this Annual Report on Form 10-K.

Revenue Recognition

We generate revenue primarily from the receipt of upfront or license fees, milestone payments and payments for procurement services that are made pursuant to license agreements or related supply agreements. Substantially all of our revenue to date has been derived from our license agreement with EA Pharma and a now-terminated license agreement with Ferring International Center S.A., or Ferring.

Where an out-license arrangement involves the provision of multiple elements that may contain different remuneration arrangements such as upfront payments, milestone payments or product sales, the arrangement is assessed to determine whether separate delivery of the individual elements of such arrangements comprises more than one unit of accounting. The delivered elements are separated if (a) they have value to the licensee on a stand-alone basis, (b) there is objective and reliable evidence of the fair value of the undelivered element(s) and (c) if the arrangement includes a general right of return relative to the delivered element(s), delivery or performance of the undelivered element(s) is considered probable and is substantially in our control. Allocation of revenue to the different elements that require separate accounting is based on the separate selling prices determined for each component, and total consideration is then allocated pro rata across the components of the arrangement. If separate selling prices are not available, we will use our best estimate of such selling prices, consistent with the overall pricing strategy and relevant market factors.

Payments resulting from procurement services are recognized into revenue as the activities are performed and are presented on a net basis. Revenue is recorded on a net basis because we act as an agent, as we do not have discretion to change suppliers and do not perform any part of the services or manufacture of the subject pharmaceutical ingredients. The costs associated with these activities are netted against the related revenue in our consolidated statement of operations.

For certain contingent payments under research and development arrangements, we recognize revenue using the milestone method. Under the milestone method, a payment that is contingent upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is an event: (i) that can be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (iii) that would result in additional payments being due to us. The determination that a milestone is substantive requires estimation and judgment and is made at the inception of the arrangement. Milestones are considered substantive when the consideration earned from the achievement of the milestone is: (A) commensurate with either our performance to achieve the milestone or the enhancement of value of the item delivered as a result of a specific outcome resulting from our performance to achieve the milestone, (B) related solely to past performance and (C) reasonable relative to all deliverables and payment terms in the arrangement. In making the determination as to whether a milestone is substantive or not, our management considers all facts and circumstances relevant to the arrangement, including factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the milestone, the level of effort and investment required to achieve the milestone and whether any portion of the milestone consideration is related to future performance or deliverables.

Research and Development 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 by CROs and other third-party vendors, including clinical trial sites. We determine accrual estimates through financial models that take into account discussion with applicable personnel and service providers as to the progress or state of completion of particular research and development activities, including clinical trials. Our preclinical study and clinical trial accrued liabilities and prepaid assets are dependent, in part, upon the receipt of timely and accurate reporting from CROs and other third party vendors, including clinical trial sites. Although we do not expect our estimates to differ materially from amounts we actually incur, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reported amounts that are too high or too low for any particular period. When contracts for research and development services require advance payment, they are recorded on our consolidated balance sheet as prepaid items and expensed when the service is provided or reaches a specific milestone outlined in the contract.
Stock-based Compensation

We recognize stock-based compensation costs related to stock options granted to personnel based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. Except as provided below, the grant date fair value of each stock-based award is recognized on a straight-line basis over the requisite service period, which is the vesting period of the award.

During the year ended December 31, 2016, we issued stock options with exercise prices denominated in a foreign currency (Euros), which are required to instead be accounted for as liabilities. We account for each liability-classified stock-based award based on its fair value at each financial reporting date until the award is settled (exercised). Changes in the amounts attributed to these awards between the reporting dates are included in stock-based compensation expense (credit) in our consolidated statement of operations. We include liability-classified stock options in noncurrent liabilities on our balance sheet as their settlement (exercise) does not require use of cash, cash equivalents or other current assets. The foreign-denominated stock options issued during 2016 were replaced with stock options denominated in U.S. dollars on the date the Transaction was completed.

The Black-Scholes option-pricing model requires the use of highly subjective and complex assumptions that which determine the fair value of stock-based awards. These assumptions include:

- **Expected term.** We estimate the expected term for stock-based awards using the simplified method due to limited historical exercise activity. The simplified method calculates the expected term as the arithmetic average between the vesting date and the contractual expiration date of the award.

- **Expected volatility.** Due to our limited history, the expected volatility was derived from the average historical stock volatilities of several unrelated public companies within our industry that we consider to be comparable to our business over a period equivalent to the expected term of the awards.

- **Risk-free interest rate.** The risk-free interest rate is based on the U.S. Government Bond rate with a maturity date commensurate with the expected term of the associated award.

- **Expected dividend.** The expected dividend is assumed to be zero. Except for a single dividend paid by Albireo Limited in 2012, we have never paid dividends and we have no current plans to pay any dividends.

In addition to the assumptions used in the Black-Scholes option-pricing model, we must also estimate a forfeiture rate to calculate the stock-based compensation for our awards. Our estimated forfeiture rate is based on an analysis of actual forfeitures. We will continue to evaluate the appropriateness of our estimated forfeiture rate based on actual experience, analysis of employee turnover and other factors. Quarterly changes in the estimated forfeiture rate could have a significant impact on stock-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. If a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in our consolidated statement of operations. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in our consolidated statement of operations.

We will continue to use judgment in evaluating the expected volatility, expected terms and forfeiture rates utilized for our stock-based compensation calculations on a prospective basis. As we continue to accumulate additional data related to our common stock and stock-based awards, there may be refinements to the estimates of expected volatility, expected terms and forfeiture rates, which could impact future stock-based compensation expense.

Some of our stock-based awards are subject to performance-based vesting conditions. Compensation expense related to awards with performance-based vesting conditions is recognized over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable or, in some cases, when the vesting condition occurs.

Fair Value of Financial Instruments

In December 2014, we executed a convertible loan instrument, which provided 1,251,000 €1.00 unsecured convertible loan notes denominated in Euros and was subsequently amended in October 2015, and issued all of the convertible loan notes to certain Albireo Limited shareholders and their affiliates. In October 2015, we executed a separate convertible loan instrument, which provided 5,000,000 $1.00 unsecured convertible loan notes denominated in U.S. dollars, and, as of December 31, 2015, issued $3.5 million of the convertible loan notes to certain Albireo Limited shareholders and their affiliates and members of management. All of the recipients of the convertible loan notes in 2014 and 2015 are considered related parties. We bifurcated the embedded conversion features of the convertible loan note instruments from the loan note payable and recorded the fair value of the conversion features as debt discount. In accordance with applicable guidance, we allocated the proceeds received based on the relative fair values of the

77
respective convertible loan notes and conversion features, which resulted in the recording of debt discount totaling $526,000 (€432,000) for the 2014 loan notes at issuance and $1.5 million for the 2015 loan notes at issuance. The debt discounts are accreted over the life of the respective convertible loan notes. In connection with the Transaction, all of the convertible loan notes issued in 2014 and 2015 were converted into equity.

Similarly, in December 2014, we entered into a loan facility agreement with Kreos Capital IV Limited, or Kreos, under which Kreos provided a €6.0 million ($7.3 million) loan facility. In connection with the agreement, we issued to an affiliate of Kreos detachable warrants that provided a right to acquire shares of Albireo Limited. In connection with the Transaction, these warrants were replaced with warrants to purchase shares of our common stock. Because the number of shares issuable upon exercise of both the initial and replacement warrants is variable, we treated the warrants as a liability under Financial Accounting Standards Board Accounting Standard Codification Topic 480, Distinguishing Liabilities From Equity, and measured them at fair value. The fair value of the warrants’ or replacement warrants’ liability is required to be remeasured at the end of each reporting period, with any change in fair value recognized in the consolidated statements of operations. In accordance with applicable guidance, we allocated the proceeds received based on the fair value of the warrants and the residual value of the debt, which resulted in us recording debt discount totaling €1.0 million ($1.2 million) at issuance. The debt discount is to be accreted over the life of the associated loan.

Results of Operations

Years Ended December 31, 2016 and December 31, 2015

Revenue

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td>Revenue</td>
<td>$11,364</td>
<td>$5,099</td>
</tr>
</tbody>
</table>

Revenue was $11.4 million for the year ended December 31, 2016 compared with revenue of $5.1 million for the year ended December 31, 2015, an increase of $6.3 million. The higher revenue was due to recognition in full of payments from EA Pharma of $8.0 million received in April 2016 in connection with a renegotiated payment stream linked to know-how and intellectual property that we had delivered upon inception of the license agreement in 2012 and €3.225 million earned in the fourth quarter of 2016 upon the decision of EA Pharma to proceed with the preparation of a new drug application for elobixibat in Japan. For the year ended December 31, 2015, we recognized into revenue $5.1 million in payments received under our license agreement with EA Pharma.

Research and development expenses

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td>Research and development expenses</td>
<td>$8,077</td>
<td>$5,634</td>
</tr>
</tbody>
</table>

Research and development expenses were $8.1 million for the year ended December 31, 2016 compared with $5.6 million for the year ended December 31, 2015, an increase of $2.4 million. The increase was principally due to a $1.7 million increase in costs incurred to third parties for preclinical research services and clinical trials, primarily related to A4250 for which we initiated a Phase 2 clinical trial in children with chronic cholestasis in the second half of 2015, as well as an increase of $755,000 primarily in fees for contract R&D consulting services and also comprising facilities and personnel costs.
The following table summarizes our principal product development programs and the out-of-pocket third-party expenses incurred with respect to each clinical-stage product candidate and our preclinical programs for the years ended December 31, 2016 and 2015.

<table>
<thead>
<tr>
<th>Direct third-party project costs:</th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td>(in thousands)</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>A4250</td>
<td>3,950</td>
<td>2,367</td>
</tr>
<tr>
<td>Eloxbibat</td>
<td>191</td>
<td>242</td>
</tr>
<tr>
<td>A3384</td>
<td>—</td>
<td>109</td>
</tr>
<tr>
<td>Preclinical</td>
<td>307</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>4,448</td>
<td>2,761</td>
</tr>
<tr>
<td>Other project costs (1):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personnel costs</td>
<td>$ 2,250</td>
<td>$ 2,193</td>
</tr>
<tr>
<td>Other costs (2)</td>
<td>1,379</td>
<td>681</td>
</tr>
<tr>
<td>Total</td>
<td>$ 3,629</td>
<td>$ 2,874</td>
</tr>
<tr>
<td>Total research and development costs</td>
<td>$ 8,077</td>
<td>$ 5,634</td>
</tr>
</tbody>
</table>

(1) Other project costs are leveraged across multiple programs.
(2) Other costs include facility, supply, consultant and overhead costs that support multiple programs.

**General and administrative expenses**

<table>
<thead>
<tr>
<th>General and administrative expenses</th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td></td>
<td>In thousands</td>
<td></td>
</tr>
<tr>
<td>General and administrative expenses</td>
<td>15,786</td>
<td>4,462</td>
</tr>
</tbody>
</table>

General and administrative expenses were $15.8 million for the year ended December 31, 2016 compared with $4.5 million for the year ended December 31, 2015, an increase of $11.3 million. The increase was principally attributable to professional fees incurred in connection with the negotiation and completion of the Transaction ($3.9 million), higher personnel and stock-based compensation costs ($2.2 million), severance costs ($1.7 million), lease termination fees ($1.2 million), accounting fees ($500,000), as well as costs associated with being a public company. We expect that we will incur increased accounting, audit, legal, regulatory, compliance, and investor and public relations expenses associated with operating as a public company.

**Other (income) expense, net**

<table>
<thead>
<tr>
<th>Other (income) expense, net</th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td></td>
<td>In thousands</td>
<td></td>
</tr>
<tr>
<td>Other (income) expense, net</td>
<td>$ (205)</td>
<td>$ (271)</td>
</tr>
</tbody>
</table>

Other (income) expense, net totaled $205,000 of income for the year ended December 31, 2016 compared with income of $271,000 for the year ended December 31, 2015, a difference of $66,000. The difference resulted from changes in currency exchange rates between the two periods.

**Interest expense, net**

<table>
<thead>
<tr>
<th>Interest expense, net</th>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td></td>
<td>In thousands</td>
<td></td>
</tr>
<tr>
<td>Interest expense, net</td>
<td>$ (1,319)</td>
<td>$ (1,722)</td>
</tr>
</tbody>
</table>
Interest expense, net totaled $1.3 million for the year ended December 31, 2016 compared with $1.7 million for 2015, a decrease of $403,000. The decrease was attributable to lower interest on convertible loan notes issued in 2014 and 2015 due to their conversion into equity in connection with the completion of the Transaction. All accrued and unpaid interest on the convertible loan notes as of November 3, 2016 was waived by the holders of the notes.

### Non-operating expense

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In thousands</td>
</tr>
<tr>
<td>Non-operating expense</td>
<td>$(2,675)</td>
</tr>
</tbody>
</table>

Non-operating expense was $2.7 million for the year ended December 31, 2016 compared with $320,000 for the year ended December 31, 2015, an increase of $2.4 million. The increase reflected adjustments for the 2016 period to fair value for derivative liabilities associated with outstanding convertible loan notes that were converted as part of the Transaction, as well as mark-to-market adjustments on warrants.

### Income tax

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In thousands</td>
</tr>
<tr>
<td>Income tax</td>
<td>$62</td>
</tr>
</tbody>
</table>

Income tax expense was $62,000 for the year ended December 31, 2016 compared to $0 for the year ended December 31, 2015.

### Liquidity and Capital Resources

#### Sources of Liquidity

We do not expect to generate revenue from product sales unless and until we or a licensee obtains regulatory approval of and commercializes its current or any potential future product candidates. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of and seek regulatory approvals for our product candidates. We are subject to all of the risks applicable to the development of new pharmaceutical products and may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may harm our business. We expect that, having become a public company upon completion of the Transaction in November 2016, we will incur additional costs associated with operating as a public company and anticipate that we will need substantial additional funding to complete development of and potentially commercialize our product candidates.

Our operations have historically been financed primarily through issuances of preference shares or convertible debt, upfront fees paid upon entering into license agreements, payments received upon the achievement of specified milestone events under license agreements, grants and venture debt borrowings. Our primary uses of capital are, and we expect will continue to be, personnel-related costs, third party expenses associated with our research and development programs, including the conduct of clinical trials, and manufacturing-related costs for our product candidates.

As of December 31, 2016, our cash and cash equivalents were approximately $29.9 million.

In November 2016, we completed the Transaction and, immediately prior to the Transaction, an associated equity financing of $10.0 million. The Transaction and the equity financing, together, provided us a net capital infusion of approximately $30 million.

In October 2015, we (Albireo Limited) entered into a loan agreement with certain of our shareholders and their affiliates and members of management and executed a related convertible loan instrument, which provided 5,000,000 $1.00 unsecured convertible loan notes denominated in U.S. dollars. We issued $3.5 million of the convertible loan notes as of December 31, 2015. Interest on the convertible loan notes accrued at a rate of 8% per annum. Unless waived, interest would have become payable on any of the outstanding convertible loan notes shortly after maturity or, if the principal amount was converted into shares, shortly after the later of such conversion into shares or repayment of the Kreos loan facility described below. The convertible loan notes were to mature on September 30, 2020 and could have been repaid earlier under certain circumstances. In connection with the Transaction, these notes were converted into 297,372 shares of our common stock based on a conversion price of $19.50 and the accrued interest was waived.
In December 2014, we (Albireo Limited) executed a convertible loan instrument, which provided 1,251,000 €1.00 unsecured convertible loan notes denominated in Euros and was subsequently amended in October 2015. We issued all of the convertible loan notes to certain of our shareholders and their affiliates. Unless waived, interest on the convertible loan notes would have accrued at a rate of 8% per annum. Interest would have become payable on any of the outstanding convertible loan notes shortly after maturity or, if the principal amount was converted into shares, shortly after the later of such conversion into shares or repayment of the Kreos loan facility described below. The convertible loan notes would have matured on December 18, 2019 and could have been repaid earlier at their nominal value of €1.3 million under certain circumstances. In connection with the Transaction, these notes were converted into 116,883 share of our common stock based on a conversion price of $19.50 and the accrued interest was waived.

Also in December 2014, we (Albireo Limited) entered into a loan facility agreement with Kreos enabling us to borrow up to €6.0 million ($7.3 million). The loan facility has a term of 36 months, with principal and interest payable monthly after an initial six-month interest-only period, at an annual rate of 11.5%. In addition, we are required to make an end-of-loan payment equal to 1.25% of the amounts lent by Kreos. On the date of the agreement, we borrowed the full €6.0 million ($7.3 million). In February 2016, we amended the loan facility to reduce principal repayments for a period of six months. As of December 31, 2016, the outstanding balance due on the loan facility, including interest and the end-of-loan payment, was €3.6 million ($3.8 million based on the Euro to U.S. dollar exchange rate at December 31, 2016).

In July 2012, we (Albireo AB) entered into a license agreement with Ferring for the development and commercialization of elobixibat outside of the territories licensed to EA Pharma in April 2012. Pursuant to the agreement, Ferring commenced a Phase 3 clinical program of elobixibat to treat CIC. In May 2014, Ferring stopped two Phase 3 clinical trials of elobixibat that Ferring had been conducting due to an issue related to the distribution of study drug to study sites that was unrelated to the performance of elobixibat. Subsequently, in March 2015, Ferring terminated the agreement, effective in September 2015. Prior to the termination of the agreement, we had received approximately $46.7 million in upfront and milestone payments from Ferring under the agreement. There was no refund of the upfront license fee or milestone fees received through the date of termination, in accordance with the agreement. The agreement is not a source of potential future funding.

In April 2012, we (Albireo AB) entered into a license agreement with EA Pharma for the development and commercialization of elobixibat in specified countries in Asia. Albireo AB subsequently transferred the agreement to its wholly owned subsidiary, Elobix AB, and the agreement was amended in January 2015 and April 2016. As of December 31, 2016, we have received approximately $34.7 million in upfront and milestone payments from EA Pharma under this agreement. We are eligible to receive additional payments of up to €13.3 million under the amended agreement ($14.0 million based on the Euro to U.S. dollar exchange rate at December 31, 2016) if specified regulatory events are achieved for elobixibat and up to ¥3.5 billion ($29.9 million based on the Japanese Yen to U.S. dollar exchange rate at December 31, 2016) if specified sales milestones are achieved for elobixibat. We are also eligible for stepped royalties at rates beginning in the high single digits on any future elobixibat product sales.

Cash Flows

**Years ended December 31, 2016 and December 31, 2015**

<table>
<thead>
<tr>
<th>Net cash (used in) provided by:</th>
<th>Year Ended December 31, 2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating activities</td>
<td>$ (8,784)</td>
<td>(4,748)</td>
</tr>
<tr>
<td>Investing activities</td>
<td>25,480</td>
<td></td>
</tr>
<tr>
<td>Financing activities</td>
<td>7,612</td>
<td>2,206</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$ 24,308</td>
<td>(2,542)</td>
</tr>
<tr>
<td>Effect of exchange rate changes on cash and cash equivalents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net (decrease) increase in cash and cash equivalents</td>
<td>24,811</td>
<td>$ (3,055)</td>
</tr>
</tbody>
</table>

Operating activities

Net cash used in operating activities for the year ended December 31, 2016 was $8.8 million compared to $4.7 million for 2015. This increase was primarily due to an increase in trade receivables, accrued expenses and stock-based compensation expense offset by a decrease in trade payables.
Investing activities

Net cash provided by investing activities was $25.5 million for the year ended December 31, 2016 compared to $0 for 2015. This increase was due to the cash acquired in the Transaction.

Financing activities

Financing activities for the year ended December 31, 2016 was $7.6 million compared to $2.2 million for 2015. In 2015, we issued $3.5 million in convertible loan notes, offset by principal payments of $1.2 million on our loan facility. In 2016, we received $9.7 million in net proceeds from an equity financing associated with the Transaction, $40,000 from issuance of Ordinary A shares and $39,000 from issuance of warrants, offset by principal payments of $2.2 million on our loan facility.

Funding Requirements

Cash used to fund operating expenses is affected by the timing of when we pay expenses, as reflected in the change in our outstanding accounts payable and accrued expenses. We believe that our existing cash and cash equivalents will be sufficient to meet our projected operating requirements through at least mid 2018. However, our operating plans may change as a result of many factors, including those described below and we may need additional funds sooner than planned to meet operational needs and capital requirements. In addition, if the conditions for raising capital are favorable we may seek to raise additional funds at any time.

Our future funding requirements will depend on many factors, including the following:

- the costs, design, timing of initiation, duration and any potential delays of the planned Phase 3 clinical trial of A4250;
- whether we will be required to conduct additional activities beyond those currently contemplated to establish the characteristics of a positive response on the patient-reported and caregiver-reported outcome instruments to assess pruritus that we are developing for potential use in the planned PFIC trial;
- the scope, number, progress, duration, cost, results and timing of clinical trials and nonclinical studies of our current or future product candidates;
- whether and to what extent milestone events are achieved under our license agreement with EA Pharma or any potential future licensee or collaborator;
- the outcomes and timing of regulatory reviews, approvals or other actions;
- our ability to obtain marketing approval for our product candidates;
- our ability to establish and maintain additional licensing, collaboration or similar arrangements on favorable terms and whether and to what extent we retain development or commercialization responsibilities under any new licensing, collaboration or similar arrangement;
- the success of any other business, product or technology that we acquire or in which we invest;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio;
- our ability to manufacture any approved products on commercially reasonable terms;
- our ability to establish a sales and marketing organization or suitable third-party alternatives for any approved product;
- the number and characteristics of product candidates and programs that we pursue;
- the costs of acquiring, licensing or investing in businesses, product candidates and technologies;
- our need and ability to hire additional management and scientific and medical personnel;
- the costs to operate as a public company in the United States, including the need to implement additional financial and reporting systems and other internal systems and infrastructure for our business;
- market acceptance of our product candidates, to the extent any are approved for commercial sale; and
- the effect of competing technological and market developments.

We cannot determine precisely the completion dates and related costs of our development programs due to inherent uncertainties in outcomes of clinical trials and the regulatory approval process. We cannot be certain that we will be able to successfully complete our research and development programs or establish licensing, collaboration or similar arrangements for our product candidates. Our failure or the failure of any current or potential future licensee to complete research and development programs for our product candidates could have a material adverse effect on our financial position or results of operations.
We expect to continue to incur losses. Our ability to achieve and maintain profitability is dependent upon the successful development, regulatory approval and commercialization of our product candidates and achieving a level of revenues adequate to support our cost structure. We may never achieve profitability.

If the conditions for raising capital are favorable, we may seek to finance future cash needs through public or private equity or debt offerings or other financings. We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on January 10, 2017 and pursuant to which we registered for sale up to $100 million of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. Any such financing could occur at any time. Additionally, if we need to raise additional capital to fund our operations, complete our ongoing and planned clinical trials, or potentially commercialize our product candidates, we may likewise seek to finance future cash needs through public or private equity or debt offerings or other financings. The necessary funding may not be available to us on acceptable terms or at all.

The sale of additional equity or convertible debt securities may result in significant dilution to our stockholders, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of additional debt financing would result in debt service obligations and the instruments governing such debt may provide for operating and financing covenants that would restrict our operations. We may also seek to finance future cash needs through potential future licensing, collaboration or similar arrangements. These arrangements may not be available on acceptable terms or at all, and we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our development programs or obtain funds through third-party arrangements that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not required for smaller reporting companies.
Item 8.  FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

ALBIREO PHARMA, INC.

Index to Consolidated Financial Statements and Financial Statement Schedules

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reports of independent registered public accounting firm</td>
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<td>Notes to Consolidated Financial Statements</td>
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</tbody>
</table>
Item 9.  **CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

Not applicable.

**Item 9A. CONTROLS AND PROCEDURES**

**Evaluation of Disclosure Controls and Procedures**

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Form 10-K, have concluded that, based on such evaluation and as discussed below, our disclosure controls and procedures were not effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

**Management’s Report on Internal Control over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our 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. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our 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. 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.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016 and, in making this assessment, used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Because of the material weakness described below, our management believes that, as of December 31, 2016, our internal control over financial reporting was not effective based on those criteria.

In connection with the audit of our 2016 financial statements, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting, specifically a lack of controls over the identification and review of complex accounting issues involving significant judgment or estimates in the financial statement closing process resulting from our limited in-house accounting and finance team. We currently rely on consultants and external advisors to provide assistance with financial reporting in accordance with the requirements of U.S. GAAP and the rules and regulations of the SEC, and these consultants and external advisors may not have direct knowledge of all of our business, transactions and contracts. Specifically, we and our independent registered public accounting firm determined that we did not have sufficient resources with U.S. GAAP and SEC financial reporting knowledge to ensure a timely and sufficient financial statement close process that includes resolution of complex accounting issues involving significant judgment and estimates.
We are working to remediate the material weakness. In particular, we hired a full-time chief financial officer in July 2016 and a controller in March 2017 and plan to develop and implement formal policies, processes and documentation procedures relating to our financial reporting. We estimate that the material weakness will be remediated prior to filing our annual report on Form 10-K for the year ending December 31, 2017.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during the fourth quarter of our last fiscal year that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. OTHER INFORMATION

Not applicable.
PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions “Management and Corporate Governance,” “Section 16(a) Beneficial Ownership Reporting Compliance,” and “Code of Conduct and Ethics” in our proxy statement for the 2017 annual meeting of stockholders.

Item 11. EXECUTIVE COMPENSATION

The response to this item is incorporated by reference from the discussion responsive thereto under the caption “Executive Officer and Director Compensation” in our proxy statement for the 2017 annual meeting of stockholders.

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The response to this item is incorporated by reference from the discussion responsive thereto under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our proxy statement for the 2017 annual meeting of stockholders.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions “Certain Relationships and Related Person Transactions” and “Management and Corporate Governance” in our proxy statement for the 2017 annual meeting of stockholders.

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the caption “Ratification of Selection of Independent Registered Public Accounting Firm” in our proxy statement for the 2017 annual meeting of stockholders.
ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

Item 15(a). The following documents are filed as part of this Annual Report on Form 10-K:

Item 15(a)(1) See “Index to Consolidated Financial Statements and Financial Statement Schedules” at Item 8 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

Item 15(a)(3) The list of exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding such exhibits and is incorporated by reference in this Item 15(a)(3).

ITEM 16. FORM 10-K SUMMARY.

None.
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.

ALBIREO PHARMA, INC.

Date: March 27, 2017

By: /s/ Ronald H.W. Cooper
    Ronald H.W. Cooper
    President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated below and on the dates indicated.

<table>
<thead>
<tr>
<th>Signatures</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>/s/ Ronald H.W. Cooper</td>
<td>President, Chief Executive Officer and Director (principal executive officer)</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Thomas A. Shea</td>
<td>Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ David Chiswell, Ph.D.</td>
<td>Chairman of the Board</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Julia R. Brown</td>
<td>Director</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Michael Gutch, Ph.D.</td>
<td>Director</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Denise Scots-Knight, Ph.D.</td>
<td>Director</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Heather Preston, M.D.</td>
<td>Director</td>
<td>March 27, 2017</td>
</tr>
<tr>
<td>/s/ Davey S. Scoon</td>
<td>Director</td>
<td>March 27, 2017</td>
</tr>
</tbody>
</table>
The Board of Directors and Stockholders of Albireo Pharma, Inc.

We have audited the accompanying consolidated balance sheet of Albireo Pharma, Inc. (the “Company”) as of December 31, 2015, and the related consolidated statement of operations, comprehensive loss, convertible preference shares and stockholders’ equity (deficit), and cash flows for the year then ended. These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company’s internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2015 and the consolidated results of its operations and its cash flows for the year then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
Reading, England

13 July 2016
The Board of Directors and Stockholders of Albireo Pharma, Inc.

We have audited the accompanying consolidated balance sheet of Albireo Pharma, Inc. as of December 31, 2016, and the related consolidated statement of operations, comprehensive loss, convertible preference shares and stockholders’ equity (deficit) and cash flows for the year then ended. These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement. We were not engaged to perform an audit of the Company’s internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the consolidated financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall consolidated financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of Albireo Pharma, Inc. as of December 31, 2016, and the consolidated results of its operations and its cash flows for the year then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
Boston, Massachusetts
March 27, 2017
<table>
<thead>
<tr>
<th>ASSETS</th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$29,931</td>
<td>$5,120</td>
</tr>
<tr>
<td>Trade receivables</td>
<td>26</td>
<td>1,272</td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>560</td>
<td>346</td>
</tr>
<tr>
<td>Other receivables</td>
<td>344</td>
<td>202</td>
</tr>
<tr>
<td><strong>Total current assets</strong></td>
<td>$30,861</td>
<td>$6,940</td>
</tr>
<tr>
<td>Equipment, net</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>Intangible assets</td>
<td>150</td>
<td>—</td>
</tr>
<tr>
<td>Goodwill</td>
<td>18,110</td>
<td>—</td>
</tr>
<tr>
<td>Other noncurrent assets</td>
<td>518</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$49,660</td>
<td>$6,974</td>
</tr>
</tbody>
</table>

| LIABILITIES, CONVERTIBLE PREFERENCE SHARES AND STOCKHOLDERS’ EQUITY (DEFICIT) | | |
| Current liabilities:                  |                  |                  |
| Trade payables                        | $972             | $1,929           |
| Accrued expenses                      | 7,548            | 2,576            |
| Advances from licensees               | 37               | 37               |
| Long-term debt, current portion       | 3,075            | 2,514            |
| Common stock warrant liability        | 25               | —                |
| Warrants liability                    | 844              | 1,163            |
| Other liabilities                     | 207              | 63               |
| **Total current liabilities**         | $12,708          | 8,282            |
| Long-term debt                        | —                | 4,866            |
| Derivative liabilities                | —                | 2,047            |
| **Total liabilities**                 | $12,708          | 15,195           |

| Temporary Equity:                      |                  |                  |
| Convertible preference shares, $0.013 par value per share — 0 and 44,945,080 shares authorized at December 31, 2016 and December 31, 2015; 0 and 39,354,000 shares issued and outstanding at December 31, 2016 and December 31, 2015 | — | 520 |
| Stockholders’ equity (deficit):        |                  |                  |
| Ordinary shares, $0.013 par value per share — 0 and 265,650 authorized and issued and outstanding at December 31, 2016 and December 31, 2015 | — | 50 |
| Common stock, $0.01 par value per share — 200,000,000 and 0 authorized at December 31, 2016 and December 31, 2015; 6,292,644 and 0 issued and outstanding at December 31, 2016 and December 31, 2015 | 63 | — |
| Additional paid in capital             | 61,338           | —                |
| Accumulated other comprehensive income | 1,496            | 804              |
| Accrued deficit                        | (25,945)         | (9,595)          |
| **Total stockholders’ equity (deficit)** | 36,952           | (8,741)          |

| Total liabilities, convertible preference shares and stockholders’ equity (deficit) | $49,660 | $6,974 |

See accompanying Notes to Consolidated Financial Statements.
## Albireo Pharma, Inc.

### Consolidated Statements of Operations

*(in thousands, except share and per share data)*

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenue</strong></td>
<td>$11,364</td>
<td>$5,099</td>
</tr>
<tr>
<td><strong>Operating expenses:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>8,077</td>
<td>5,634</td>
</tr>
<tr>
<td>General and administrative</td>
<td>15,786</td>
<td>4,462</td>
</tr>
<tr>
<td>Other (income) expense, net</td>
<td>(205)</td>
<td>(271)</td>
</tr>
<tr>
<td><strong>Total operating expenses</strong></td>
<td>23,658</td>
<td>9,825</td>
</tr>
<tr>
<td><strong>Operating loss</strong></td>
<td>(12,294)</td>
<td>(4,726)</td>
</tr>
<tr>
<td><strong>Interest expense, net</strong></td>
<td>(1,319)</td>
<td>(1,722)</td>
</tr>
<tr>
<td><strong>Non-operating expense, net</strong></td>
<td>(2,675)</td>
<td>(320)</td>
</tr>
<tr>
<td><strong>Net loss before income taxes</strong></td>
<td>(16,288)</td>
<td>(6,768)</td>
</tr>
<tr>
<td><strong>Income tax</strong></td>
<td>62</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>$ (16,350)</td>
<td>$ (6,768)</td>
</tr>
<tr>
<td><strong>Net loss per share attributable to holders of common stock:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic and diluted</td>
<td>$ (13.19)</td>
<td>$ (25.49)</td>
</tr>
<tr>
<td><strong>Weighted-average shares outstanding:</strong></td>
<td>1,239,694</td>
<td>265,560</td>
</tr>
<tr>
<td>Basic and diluted</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See accompanying Notes to Consolidated Financial Statements.

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Albireo Pharma, Inc.

Consolidated Statements of Comprehensive Loss
(in thousands)

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(16,350)</td>
</tr>
<tr>
<td>Other comprehensive income:</td>
<td></td>
</tr>
<tr>
<td>Foreign currency translation adjustment</td>
<td>692</td>
</tr>
<tr>
<td>Total other comprehensive (loss) income</td>
<td>692</td>
</tr>
<tr>
<td>Total comprehensive loss</td>
<td>$(15,658)</td>
</tr>
</tbody>
</table>

See accompanying Notes to Consolidated Financial Statements.

F-5
### Albireo Pharma, Inc.

**Consolidated Statements of Convertible Preference Shares and Stockholders' Equity (Deficit)**

*(in thousands, except share amounts)*

<table>
<thead>
<tr>
<th>Convertible Preference Shares</th>
<th>Ordinary Shares</th>
<th>Common Stock</th>
<th>Additional Paid-In Capital</th>
<th>Accumulated Other Comprehensive Income</th>
<th>Accumulated Deficit</th>
<th>Total Stockholders' Equity (Deficit)</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>Balance—December 31, 2014</td>
<td>39,354,000</td>
<td>265,560</td>
<td>50</td>
<td>—</td>
<td>451</td>
<td>(2,827)</td>
</tr>
<tr>
<td>Other comprehensive income</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>353</td>
<td>$353</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>$(6,768)</td>
</tr>
<tr>
<td>Balance—December 31, 2015</td>
<td>39,354,000</td>
<td>265,560</td>
<td>50</td>
<td>—</td>
<td>—</td>
<td>$(6,768)</td>
</tr>
<tr>
<td>Issuance of Ordinary A shares</td>
<td>—</td>
<td>—</td>
<td>42,726</td>
<td>6</td>
<td>34</td>
<td>$40</td>
</tr>
<tr>
<td>Issuance of warrants</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>39</td>
<td>$39</td>
</tr>
<tr>
<td>Issuance of Series C preference shares</td>
<td>9,708,740</td>
<td>9,655</td>
<td>—</td>
<td>—</td>
<td>39</td>
<td>—</td>
</tr>
<tr>
<td>Conversion of 2014 and 2015 conversion loans</td>
<td>5,918,777</td>
<td>8,074</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>$39</td>
</tr>
<tr>
<td>Notes to common stock</td>
<td>(54,981,517)</td>
<td>(18,249)</td>
<td>—</td>
<td>—</td>
<td>3,846,083</td>
<td>38</td>
</tr>
<tr>
<td>Share exchange and adjustment for reverse acquisition</td>
<td>—</td>
<td>—</td>
<td>(308,286)</td>
<td>(56)</td>
<td>2,446,561</td>
<td>25</td>
</tr>
<tr>
<td>Share based compensation expense</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1,138</td>
<td>—</td>
</tr>
<tr>
<td>Other comprehensive loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>692</td>
<td>$692</td>
</tr>
<tr>
<td>Net loss</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>$(16,350)</td>
</tr>
<tr>
<td>Balance—December 31, 2016</td>
<td>—</td>
<td>—</td>
<td>6,292,644</td>
<td>63</td>
<td>61,338</td>
<td>$(25,945)</td>
</tr>
</tbody>
</table>

See accompanying Notes to Consolidated Financial Statements.

F-6
## Albireo Pharma, Inc.

### Consolidated Statements of Cash Flows

(in thousands)

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cash flows from operating activities:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(16,350)</td>
<td>$(6,768)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash used in operating activities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accretion of debt discount and amortization of issuance costs</td>
<td>1,065</td>
<td>777</td>
</tr>
<tr>
<td>Depreciation and amortization</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Loss on settlement of 2014 Convertible Loans and 2015 Convertible Loans</td>
<td>2,095</td>
<td>—</td>
</tr>
<tr>
<td>Change in fair value of financial instruments</td>
<td>(13)</td>
<td>320</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>1,138</td>
<td>—</td>
</tr>
<tr>
<td>Changes in operating assets and liabilities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trade receivables</td>
<td>1,246</td>
<td>(1,258)</td>
</tr>
<tr>
<td>Prepaid expenses and other current assets</td>
<td>(214)</td>
<td>(282)</td>
</tr>
<tr>
<td>Other receivables</td>
<td>(142)</td>
<td>(80)</td>
</tr>
<tr>
<td>Other non current assets</td>
<td>183</td>
<td>—</td>
</tr>
<tr>
<td>Trade payables</td>
<td>(1,164)</td>
<td>1,319</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>3,214</td>
<td>1,196</td>
</tr>
<tr>
<td>Other liabilities</td>
<td>144</td>
<td>13</td>
</tr>
<tr>
<td><strong>Net cash used in operating activities</strong></td>
<td>(8,784)</td>
<td>(4,748)</td>
</tr>
<tr>
<td><strong>Cash flows from investing activities:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchase of property, plant and equipment</td>
<td>(3)</td>
<td>—</td>
</tr>
<tr>
<td>Cash acquired in business combinations</td>
<td>25,483</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net cash provided by investing activities</strong></td>
<td>25,480</td>
<td>—</td>
</tr>
<tr>
<td><strong>Cash flows from financing activities:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proceeds from issuance of Ordinary A shares</td>
<td>40</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of warrants, net of issuance costs</td>
<td>39</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of convertible loan notes, net</td>
<td>—</td>
<td>3,429</td>
</tr>
<tr>
<td>Proceeds from issuance of Series C preference shares</td>
<td>9,690</td>
<td>—</td>
</tr>
<tr>
<td>Payments of principal on borrowings</td>
<td>(2,157)</td>
<td>(1,223)</td>
</tr>
<tr>
<td><strong>Net cash provided by in financing activities</strong></td>
<td>7,612</td>
<td>2,206</td>
</tr>
<tr>
<td><strong>Effect of exchange rate changes on cash and cash equivalents</strong></td>
<td>503</td>
<td>(513)</td>
</tr>
<tr>
<td><strong>Net increase (decrease) in cash and cash equivalents</strong></td>
<td>24,811</td>
<td>(3,055)</td>
</tr>
<tr>
<td><strong>Cash and cash equivalents—beginning of period</strong></td>
<td>5,120</td>
<td>8,175</td>
</tr>
<tr>
<td><strong>Cash and cash equivalents—end of period</strong></td>
<td>$29,931</td>
<td>$5,120</td>
</tr>
</tbody>
</table>

### Supplemental disclosures of cash flow information:

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash paid for interest</td>
<td>$450</td>
<td>$761</td>
</tr>
<tr>
<td>Settlement of derivative liabilities</td>
<td>2,343</td>
<td>—</td>
</tr>
<tr>
<td>Conversion of convertible preference shares and the 2014 and 2015 Convertible Notes to common stock</td>
<td>8,563</td>
<td>—</td>
</tr>
<tr>
<td>Value of shares issued to acquire Biodel</td>
<td>41,886</td>
<td>—</td>
</tr>
</tbody>
</table>

See accompanying Notes to Consolidated Financial Statements.
Albireo Pharma, Inc.
Notes to Consolidated Financial Statements

1. Summary of significant accounting policies and basis of presentation

Organization and Share Exchange

Albireo Pharma, Inc. (Parent), together with its direct and indirect subsidiaries (the Company), is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel bile acid modulators to treat orphan pediatric liver diseases and other liver and gastrointestinal diseases and disorders. The Company’s clinical pipeline includes two Phase 2 product candidates, plus a third product candidate for which an application for regulatory approval has been filed in Japan. A4250, the Company’s lead product candidate, is in development initially for the treatment of progressive familial intrahepatic cholestasis (PFIC), a rare, life-threatening genetic disorder affecting young children. A4250 is currently being evaluated in a Phase 2 clinical trial in children with chronic cholestasis.

Prior to November 3, 2016, Parent’s name was Biodel Inc. (Biodel). On that date, Biodel effected a 1-for-30 reverse stock split of its common stock (Reverse Stock Split) and completed a share exchange transaction with Albireo Limited, a limited company domiciled in London, United Kingdom, in accordance with the terms of an Amended and Restated Share Exchange Agreement (the Agreement), dated as of July 13, 2016, by and among Biodel, Albireo Limited and the shareholders and noteholders of Albireo Limited. Pursuant to the Agreement, each holder of shares or notes convertible into shares of Albireo Limited received newly issued shares of Biodel common stock and Albireo Limited became a wholly owned subsidiary of Biodel (the Transaction). Following completion of the Transaction, the business of Albireo Limited became the business of Parent and Parent changed its name to Albireo Pharma, Inc.

For accounting purposes, the Transaction was treated as a “reverse acquisition” and Albireo Limited was considered the accounting acquirer. Accordingly, these Consolidated Financial Statements reflect the historical results of Albireo Limited and its direct and indirect subsidiaries prior to completion of the Transaction and do not include the historical results of Biodel prior to completion of the Transaction. See Note 6. Except as provided in Note 10, all 2016 and 2015 share and per share information has been retroactively adjusted to reflect the exchange of shares in the Transaction based on an exchange ratio of 0.06999 and, where applicable, the Reverse Stock Split.

Basis of presentation

These audited Consolidated Financial Statements have been prepared in conformity with generally accepted accounting principles in the United States (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB). Any reference in these Consolidated Financial Statements to common stock or options or warrants to purchase shares of common stock of the Company means the common stock or options or warrants to purchase shares of common stock of Parent. Any reference in these Consolidated Financial Statements to common stock means, for periods prior to November 3, 2016, Ordinary shares of Albireo Limited.

Principles of consolidation

The accompanying Consolidated Financial Statements include the accounts of Parent and its direct or indirect wholly owned subsidiaries, Albireo Limited, Albireo AB, Elobix AB and Albireo, Inc. All intercompany balances and transactions have been eliminated in consolidation. In the opinion of management, all adjustments (including normal recurring accruals) considered necessary for fair presentation have been included in the Consolidated Financial Statements.

Foreign currency translation

Functional and presentation currency

Items included in the financial statements of each entity comprising the Company are measured using the currency of the primary economic environment in which the entity operates (the functional currency). The functional currency for Parent and Albireo, Inc. is the U.S. Dollar (USD), the functional currency for Albireo Limited and Elobix AB is the Euro, and the functional currency for Albireo AB is the Swedish Krona (SEK). The Company consolidates its financial statements in USD.
Transactions and balances

Foreign currency transactions in each entity comprising the Company are translated into the functional currency of the entity using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized within Other income (expense), net in the Consolidated Statements of Operations.

The results and financial position of the Company and its subsidiaries that have a functional currency different from the presentation currency are translated into the presentation currency as follows:

a. assets and liabilities presented are translated at the closing exchange rate as of December 31, 2016 and 2015;

b. income and expenses for each statement of comprehensive loss are translated at annual average exchange rates that are relevant for the respective period reported;

c. significant transactions use the exchange rate on the date of the transaction; and

d. all resulting exchange differences arising from such translation are recognized directly in other comprehensive loss and presented as a separate component of equity.

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Management must apply significant judgment in this process. Actual results could materially differ from those estimates.

Segment information

The Company’s entire business is managed by a single management team, which reports to the Chief Executive Officer. No separate lines of business or separate business entities have been identified with respect to any product candidate or geographical market and one operating segment is currently disclosed in the Company’s internal reporting.

Accordingly, the Company has one reporting segment which is the research and development of novel treatments for liver and gastrointestinal diseases and disorders.

Cash and cash equivalents

The Company considers all short-term highly liquid investments with an original maturity at the date of purchase of three months or less to be cash equivalents.

Concentration of risk

Credit risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash and cash equivalents and accounts receivable. For banks and financial institutions, only independent financial institutions with high credit ratings are engaged. The Company’s license agreements are with established and reputable pharmaceutical companies and, historically, the Company has not needed to impair accounts receivable.

Concentration of revenue and accounts receivable

The Company generally does not require collateral or other security in support of accounts receivable. Allowances are provided for individual accounts receivable when the Company becomes aware of a customer’s inability to meet its financial obligations, such as in the case of bankruptcy, deterioration in the customer’s operating results or change in financial position. If circumstances related to a customer change, estimates of the recoverability of receivables would be further adjusted. The Company also considers broad factors in evaluating the sufficiency of its allowances for doubtful accounts, including the length of time receivables are past due, significant one-time events, creditworthiness of customers and historical experience. There is no allowance for doubtful accounts as of December 31, 2016 or 2015.
Equipment, net

Equipment is stated at historical cost less depreciation and consists of computers, furniture and fixtures, and other equipment. Depreciation is computed using a straight-line method over the estimated useful lives, determined to be five years. Computers and other equipment purchased for less than $2,000 or the equivalent thereof are expensed immediately.

Gains and losses on disposals of equipment are determined by comparing the proceeds with the carrying amount and are recognized within Other income (expense), net in the Consolidated Statements of Operations.

Impairment of long-lived assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. In such instances, the recoverability of assets to be held and used is measured first by a comparison of the carrying amount of an asset group to future undiscounted net cash flows expected to be generated by the assets. If such assets are considered to be impaired, an impairment loss would be recognized if the carrying amount of the asset exceeds the fair value of the asset. There were no impairments recorded for the years ended December 31, 2016 and 2015.

Research and development expenses

Research and development costs are expensed as incurred and include primarily salaries, benefits and other staff-related costs; clinical trial and related clinical manufacturing costs; contract services and other outside costs.

The Company’s preclinical studies and clinical trials are performed by third-party contract research organizations (CROs). Some of these expenses are billed monthly for services performed, while others are billed based upon milestones achieved. For preclinical studies, the significant factors used in estimating accruals include the percentage of work completed to date and contract milestones achieved. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled and percentage of work completed to date or contract milestones achieved. The Company’s estimates are highly dependent upon the timeliness and accuracy of the data provided by the respective CROs regarding the status of the contracted activity, with adjustments made when deemed necessary.

Revenue recognition

Revenue is generated from the receipt of upfront or license fees, milestone payments and payments for procurement services that are made pursuant to out-licensing or related supply agreements.

Where an out-licensing arrangement of the Company involves the provision of multiple elements that may contain different remuneration arrangements such as upfront payments, milestone payments or product sales, the arrangement is assessed to determine whether separate delivery of the individual elements of such arrangement comprises more than one unit of accounting. The delivered elements are separated if (a) they have value to the licensee on a stand-alone basis, (b) there is objective and reliable evidence of the fair value of the undelivered element(s) and (c) if the arrangement includes a general right of return relative to the delivered element(s), delivery or performance of the undelivered element(s) is considered probable and is substantially in the control of the Company. Allocation of revenue to the different elements that require separate accounting is based on the separate selling prices determined for each component, and total consideration is then allocated pro rata across the components of the arrangement. If separate selling prices are not available, the Company will use its best estimate of such selling prices, consistent with the overall pricing strategy and relevant market factors.

The Company has determined that each element of its out-licensing agreements is a separate and distinct unit of accounting, and, as such, the fair value of each element has been subscribed and recognized as follows:

- Nonrefundable upfront payments received from the Company’s out-licensing agreements relating to technical expertise and intellectual property are recognized in income if all rights relating to the intellectual property and all obligations resulting from them have been relinquished under the contract terms and the Company has no continuing material obligation to perform under the agreement. However, if rights to the intellectual property continue to exist or obligations resulting from them have yet to be fulfilled, the payments received would be deferred until all rights and obligations have been fulfilled.
As of December 31, 2016, the Company had a license agreement with EA Pharma Co., Ltd. (EA Pharma, formerly Ajinomoto Pharmaceuticals Co., Ltd.), entered into in 2012, to develop a select product candidate (elobixibat) for registration and subsequent commercialization in select markets. The Company satisfied its material performance obligations under the agreement in 2012, upon the delivery of technical expertise and intellectual property rights to EA Pharma.

In March 2015, a second licensee of the Company (Ferring International Center S.A., or Ferring) gave notice of termination of its license agreement with the Company. The termination eliminated any prospect of future contingent income under that license agreement. There was no refund of the upfront license fee or milestone fees received by the Company through the date of termination, in accordance with the agreement.

Payments resulting from procurement services are recognized as revenue as the activities are performed and are presented on a net basis. Revenue is recorded on a net basis because the Company acts as an agent, as it does not have discretion to change suppliers and does not perform any part of the services or manufacture of the subject pharmaceutical ingredients. The costs associated with these activities are netted against the related revenue in the Consolidated Statements of Operations.

For certain contingent payments under research and development arrangements, the Company recognizes revenue using the milestone method. Under the milestone method, a payment that is contingent upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is an event: (i) that can be achieved based in whole or in part on either the Company’s performance or on the occurrence of a specific outcome resulting from the Company’s performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (iii) that would result in additional payments being due to the Company. The determination that a milestone is substantive requires estimation and judgment and is made at the inception of the arrangement. Milestones are considered substantive when the consideration earned from the achievement of the milestone is: (i) commensurate with either the Company’s performance to achieve the milestone or the enhancement of value of the item delivered as a result of a specific outcome resulting from the Company’s performance, (ii) related solely to past performance and (iii) reasonable relative to all deliverables and payment terms in the arrangement. In making the determination as to whether a milestone is substantive or not, management of the Company considers all facts and circumstances relevant to the arrangement, including factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the milestone, the level of effort and investment required to achieve the milestone and whether any portion of the milestone consideration is related to future performance or deliverables. The Company has evaluated each milestone specified under its license agreement with EA Pharma and its now-terminated license agreement with Ferring and determined the milestone to be substantive.

For the year ended December 31, 2016, the Company recognized in full into revenue nonrefundable payments of (a) $8.0 million received in April 2016 in connection with a renegotiated payment stream with EA Pharma linked to know-how and intellectual property delivered by the Company upon inception of the license agreement in 2012 and (b) $3.6 million triggered by the decision of EA Pharma to proceed with the preparation of a new drug application for elobixibat in Japan. The renegotiated payment stream was implemented via an amendment to the license agreement that did not change the contingent nature of the remaining deliverables or the parties’ respective obligations under the agreement.

Under the terms of the license agreement with EA Pharma, the Company was eligible as of December 31, 2016 to receive up to approximately (a) €13.3 million ($14.0 million based on the Euro to USD exchange rate at December 31, 2016) if specified regulatory events are achieved for elobixibat in Japan and (b) ¥3.5 billion ($29.9 million based on the Japanese Yen to USD exchange rate at December 31, 2016) if specified sales milestones are achieved for elobixibat following regulatory approval in any country in EA Pharma’s licensed territory. The likelihood that the Company will achieve any particular milestone event with respect to elobixibat in any particular period, or at all, is uncertain, and the Company may not earn any future milestone payment with respect to elobixibat in any particular period, or ever. In addition, the Company is eligible to receive stepped royalties beginning in the high single digits on any future elobixibat product sales. The Company will recognize royalty revenue in the period of sale of elobixibat, based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.
Stock-based compensation

The Company accounts for stock-based compensation awards in accordance with FASB ASC Topic 718, Compensation—Stock Compensation (ASC 718). ASC 718 requires all stock-based payments, including grants of stock options, to be recognized in the consolidated statements of operations based on their respective fair values.

The fair value of the Company’s stock options has been determined using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. For the year ended December 31, 2016, due to the lack of historical and implied volatility data of the Company’s common stock and, prior to completion of the Transaction, the Ordinary shares and Ordinary A shares of Albireo Limited, the expected volatility has been estimated based on the historical volatilities of peer companies in the Company’s industry that are publicly traded. The Company selected companies that it considers to have comparable characteristics to the Company, including enterprise value, risk profiles and position within the industry and with historical share price information sufficient to meet the expected term of the stock options. The historical volatility data has been computed using the daily closing prices for the selected companies.

Due to the lack of sufficient historical trade data, the Company used the “simplified” method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the award, to determine the expected term of stock options. For periods prior to completion of the Transaction, the risk-free interest rate for periods within the expected term of the option were based on the United Kingdom Government Bond rate with a maturity date commensurate with the expected term of the associated award. For the periods after completion of the Transaction, the risk-free interest rate for periods within the expected term of the option is based on the United States Government Bond rate with a maturity date commensurate with the expected term of the associated award. In addition, it is assumed that the Company will not pay dividends in the near future.

The Company’s stock-based awards are subject to either service-based or service and performance-based vesting conditions. Prior to the Transaction, the Company issued certain stock options with exercise prices denominated in a foreign currency (Euro) that were required to be accounted for as liabilities. The Company accounted for liability-classified stock-based awards based on the then-current fair values at each financial reporting date. Changes in the amounts attributed to these awards between the reporting dates were included in the Consolidated Statement of Operations. On November 3, 2016, these stock options were replaced with stock options denominated in USD. The replacement was accounted for as a modification and the awards are included in equity.

The Company records compensation expense for service-based awards over the vesting period of the award on a straight-line basis. For awards with service and performance based conditions, compensation related to the performance-based vesting conditions is recognized when achievement of the performance condition is considered probable and the compensation expense related to the service condition is recorded using the accelerated method.

Modifications to stock-based awards are treated as an exchange of the original award for a new award with total compensation equal to the grant-date fair value of the original award plus any incremental value of the modification. The incremental value is based on the excess of the fair value of the modified award over the fair value of the original award immediately before the modification.

Temporary equity

The Series A and B preference shares of Albireo Limited prior to completion of the Transaction are classified outside of Stockholders’ Equity (Deficit) on the basis that the shares were redeemable upon a liquidation event that could be forced by the holders of preference shares through their voting rights on the Albireo Limited Board of Directors. Any undeclared dividends are not recognized until the time it becomes probable that the preference shares will be redeemable. No dividends were recognized for either of the years ended December 31, 2016 or 2015. All preference shares of Albireo Limited were converted into Ordinary shares that were exchanged for shares of common stock of the Company as part of the Transaction.

Employee benefits

Pension obligations

The Company has defined contribution plans for its Sweden-based employees whereby the Company pays contributions to employee benefit or insurance plans on a mandatory, contractual or voluntary basis. The Company has no legal or constructive obligations to pay further contributions if the fund does not hold sufficient assets to pay all employees the benefits relating to employee service in the current and prior periods.
The Company has no further payment obligations once the contributions have been paid. The contributions are recognized as employee benefit expense when they are due. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

401(k)

The Company has a 401(k) retirement plan in which all U.S.-based employees are eligible to participate. The Company contributed $33,000 and $3,000 to the plan for the years ended December 31, 2016 and 2015, respectively. The Company matches employee contributions to the plan, on a per employee basis, up to 4% of each employee’s wages for the years ended December 31, 2016 and 2015.

Loss contingencies

Loss contingencies are recorded as liabilities when it is probable that a liability has occurred and the amount of loss is reasonably estimable. Disclosure is required when there is a reasonable possibility that an ultimate loss will be material. Contingent liabilities are often resolved over long periods of time. Estimating probable losses requires analysis that often depends on judgments about potential actions by third parties, such as regulators.

Income taxes

The Company accounts for income taxes in accordance with ASC 740, *Income Taxes* (ASC 740). Deferred income taxes are recorded for the expected tax consequences of temporary differences between the tax basis of assets and liabilities for financial reporting purposes and amounts recognized for income tax purposes. The Company records a valuation allowance to reduce its deferred tax assets to the amount of future tax benefit that is more likely than not to be realized.

Income tax expense consists of taxes currently payable and changes in deferred tax assets and liabilities calculated according to local tax rules. Deferred tax assets and liabilities are based on temporary differences that arise between carrying values used for financial reporting purposes and amounts used for taxation purposes of assets and liabilities and the future tax benefits of tax loss carry forwards. A deferred tax asset is recognized only to the extent that it is more likely than not that future taxable profits will be available against which the asset can be utilized.

Significant judgment is required in determining any valuation allowance recorded against deferred tax assets. In assessing the need for a valuation allowance, the Company considers all available evidence for each jurisdiction including past operating results, estimates of future taxable income and the feasibility of ongoing tax planning strategies. In the event that the Company changes its determination as to the amount of deferred tax assets that can be realized, the Company will adjust its valuation allowance with a corresponding impact to income tax expense in the period in which such determination is made.

The amount of deferred tax provided is calculated using tax rates in effect at the balance sheet date. The impact of tax law changes is recognized in periods when the change is enacted.

A two-step approach is applied pursuant to ASC 740 in the recognition and measurement of uncertain tax positions taken or expected to be taken in a tax return. The first step is to determine if the weight of available evidence indicates that it is more likely than not that the tax position will be sustained in an audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement.

The Company’s policy is to recognize interest and penalty expenses associated with uncertain tax positions as a component of income tax expense in the Consolidated Statements of Operations. As of the years ended December 31, 2016 and 2015, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Consolidated Statements of Operations.

Net loss per share

Basic net loss per share is calculated by dividing the net loss attributable to holders of common stock by the weighted average number of shares of common stock outstanding. Diluted net loss per share is calculated by dividing the net loss attributable to holders of common stock by the weighted-average number of shares of common stock outstanding. If the Company were in a net income position, diluted net income per share would be calculated by dividing the net income attributable to holders of common stock by the weighted-average number of shares of common stock plus dilutive common stock equivalents outstanding, including any dilutive effect from such shares.
For the years ended December 31, 2016 and 2015, common stock equivalents included convertible preference shares, stock options and warrants. The Company’s Convertible Loan Notes (see Note 13) were not included in common stock equivalents, as they were not readily convertible at the option of the respective holders.

**Goodwill and long-lived assets**

Goodwill is the excess of the purchase price in a business combination over the fair value of identifiable net assets acquired. Goodwill and certain other intangible assets having indefinite lives are not amortized to earnings, but instead are subject to periodic testing for impairment.

Goodwill and indefinite-lived intangible assets are assessed at least annually, but also whenever events or changes in circumstances indicate the carrying values may not be recoverable. Factors that could trigger an impairment review, include: (a) significant underperformance relative to historical or projected future operating results; (b) significant changes in the manner of use of the acquired assets or the strategy for the Company’s overall business; (c) significant negative industry or economic trends; (d) significant decline in the Company’s stock price for a sustained period; and (e) a decline in the Company’s market capitalization below net book value.

When performing the evaluation of goodwill for impairment, if the Company concludes qualitatively that it is more likely than not that the fair value of the reporting unit is not less than its carrying amount, then the two-step impairment test is not required. If the Company is unable to reach this conclusion, then it would perform the two-step impairment test. Initially, the fair value of the reporting unit is compared to its carrying amount. To the extent the carrying amount of a reporting unit exceeds the fair value of the reporting unit, the Company is required to perform a second step, as this is an indication that the reporting unit goodwill may be impaired. In this step, the Company compares the implied fair value of the reporting unit goodwill with the carrying amount of the reporting unit goodwill and recognizes a charge for impairment to the extent the carrying value exceeds the implied fair value. The implied fair value of goodwill is determined by allocating the fair value of the reporting unit to all of the assets (recognized and unrecognized) and liabilities of the reporting unit in a manner similar to a purchase price allocation. The residual fair value after this allocation is the implied fair value of the reporting unit goodwill.

There are inherent assumptions and estimates used in developing future cash flows requiring management judgment in applying these assumptions, including projecting revenues, interest rates and the cost of capital. Many of the factors used in assessing fair value are outside the Company’s control and it is reasonably likely that assumptions and estimates will change in future periods. These changes can result in future impairments. In the event the Company’s planning assumptions are modified and result in an impairment, the associated expense would be included in the Consolidated Statements of Operations, which could materially impact the Company’s results of operations.

In connection with the Transaction, the Company performed a valuation of the acquired goodwill and intangible assets and recorded $18.1 million of goodwill based on the fair values of the assets acquired and liabilities assumed. The Company will conduct an impairment assessment on October 1 each year taking a qualitative evaluation approach to determine if there are any adverse market factors or changes in circumstances indicating that the carrying value of goodwill as determined in connection with the Transaction may not be recoverable.

Assessment for possible impairment of long-lived assets is based on the Company’s ability to recover the carrying value of the long-lived asset from the expected future pre-tax cash flows. The expected future pre-tax cash flows are estimated based on historical experience, knowledge and market data. Estimates of future cash flows require the Company to make assumptions and to apply judgment, including forecasting future sales and expenses and estimating the useful lives of assets. If the expected future cash flows related to a long-lived asset are less than the asset’s carrying value, an impairment charge is recognized for the difference between estimated fair value and carrying value.

**Recently adopted accounting pronouncements**

In April 2015, the FASB issued ASU No. 2015-03, “Simplifying the Presentation of Debt Issuance Costs,” which updated guidance to clarify the required presentation of debt issuance costs. The updated guidance requires that debt issuance costs be presented in the balance sheet as a direct reduction from the carrying amount of the recognized debt liability, consistent with the treatment of debt discounts. Amortization of debt issuance costs is to be reported as interest expense. The recognition and measurement guidance for debt issuance costs is not affected by the updated guidance. The update requires retrospective application and represents a change in accounting principles. The updated guidance is effective for reporting periods beginning after December 15, 2015, with early adoption permitted. The Company elected to early adopt the ASU during 2015 and has recorded $0 and $42,000 of transaction costs as reduction of long-term debt as of December 31, 2016 and 2015, respectively.
In September 2014, the FASB issued ASU No. 2014-15, “Presentation of Financial Statements—Going Concern” (ASU No. 2014-15). The guidance addresses management’s responsibility to evaluate whether there is substantial doubt about an entity’s ability to continue as a going concern and to provide related footnote disclosures. Management’s evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The standard will be effective for the first interim period within annual reporting periods beginning after December 15, 2016 and for annual and interim periods thereafter. Early adoption is permitted. The Company early adopted this ASU during 2015 in its consolidated financial statements.

In November 2015, the FASB issued ASU No. 2015-17, “Balance Sheet Classification of Deferred Taxes,” (ASU 2015-17), which amends the accounting guidance related to balance sheet classification of deferred taxes. The amendment requires that deferred tax assets and liabilities be classified as noncurrent in the statement of financial position, thereby simplifying the current guidance that requires an entity to separate deferred tax assets and liabilities into current and noncurrent amounts. ASU 2015-17 will be effective beginning in the first quarter of fiscal year 2018. Early adoption is permitted. The amendment can be adopted either prospectively or retrospectively. The Company adopted this standard on a retrospective basis on December 31, 2016. There was no change or reclassification recorded to the prior year presentation as a result of adopting this standard.

Accounting pronouncements issued but not yet adopted

In May 2014, the FASB issued ASU No. 2014-09, “Revenue from Contracts with Customers: (Topic 606)” This ASU affects any entity that either enters into contracts with customers to transfer goods or services or enters into contracts for the transfer of nonfinancial assets unless those contracts are within the scope of other standards (e.g., insurance contracts or lease contracts). This ASU will supersede the revenue recognition requirements in ASC Topic 605, “Revenue Recognition,” and most industry-specific guidance. In addition, the existing requirements for the recognition of a gain or loss on the transfer of nonfinancial assets that are not in a contract with a customer (e.g., assets within the scope of ASC Topic 360, “Property, Plant, and Equipment,” and intangible assets within the scope of ASC Topic 350, “Intangibles—Goodwill and Other”) are amended to be consistent with the guidance on recognition and measurement (including the constraint on revenue) in this ASU. The core principle of the guidance is that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In July 2015, the FASB deferred the effective date of ASU 2014-09. This ASU will be effective for the Company on January 1, 2018 (for the Company’s 2018 fiscal year). The Company is currently evaluating the impact this ASU will have on its consolidated financial statements, including method of adoption. The Company will not be early-adopting this standard. The Company currently has one contract that generates revenue.

In February 2016, the FASB issued ASU 2016-02, “Leases (Topic 842).” The new standard establishes a right-of-use (ROU) model that requires a lessee to record a ROU asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. The new standard is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. A modified retrospective transition approach is required for lessees for capital and operating leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The Company is currently evaluating the impact this ASU will have on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, “Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting,” which changes the accounting for stock-based payment transactions, including income tax consequences, classification of awards as either equity or liabilities, and classification in the statement of cash flows. The new standard is effective for fiscal years beginning after December 15, 2016 and for interim periods therein, with early adoption permitted. The Company is currently evaluating the impact this ASU will have on its consolidated financial statements.

In September 2016, the FASB issued ASU 2016-15, “Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments (a consensus of the Emerging Issues Task Force),” which changes how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The new standard is effective for fiscal years beginning after December 15, 2017 and for interim periods therein, with early adoption permitted. The Company is currently evaluating the impact this ASU will have on its consolidated financial statements.

2. Fair value of financial instruments

In measuring fair value, the Company evaluates valuation techniques such as the market approach, the income approach and the cost approach. A three-level valuation hierarchy, which prioritizes the inputs to valuation techniques that are used to measure fair value, is based upon whether such inputs are observable or unobservable.
Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1—Observable inputs such as quoted prices (unadjusted) for identical instruments in active markets;

Level 2—Observable inputs such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model-derived valuations whose significant inputs are observable for substantially the full term of the assets or liabilities; and

Level 3—Unobservable inputs that reflect the reporting entity’s estimate of assumptions that market participants would use in pricing the asset or liability.

The following tables present the fair values for the Company’s financial instruments as well as the input levels used to determine these fair values as of December 31, 2016 and 2015. The Company values its current assets, which include trade and other receivables, and liabilities, which include advances from licensees and accounts payable, at historical cost, which approximates fair value. The fair value of the Loan Facility (see Note 13) was $3.4 million as of December 31, 2016. The valuation method used to value the Loan Facility was the income approach.

On December 17, 2014, the Company executed a convertible loan instrument, which provided 1,251,000 €1.00 ($1.12) unsecured convertible loan notes (2014 Convertible Loans), denominated in Euros, and was subsequently amended on October 1, 2015. On October 1, 2015, the Company executed a convertible loan instrument which provided 5,000,000 $1.00, unsecured convertible loan notes (the 2015 Convertible Loans), denominated in USD. See Note 13 for a further understanding of these instruments. Immediately prior to completion of the Transaction on November 3, 2016, the conversion rights for the 2014 and 2015 Convertible Loans were exercised.

The fair value of the 2015 Convertible Loans was $2.1 million as of December 31, 2015. The fair value of the 2014 Convertible Loans was $954,000 (€874,000) as of December 31, 2015. The valuation methods used to value the 2014 Convertible Loans and the 2015 Convertible Loans were the income approach and Monte Carlo simulation analysis. The key assumptions are the same as those used to determine the fair value of derivative liabilities as described below.

<table>
<thead>
<tr>
<th>Financial Instruments Recorded at Fair Value on a Recurring Basis</th>
<th>Fair Value Level</th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
<th>Fair Value Measurements</th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current liabilities: Warrants</td>
<td>3</td>
<td>$844</td>
<td>$1,163</td>
<td>$844</td>
<td>$1,163</td>
<td></td>
</tr>
<tr>
<td>Noncurrent liabilities: Derivative liabilities</td>
<td>3</td>
<td>—</td>
<td>2,047</td>
<td>—</td>
<td>2,047</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance, beginning</td>
<td>$2,047</td>
<td>$486</td>
<td>$1,163</td>
<td>$1,141</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Income) loss recognized in earnings</td>
<td>261</td>
<td>172</td>
<td>(294)</td>
<td>148</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchases, sales, issues and settlements</td>
<td>(2,343)</td>
<td>1,485</td>
<td>—</td>
<td>—</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foreign currency (gains) losses</td>
<td>35</td>
<td>(96)</td>
<td>(25)</td>
<td>(126)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfers in (out)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance, ending</td>
<td>$2,047</td>
<td>$486</td>
<td>$1,163</td>
<td>$1,141</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There were no transfers from one level to the other during the reporting periods.
**Derivative liabilities**

As of December 31, 2015, the fair values of the derivative liabilities related to the convertible features associated with the 2014 Convertible Loans and 2015 Convertible Loans were determined using the income approach and Monte Carlo simulation analysis on inception. See Note 13 for a further understanding of these instruments. The income approach was used as the starting point to determine the Company’s equity value. The Monte Carlo simulation was then used to determine possible future values of the Company’s equity. Using the Monte Carlo simulation, the Company considered the following scenarios as of December 31, 2015:

- **Series C preference shares financing (Round C):** In this scenario, the 2014 Convertible Loans and 2015 Convertible Loans would convert into a known number of Series C preference shares at a known price, which was based on the expected conversion price of Series C preference shares. It should be noted that this scenario would not have precluded the Company from filing for an initial public offering in the future.Convertible value was based on Series C preference shares conversion and accrued interests. The Company then used the estimated value of the total Series C preference shares and accrued interest and discounted the value using a risk-free interest rate of 0.39% per annum as of December 31, 2015.

- **IPO:** In this scenario, the Company would file for an IPO without first raising equity financing. The 2014 Convertible Loans and 2015 Convertible Loans would convert into a known number of Series C preference shares at a known price, which was based on the expected conversion price of Series C preference shares. Convertible value was based on the higher of Series C preference shares conversion and accrued interests, or fixed income component value.

- **No IPO:** In this scenario, the Company assumed that no conversion would take place. The Company valued the 2014 Convertible Loans and 2015 Convertible Loans using the income approach. The cash flows were based on principal and a contractual 8% annual interest rate. This amount was then discounted at the estimated market rate of 21.0% per annum as of December 31, 2015. Convertible value was based on the lower of equity value at exit or fixed income component value.

The scenarios were determined based on the amount of equity at the time of exit, which is driven by Monte Carlo simulation. The Company then used the convertible value and discounted the value using a risk-free interest rate of 0.65% per annum as of December 31, 2015.

Based upon these methodologies, the fair value of the derivative liabilities associated with the 2014 Convertible Loans was determined to be $566,000 (€519,000) as of December 31, 2015.

Using the same methods, the fair value of the derivative liabilities associated with the 2015 Convertible Loans was determined to be $1.5 million as of December 31, 2015.

The derivative liabilities were recorded for the year ended December 31, 2015 as a noncurrent liability, as the Company had an unconditional right to defer settlement for at least 12 months after December 31, 2015.

Significant unobservable inputs used in the measurement of the derivative liabilities associated with the 2014 Convertible Loans and 2015 Convertible Loans included the discount rate and the probability of the issuance and sale of Series C preference shares in Round C.

The Company performed a sensitivity analysis for the 2014 Convertible Loans regarding the discount rate. By varying the discount rate by 0.5%, the resulting values of the derivative liabilities that were bifurcated from the 2014 Convertible Loans were as follows (in thousands):

<table>
<thead>
<tr>
<th>Assumptions:</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discount rate</td>
<td>+0.5% 697</td>
</tr>
<tr>
<td></td>
<td>-0.5% 445</td>
</tr>
</tbody>
</table>

By varying the probability of Round C by 25% at December 31, 2015, the resulting value of the 2014 Convertible Loans was as follows (in thousands):

<table>
<thead>
<tr>
<th>Assumptions:</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of Round C</td>
<td>+25% 1,641</td>
</tr>
<tr>
<td></td>
<td>-25% 1,391</td>
</tr>
</tbody>
</table>
The Company also performed a sensitivity analysis for the 2015 Convertible Loans regarding the discount rate. By varying the discount rate by 0.5%, the resulting values of the derivative liabilities that were bifurcated from the 2015 Convertible Loans were as follows (in thousands):

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+0.5%</td>
</tr>
<tr>
<td>Discount rate</td>
<td>$1,852</td>
</tr>
</tbody>
</table>

By varying the probability of the Round C by 25% at December 31, 2015, the resulting value of the 2015 Convertible Loans was as follows (in thousands):

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of Round C</td>
<td>$3,973</td>
</tr>
</tbody>
</table>

**Warrants**

In connection with the Loan Facility, the Company issued to Kreos Capital IV (Expert Fund) Limited (Kreos Capital) detachable warrants with a right to acquire shares at €720,000 (the Warrants). The Company recognized the Warrants at fair value at the time of execution of the Loan Facility and remeasured their fair value on a recurring basis thereafter. In connection with the Transaction, the Warrants were replaced with warrants to purchase 67,271 shares of the Company’s common stock at an exercise price of $11.78 per share (the Replacement Kreos Warrants). The Replacement Kreos Warrants were valued as of December 31, 2016 at $844,000. The exchange was accounted for as a modification whereby the fair value of the Replacement Kreos Warrants was compared to the fair value of the Warrants immediately before the terms were modified, measured based on the market price of the common stock of the Company and other pertinent factors on the date of the modification. See Note 13 for a further description of the Warrants and Loan Facility.

Beginning with the quarter ended June 30, 2016, the Company estimated the fair value of the Warrants, primarily using the binomial method. The revision from December 31, 2015 was due to the execution of the agreement for the Transaction in 2016. The binomial method used assumptions that were based on the Warrants being exchanged for warrants exercisable for shares of the Company’s common stock.

The key assumptions used in the binomial method as of December 31, 2016 included the following:

<table>
<thead>
<tr>
<th>Assumption</th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock price</td>
<td>$17.73</td>
</tr>
<tr>
<td>Exercise price</td>
<td>$11.78</td>
</tr>
<tr>
<td>Term (in years)</td>
<td>1.00</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>0.85%</td>
</tr>
<tr>
<td>Volatility</td>
<td>83.4%</td>
</tr>
</tbody>
</table>

As of December 31, 2015, the Company calculated the Warrants’ fair value as follows:

- The Company’s equity value was estimated using the income approach.
- The Company’s equity value was then allocated among classes of its capital structure. The allocation was performed using the Option Pricing Methodology (OPM). This method treats securities as options with the Company. The allocation was used to determine the value of Series B preference shares. The Company assumed that any exercise of the Warrants would be to purchase Series B preference shares, as this class had the lowest exercise price, and also assumed scenarios where the Warrants would not be exercised.
As of December 31, 2015, a weighted average of the values derived using the OPM and a traditional Black-Scholes formula was used to calculate the fair value of the Warrants. The key assumptions used in the OPM as of December 31, 2015, included the following:

<table>
<thead>
<tr>
<th>December 31, 2015</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Term (in years)</td>
<td>1.0</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>0.7%</td>
</tr>
<tr>
<td>Volatility</td>
<td>85%</td>
</tr>
</tbody>
</table>

A traditional Black-Scholes formula was then used to calculate the fair value of the Warrants with the strike price of €1 and stock price as calculated in the allocation. The assumptions used in applying the Black-Scholes formula include the following:

<table>
<thead>
<tr>
<th>December 31, 2015</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock price</td>
<td>$ 1.77</td>
</tr>
<tr>
<td>Exercise price</td>
<td>$ 1.09</td>
</tr>
<tr>
<td>Term (in years)</td>
<td>7.50</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>2.12%</td>
</tr>
<tr>
<td>Volatility</td>
<td>90%</td>
</tr>
<tr>
<td>Dividend</td>
<td>0%</td>
</tr>
</tbody>
</table>

Based on these different methods, the fair value of the Warrants was determined to be $1.2 million (€1.1 million) as of December 31, 2015 and the fair value of the Replacement Kreos Warrants was determined to be $844,000 (€762,000) as of December 31, 2016. Each of these fair values was classified as a current liability because the Warrants were, and the Replacement Kreos Warrants are, immediately exercisable.

Under the binomial method, the fair value of the Warrants or Replacement Kreos Warrants decreased by $294,000 for the year ended December 31, 2016.

The significant unobservable input used in the measurement of the Warrants’ or Replacement Kreos Warrants’ liability was the term used in the OPM. The Company performed sensitivity analysis regarding this input and the value of the Warrants was found to be as follows using a 0.5 year decrease or 0.5 year increase in the term (in thousands):

<table>
<thead>
<tr>
<th>December 31, 2016</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>$(829)</td>
</tr>
<tr>
<td></td>
<td>$(829)</td>
</tr>
</tbody>
</table>

3. Equipment, net

Equipment, net consisted of the following (in thousands):

<table>
<thead>
<tr>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost:</td>
<td></td>
</tr>
<tr>
<td>Equipment cost as of January 1,</td>
<td>$142</td>
</tr>
<tr>
<td>Additions</td>
<td>3</td>
</tr>
<tr>
<td>Exchange differences</td>
<td>(2)</td>
</tr>
<tr>
<td>Equipment cost as of period end</td>
<td>$143</td>
</tr>
<tr>
<td>Less:</td>
<td></td>
</tr>
<tr>
<td>Accumulated depreciation as of January 1</td>
<td>(108)</td>
</tr>
<tr>
<td>Amortization for the period</td>
<td>(12)</td>
</tr>
<tr>
<td>Exchange differences</td>
<td>(2)</td>
</tr>
<tr>
<td>Accumulated depreciation as of period end</td>
<td>(122)</td>
</tr>
<tr>
<td>Total equipment, net</td>
<td>$21</td>
</tr>
</tbody>
</table>
Depreciation expense for the years ended December 31, 2016 and 2015 was $14,000 and $15,000, respectively.

4. Accrued expenses

Accrued expenses consist of the following (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accrued bonuses</td>
<td>$849</td>
<td>$392</td>
</tr>
<tr>
<td>Accrued vacation pay</td>
<td>$318</td>
<td>$368</td>
</tr>
<tr>
<td>Accrued social security pay</td>
<td>$1,461</td>
<td>$150</td>
</tr>
<tr>
<td>Accrued interest</td>
<td>—</td>
<td>$243</td>
</tr>
<tr>
<td>Accrued professional fees</td>
<td>$730</td>
<td>$758</td>
</tr>
<tr>
<td>Accrued development costs</td>
<td>$522</td>
<td>$665</td>
</tr>
<tr>
<td>Accrued severance</td>
<td>$2,864</td>
<td>—</td>
</tr>
<tr>
<td>Accrued other</td>
<td>$804</td>
<td>—</td>
</tr>
<tr>
<td>Total accrued expenses</td>
<td>$7,548</td>
<td>$2,576</td>
</tr>
</tbody>
</table>

5. Commitments and contingencies

Operating lease commitments

In July 2015, the Company entered into a month-to-month lease agreement for office space in Boston, Massachusetts.

In July 2014, the Company entered into a 36-month building lease for approximately 2,900 square feet of office space in Gothenburg, Sweden. The lease does not have stated escalating rent clauses, except for changes in the Swedish Consumer Price Index (CPI). The lease renews automatically for consecutive three-year terms, unless notice of nonrenewal is given by either party at least nine months prior to the end of the current term and subject to the Company’s right to terminate the lease at any time upon six months’ notice.

As of December 31, 2016, future minimum commitments under facility operating leases were $57,000.

Rent expense recognized under the Company’s operating leases was $122,000 and $93,000 for the years ended December 31, 2016 and 2015, respectively.

Agreements with CROs

As of December 31, 2016, the Company had various agreements with CROs for the conduct of specified research and development activities and, based on the terms of the respective agreements, may be required to make future payments of up to $3.5 million upon the completion of contracted work.

Other Commitments

In connection with the spin-off from AstraZeneca in 2008 and associated transfer agreements, the Company became party to an assignment agreement between AstraZeneca and a named inventor on a patent related to elobixibat. In connection with this agreement, the inventor is entitled upon the initial launch of a pharmaceutical product that constitutes an IBAT-inhibitor in specified countries to a one-time “launch fee” payment of SEK 4.0 million ($441,000, based on the SEK to USD exchange rate at December 31, 2016).

6. Business Combination

On November 3, 2016, the Company completed the Transaction pursuant to the Agreement. Subsequent to the Transaction, the Company is under the leadership of the former management team of Albireo Limited and a board of directors comprised of two former directors of Biodel and five former directors of Albireo Limited.
In the Transaction, Biodel issued to the former holders of shares of Albireo Limited an aggregate of 4,154,369 shares of Biodel common stock, representing approximately two-thirds of the combined organization’s common stock outstanding at the completion of the Transaction. The number of shares of Biodel common stock issued was determined based on a negotiated exchange ratio of 0.06999. In addition, in accordance with the terms of the Agreement, all outstanding options or warrants to purchase Albireo Limited shares immediately prior to the Transaction were converted into options to purchase 351,550 shares of Biodel common stock.

The Transaction was accounted for as a “reverse acquisition” pursuant to which Albireo Limited was considered the accounting acquirer. As such, these Consolidated Financial Statements reflect the historical results of Albireo Limited prior to completion of the Transaction and do not include the historical results of Biodel prior to completion of the Transaction.

Transaction Costs

The Company incurred costs related to the Transaction, which were expensed in the period ended December 31, 2016. The expensed transaction costs include:

<table>
<thead>
<tr>
<th></th>
<th>(in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legal fees</td>
<td>1,187</td>
</tr>
<tr>
<td>Accounting fees</td>
<td>653</td>
</tr>
<tr>
<td>Advisory fees</td>
<td>2,031</td>
</tr>
<tr>
<td>Termination and severance</td>
<td>1,749</td>
</tr>
<tr>
<td><strong>Total Transaction Costs</strong></td>
<td><strong>5,620</strong></td>
</tr>
</tbody>
</table>

In addition to the Transaction-related costs described above, the Company also recorded general and administrative expense of $1.2 million for the period ended December 31, 2016 associated with a lease termination payment obligation incurred for Biodel’s corporate offices in Danbury, Connecticut.

Purchase Consideration and Net Assets Acquired

The fair value of Biodel common stock used in determining the purchase price was $19.50 per share, the closing price on November 3, 2016. The acquisition-date fair value of the outstanding stock options of Biodel is included in the purchase consideration based on the amount attributable to services provided by the Biodel employees prior to the Transaction, calculated using the Black-Scholes option pricing model. In accordance with the change of control provisions, all Biodel options vested on November 3, 2016. Assumptions used in Black-Scholes calculations during such periods included: volatility ranging from 75.7% to 79.0%; risk-free interest rates ranging between 0.64% and 0.72%; and the expected terms ranging from 1.0 to 1.5 years.

The purchase price is as follows:

<table>
<thead>
<tr>
<th></th>
<th>(in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair value of Biodel shares outstanding</td>
<td>41,696</td>
</tr>
<tr>
<td>Fair value of Biodel stock options</td>
<td>242</td>
</tr>
<tr>
<td><strong>Purchase price</strong></td>
<td><strong>41,938</strong></td>
</tr>
</tbody>
</table>

The following presents the preliminary allocation of the purchase consideration to the assets acquired and liabilities assumed on November 3, 2016:

<table>
<thead>
<tr>
<th></th>
<th>(in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td>$ 25,483</td>
</tr>
<tr>
<td>Other current assets</td>
<td>701</td>
</tr>
<tr>
<td>Intangible assets</td>
<td>150</td>
</tr>
<tr>
<td>Goodwill</td>
<td>18,110</td>
</tr>
<tr>
<td>Accounts payable and accrued liabilities</td>
<td>(2,215)</td>
</tr>
<tr>
<td>Other current liabilities</td>
<td>(286)</td>
</tr>
<tr>
<td>Warrant liabilities</td>
<td>(5)</td>
</tr>
<tr>
<td><strong>Total Net Assets Acquired</strong></td>
<td><strong>41,938</strong></td>
</tr>
</tbody>
</table>
Any changes in the estimated fair values of the net assets recorded for this business combination upon the finalization of more detailed analyses of the facts and circumstances that existed at the date of the transaction will change the allocation of the purchase price. Any subsequent changes to the purchase allocation during the measurement period that are material will be adjusted retrospectively.

The amount allocated to in-process research and development represents an estimate of the fair value of purchased in-process technology for research projects (IPR&D), primarily related to Biodel’s glucagon emergency management product candidate and BIOD-531 concentrated prandial/basal insulin combination product candidate. IPR&D is considered an indefinite-lived intangible asset until the completion or abandonment of the associated research and development efforts. Accordingly, during the development period, the IPR&D is not amortized but subject to impairment review. No amortization of the IPR&D has been reflected in these Consolidated Financial Statements as the assets are considered indefinite-lived.

The excess purchase consideration over the fair values of assets acquired and liabilities assumed is recorded as goodwill. Goodwill is not amortized but tested for impairment on an annual basis or when an indicator for impairment exists. The goodwill recorded is not tax deductible since the Transaction was structured as a tax-free exchange.

**Unaudited Pro Forma Information**

Supplemental information on a pro forma basis assuming the Transaction occurred on January 1, 2015 is presented below for the years ended December 31, 2015 and 2016:

<table>
<thead>
<tr>
<th>Year Ended December 31, 2016 (in thousands)</th>
<th>Year Ended December 31, 2015 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pro Forma Net Revenues</td>
<td>$11,364</td>
</tr>
<tr>
<td></td>
<td>$5,099</td>
</tr>
<tr>
<td>Pro Forma Loss</td>
<td>$(32,609)</td>
</tr>
<tr>
<td></td>
<td>$(23,667)</td>
</tr>
</tbody>
</table>

Pro forma results for the year ended December 31, 2016 include adjustments to accrued interest and accretion of the debt discounts associated with, the 2014 Convertible Loans and 2015 Convertible Loans upon their conversion into equity immediately prior to completion of the Transaction.

7. **Employee benefits expense**

The Company has defined contribution retirement benefit plans for its Sweden-based employees. The expenses for the Company’s employee benefits recognized in the Consolidated Statements of Operations were as follows (in thousands):

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wages and salaries</td>
<td>$3,279</td>
<td>$1,610</td>
</tr>
<tr>
<td>Social security expenses</td>
<td>575</td>
<td>169</td>
</tr>
<tr>
<td>Pension expenses – defined contribution plans</td>
<td>331</td>
<td>218</td>
</tr>
<tr>
<td></td>
<td>$4,185</td>
<td>$1,997</td>
</tr>
</tbody>
</table>

The Company has a 401(k) retirement plan in which all U.S.-based employees are eligible to participate. The Company contributed $33,000 and $3,000 to the plan for the years ended December 31, 2016 and 2015, respectively. The Company matched employee contributions to the plan, on a per employee basis, up to 4% of each employee’s wages for the years ended December 31, 2016 and 2015.

8. **Net loss per share**

Basic net loss per share, or Basic EPS, is calculated by dividing the net loss attributable to holders of common stock by the weighted average number of shares of common stock outstanding. Diluted net loss per share, or Diluted EPS, is calculated by dividing the net loss attributable to holders of common stock by the weighted-average number of common stock outstanding. If the Company were in a net income position, Diluted EPS would be calculated by dividing the net income attributable to holders of common stock by the weighted-average number of common stock plus dilutive common stock equivalents outstanding.
The following table sets forth the computation of Basic EPS and Diluted EPS (in thousands, except for share and per share data):

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td><strong>Basic and Diluted EPS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Numerator</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (16,350)</td>
<td>$ (6,768)</td>
</tr>
<tr>
<td>Net loss attributable to holders of common stock</td>
<td>$ (16,350)</td>
<td>$ (6,768)</td>
</tr>
<tr>
<td><strong>Denominator</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weighted average number of shares</td>
<td>1,239,694</td>
<td>265,560</td>
</tr>
<tr>
<td>Number of shares used for basic and diluted EPS computation</td>
<td>1,239,694</td>
<td>265,560</td>
</tr>
<tr>
<td>Basic and Diluted EPS</td>
<td>$ (13.19)</td>
<td>$ (25.49)</td>
</tr>
</tbody>
</table>

The following weighted-average outstanding common stock equivalents were excluded from the computation of Diluted EPS for the periods presented because including them would have been anti-dilutive:

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td>Convertible preference shares (on an as-converted basis)</td>
<td>2,317,898</td>
<td>2,754,386</td>
</tr>
<tr>
<td>Warrants to purchase convertible preference shares (on an as-converted basis)</td>
<td>6,946</td>
<td>50,392</td>
</tr>
<tr>
<td>Warrants to purchase common stock</td>
<td>48,543</td>
<td>—</td>
</tr>
</tbody>
</table>

9. Income taxes

The Company recorded income tax expense in relation to its U.S. operations in the year ended December 31, 2016. No income tax provision or benefit was recorded for the year ended December 31, 2015. The Company has had an overall net operating loss position since its inception.

For the years ended December 31, 2016 and 2015, the components of loss before income taxes were as follows (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
<td>2015</td>
</tr>
<tr>
<td>U.S.</td>
<td>$ (5,555)</td>
<td>$ (69)</td>
</tr>
<tr>
<td>Foreign</td>
<td>(10,733)</td>
<td>(6,699)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$ (16,288)</td>
<td>$ (6,768)</td>
</tr>
</tbody>
</table>
The components of income tax (benefit) for the years ended December 31, 2016 and 2015 were as follows (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td><strong>Current tax expense:</strong></td>
<td></td>
</tr>
<tr>
<td>Federal</td>
<td>$50</td>
</tr>
<tr>
<td>State</td>
<td>$12</td>
</tr>
<tr>
<td>Foreign</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$62</td>
</tr>
<tr>
<td><strong>Deferred tax benefit:</strong></td>
<td></td>
</tr>
<tr>
<td>Federal</td>
<td>—</td>
</tr>
<tr>
<td>State</td>
<td>—</td>
</tr>
<tr>
<td>Foreign</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>—</td>
</tr>
<tr>
<td><strong>Total provision for income taxes</strong></td>
<td>$62</td>
</tr>
<tr>
<td><strong>Effective tax rate</strong></td>
<td>0%</td>
</tr>
</tbody>
</table>

A reconciliation of the U.S. statutory income tax rate to the consolidated effective income tax rate was as follows:

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td>U.K. statutory income tax rate</td>
<td>—</td>
</tr>
<tr>
<td>U.S. statutory income tax rate</td>
<td>34%</td>
</tr>
<tr>
<td>Non-deductible interest expense</td>
<td>(6%)</td>
</tr>
<tr>
<td>Kreos warrant replacement</td>
<td>(2%)</td>
</tr>
<tr>
<td>Other permanent differences</td>
<td>(1%)</td>
</tr>
<tr>
<td>State taxes, net of federal tax effect</td>
<td>2%</td>
</tr>
<tr>
<td>Increase in valuation allowance</td>
<td>(20%)</td>
</tr>
<tr>
<td>Foreign tax rate differences</td>
<td>(7%)</td>
</tr>
<tr>
<td><strong>Effective income tax rate</strong></td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Deferred taxes are recognized for temporary differences between the bases of assets and liabilities for financial statement and income tax purposes. The tax effect of temporary differences that give rise to significant portions of the deferred tax assets are as follows (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td><strong>Deferred tax assets:</strong></td>
<td></td>
</tr>
<tr>
<td>Tax loss carryforwards</td>
<td>$15,420</td>
</tr>
<tr>
<td>Capitalized expenses</td>
<td>36,254</td>
</tr>
<tr>
<td>Research and development credits</td>
<td>140</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>1,088</td>
</tr>
<tr>
<td>Stock compensation</td>
<td>383</td>
</tr>
<tr>
<td>Other</td>
<td>43</td>
</tr>
<tr>
<td><strong>Total gross deferred tax assets</strong></td>
<td>53,328</td>
</tr>
<tr>
<td>Valuation allowance</td>
<td>(53,257)</td>
</tr>
<tr>
<td><strong>Total deferred tax assets</strong></td>
<td>71</td>
</tr>
<tr>
<td><strong>Deferred tax liabilities:</strong></td>
<td></td>
</tr>
<tr>
<td>Intangible assets</td>
<td>$40</td>
</tr>
<tr>
<td>Temporary difference on financial instruments</td>
<td>31</td>
</tr>
<tr>
<td><strong>Total deferred tax liabilities</strong></td>
<td>71</td>
</tr>
<tr>
<td><strong>Net deferred tax assets</strong></td>
<td>$—</td>
</tr>
</tbody>
</table>
A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future returns, the Company has recorded a full valuation allowance against the Company’s otherwise recognizable net deferred tax assets. The Company had approximately $53.3 million and $2.7 million in valuation allowances recorded against its deferred tax assets as of December 31, 2016 and 2015, respectively.

Total net deferred taxes are classified as follows (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>As of December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td>Noncurrent deferred tax assets</td>
<td>$ —</td>
</tr>
<tr>
<td>Noncurrent deferred tax liabilities</td>
<td>—</td>
</tr>
</tbody>
</table>

As of December 31, 2016, deferred tax assets related to net operating loss (NOL) carryforwards was $15.4 million, which may be used subject to certain limitations to offset future taxable income, if any. The NOL includes approximately $11.2 million for U.S. federal tax purposes (net of Section 382 limitations) and $151.0 million for U.S. state tax purposes. These loss carryforwards expire between 2024 and 2036. Additional NOL of approximately $18.9 million were generated in various non-U.S. jurisdictions and will not expire.

Utilization of the NOL and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. As a result of previous ownership changes, approximately $141.2 million of the $152.5 million of NOL carryforwards as of December 31, 2016 are subject to a Section 382 limitation.

The Company also has state research and development credit carry-forwards of approximately $212,000, which expire commencing in fiscal 2022. A valuation allowance of $16 million has been established on the NOL carryforward and research and development credits as it is uncertain as to whether future taxable income will be generated.

The Company’s policy is for any earnings of non-U.S. subsidiaries to be indefinitely invested outside the United States on the basis of estimates that future domestic cash generation will be sufficient to meet future domestic cash needs and the Company’s specific plans for reinvestment of those subsidiary earnings, if any.

**Uncertain tax positions**

The Company records uncertain tax positions in accordance with ASC 740 on the basis of a two-step process whereby

1. the Company determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position; and
2. for those tax positions that meet the more-likely-than-not recognition threshold, the Company recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority.

The following table summarized the activity related to the Company's liabilities for uncertain tax positions:

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td>Balance, beginning of year</td>
<td>$ —</td>
</tr>
<tr>
<td>Decrease related to prior year's tax position</td>
<td>—</td>
</tr>
<tr>
<td>Balance, at end of year</td>
<td>$ —</td>
</tr>
</tbody>
</table>
The Company files U.S. federal and state tax returns and has determined that its major tax jurisdictions are the United States, Massachusetts and Connecticut, as well as United Kingdom and Sweden. There have been no uncertain tax benefits recognized, or related interest or potential penalties, as of December 31, 2016 or 2015. The Company’s tax returns may be examined for certain tax jurisdictions back to December 31, 2013. The Company’s 2015 federal tax return, in respect of its predecessor (Biodel), is under examination.

10. Stockholders’ equity

As of December 31, 2016, the number of shares of common stock authorized and outstanding is as follows:

<table>
<thead>
<tr>
<th>Type of share</th>
<th>Authorized</th>
<th>Issued and Outstanding</th>
<th>Nominal value</th>
<th>Voting right</th>
<th>Book value (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common stock</td>
<td>200,000,000</td>
<td>6,292,644</td>
<td>$0.01</td>
<td>1</td>
<td>$63</td>
</tr>
</tbody>
</table>

In addition, as of December 31, 2016, the Company has 50,000,000 shares of preferred stock authorized. There are no shares of preferred stock issued or outstanding.

Prior to the closing date of the Transaction, Albireo Limited had collectively 308,286 Ordinary shares and Ordinary A shares outstanding (pre-exchange ratio 4,404,817 Ordinary shares and Ordinary A shares). In conjunction with the Transaction:

• immediately prior to completion of the Transaction, Albireo Limited received an investment of $10.0 million in exchange for 9,708,740 Series C preference shares from certain of its existing shareholders;
• the 2015 Convertible Loans were converted into 4,248,780 Series C preference shares and the 2014 Convertible Loans were converted into 1,669,997 Series C preference shares, at a conversion rate of €0.749;
• 4,679,365 Series A preference shares, 34,674,635 Series B preference shares and 15,627,517 Series C preference shares were converted into 54,981,517 Ordinary shares; and
• 59,386,334 Ordinary shares were exchanged for 4,154,639 shares of the Company’s common stock, based on an exchange ratio of 0.06999.

Immediately following the Transaction, the Company had 6,292,644 issued and outstanding shares of common stock.

The following table summarizes the Ordinary shares of Albireo Limited outstanding as of December 31, 2015.

<table>
<thead>
<tr>
<th>Type of share</th>
<th>Authorized</th>
<th>Issued and Outstanding</th>
<th>Nominal value</th>
<th>Voting right</th>
<th>Book value (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Stock</td>
<td>265,560</td>
<td>265,560</td>
<td>$0.01</td>
<td>1</td>
<td>$50</td>
</tr>
</tbody>
</table>

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11. Temporary equity

The Company had no temporary equity as of December 31, 2016 following completion of the Transaction on November 3, 2016. Temporary equity as of December 31, 2015 consisted of the following:

<table>
<thead>
<tr>
<th>Type of Preference shares</th>
<th>Authorized</th>
<th>Issued and Outstanding</th>
<th>Nominal value</th>
<th>Voting right</th>
<th>Book value (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A Convertible Preference shares – voting</td>
<td>1,504,291</td>
<td>1,504,291</td>
<td>$0.013</td>
<td>1</td>
<td>$19</td>
</tr>
<tr>
<td>Series B Convertible Preference shares – nonvoting</td>
<td>3,175,074</td>
<td>3,175,074</td>
<td>0.013</td>
<td>—</td>
<td>43</td>
</tr>
<tr>
<td>Series C Convertible Preference shares – voting</td>
<td>35,394,635</td>
<td>34,674,635</td>
<td>0.013</td>
<td>1</td>
<td>458</td>
</tr>
<tr>
<td>Total</td>
<td>44,945,080</td>
<td>39,354,000</td>
<td>0.013</td>
<td>1</td>
<td>520</td>
</tr>
</tbody>
</table>

Significant provisions of the preference shares of Albireo Limited as of December 31, 2015 were as described below. Upon completion of the Transaction on November 3, 2016, all outstanding convertible preference shares converted to Ordinary shares and with all preferential rights terminating at that time.

**Voting** — Each Series A, Series B and Series C preference share was entitled to one vote per share on an as-converted basis. Each Series A and Series B preference share that was classified as nonvoting was not entitled to any voting rights.

**Transfers** — Shareholders in each class had certain transfer rights. Transfer rights included, for holders of Series B preference shares or Series C preference shares, but who were not holders of Series A preference shares or specified members of management, the right to transfer any shares held (where the holder is a company or other entity or investment vehicle) to its holding company or to any subsidiary of that holding company or to any entity or investment vehicle in which the holder, its holding company or any subsidiary of that holding company has a majority economic interest, or to any affiliate or (where the holder is an investment fund or investment fund manager or nominee thereof) to any successor investment fund, or investment manager of any nominee thereof or to the general partner of such fund (or solely in connection with a dissolution any participant or partner in such fund).

**Conversion** — Series A preference shares had conversion rights that enabled any holder of such shares to at any time convert the whole or part of its holding into Ordinary shares. In addition, upon notice by the holders of 65% of the outstanding voting preference shares, immediately prior to a defined “Qualifying IPO” or immediately prior to a sale of the Company, each Series A preference share was automatically to be converted into Ordinary shares at a ratio of 1:1 (subject to adjustment in accordance with the anti-dilution mechanism provided for in the then articles of association of Albireo Limited). The holders of Series B preference shares and Series C preference shares had conversion rights that were broadly equivalent to conversion rights of the holders of Series A preference shares as described in this paragraph.

Series A preference shares had additional conversion rights whereby a holder of Series A preference shares could at any time convert part of its holding of Series A voting preference shares into a like number of equivalently paid Series A nonvoting preference shares, provided such holder held at least one Series A preference share (and vice versa).

Series B preference shares also had additional conversion rights whereby a holder of the Series B shares, who was also a holder of Series A preference shares, could at any time convert part of its holding of Series B voting preference shares into a like number of equivalently paid Series B nonvoting preference shares (and vice versa).

All preferential income and capital rights granted to holders of convertible preference shares were to terminate immediately prior to a Qualifying IPO with any income or capital subsequently distributed to the holders of the Ordinary shares in proportion to the number of Ordinary shares held.

**Dividends** — Holders of Series A, Series B or Series C preference shares were entitled to dividends in the same order of priority as would apply upon a liquidation, if and when declared by the Albireo Limited Board of Directors. Certain of these rights were settled with the payment of a dividend in the cumulative amount of approximately $47 million (€36 million) in 2012. No dividends have been declared from December 21, 2012 through December 31, 2016.
**Liquidation preferences** — In the event of any voluntary or involuntary liquidation, dissolution or winding up of Albireo Limited, holders of Series C preference shares were entitled to receive, prior and in preference to holders of Ordinary shares and the holders of Series B and Series A preference shares, an amount per share calculated by reference to the subscription price paid. After this, certain holders of Ordinary shares, subject to satisfaction of applicable conditions, were entitled to receive, prior and in preference to holders of Series B and Series A preference shares, fixed sums to be paid amongst those certain holders. Upon completion of the distribution to those certain holders of Ordinary shares, holders of Series B preference shares were entitled to receive prior and in preference to holders of Series A preference shares, amounts calculated by reference to a cumulative dividend at the annual rate of 8% of the original subscription price, from the date of issuance to December 1, 2012, and historic interest payments on related loan notes together with €1.00 for each such share held. Further preferential rights for determinable amounts were then reserved to holders of Series C, Series B and Series A preference shares and certain holders of Ordinary shares, collectively. In each case entitlements of shareholders were calculated to take account of prior distributions that have been made, and were subject to the conditional and accelerated entitlements expressly provided for in the articles of association and the satisfaction of any declared but unpaid dividends. All remaining legally available assets of the Company were to be distributed to holders of Ordinary shares and Series C, Series B and Series A preference shares in proportion to the number of shares held (with the holders of convertible preference shares participating on an as-converted basis).

12. Stock-based Compensation

On November 3, 2016, the Albireo Pharma, Inc. 2016 Equity Incentive Plan (the 2016 Equity Plan) was approved by the Company’s stockholders. The 2016 Equity Plan replaced Biodel’s 2010 Stock Incentive Plan, as amended (the 2010 Plan), in connection with completion of the Transaction. The 2016 Equity Plan authorized the issuance of up to 635,000 shares, plus up to 249,059 shares issued if awards outstanding under the 2010 Plan were cancelled, forfeited or expired on or after the Transaction. All stock options outstanding under the 2010 Plan remain in full force and effect pursuant to their terms and the terms of the 2010 Plan. The 2016 Equity Plan is structured to comply with the requirements imposed by Section 162 (m) of the Internal Revenue Code of 1986, as amended, and related regulations.

Prior to completion of the Transaction, Albireo Limited adopted a share option plan on March 18, 2016, providing for the grant of share options to employees, consultants, officers and directors of Albireo Limited or its subsidiaries (the Pre-Transaction Plan). The Pre-Transaction Plan was amended by Albireo Limited on April 18, 2016. Pursuant to the terms of the Pre-Transaction Plan and prior to completion of the Transaction, Albireo Limited issued or granted options to purchase 246,666 Ordinary A shares. These options were classified as a liability on the basis that they were granted in a currency other than the functional currency of the employing entity of the recipients and were subject to revaluation until exercised or forfeited. The options were replaced with options to purchase shares of the Company’s common stock in conjunction with the Transaction. The replacement was accounted for as a modification whereby the fair value of the replacement awards was compared to the fair value of the original award immediately before the terms were modified, measured based on the market price of the common stock of Biodel and other pertinent factors on the date of the modification. The options were then classified as equity awards with the liability reclassified to Additional paid in capital.

The Company’s employment agreements with certain of its executives provide that, upon a change of control as defined, all of the then outstanding unvested options and any other rights to purchase Company shares will become fully vested and exercisable and any vesting-like restrictions will lapse in full, unless earlier vesting is provided for in the applicable program under which such option or other right to purchase Company shares was granted or under applicable law. The Transaction was not a change of control under the employment agreements.

The Company recognized stock-based compensation expense for employees in the accompanying Consolidated Statements of Operations as follows (in thousands):

<table>
<thead>
<tr>
<th>Years Ended December 31,</th>
<th>2016</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>General and administrative</td>
<td>$1,138</td>
<td>—</td>
</tr>
<tr>
<td>Total stock-based compensation</td>
<td>$1,138</td>
<td>—</td>
</tr>
</tbody>
</table>

As of December 31, 2016, there were options to purchase 692,384 shares of common stock outstanding.
A summary of the outstanding stock options as of December 31, 2016 is as follows:

<table>
<thead>
<tr>
<th>Stock Options Outstanding</th>
<th>Number of Shares</th>
<th>Weighted-Average Exercise Price Per Share</th>
<th>Weighted-Average Remaining Contractual Term (Years)</th>
<th>Aggregate Intrinsic Value (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outstanding—December 31, 2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granted</td>
<td>454,391</td>
<td>$10.87</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Replacement of 2016 warrants</td>
<td>104,883</td>
<td>$1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Assumed in acquisition</td>
<td>138,346</td>
<td>$102.59</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Expirations</td>
<td>(2,573)</td>
<td>$—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Outstanding—December 31, 2016</td>
<td>695,047</td>
<td>$26.71</td>
<td>7.35</td>
<td>$6,435</td>
</tr>
<tr>
<td>Exercisable—December 31, 2016</td>
<td>192,499</td>
<td>$70.19</td>
<td>3.33</td>
<td>$1,526</td>
</tr>
<tr>
<td>Vested or expected to vest at—December 31, 2016</td>
<td>672,962</td>
<td>$27.46</td>
<td>7.29</td>
<td>$6,075</td>
</tr>
</tbody>
</table>

Aggregate intrinsic value represents the difference between the estimated fair value of the underlying common stock and the exercise price of outstanding, in-the-money options.

Options to purchase 19,422 shares of common stock vested upon completion of the Transaction and are exercisable as of December 31, 2016. In addition, options to purchase 19,422 shares of common stock are performance based and vest upon the date the Company files a new drug application with the U.S. Food and Drug Administration for A4250 for any orphan indication, if such filing occurs prior to a specified date. This unvested performance-based option is excluded from the vested or expected to vest balance as of December 31, 2016.

As of December 31, 2016, the total unrecognized compensation expense related to unvested options was $7.8 million, which the Company expects to recognize over a weighted average vesting period of 2.0 years.

In determining the estimated fair value of the stock-based awards, the Company uses the Black-Scholes option pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

The fair value of share option awards was estimated with the following assumptions:

<table>
<thead>
<tr>
<th>As of December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price per share of common stock</td>
</tr>
<tr>
<td>Expected term (in years)</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
</tr>
<tr>
<td>Expected volatility</td>
</tr>
<tr>
<td>Dividend rate</td>
</tr>
</tbody>
</table>

Employee Warrants

Prior to completion of the Transaction, Albireo Limited entered into a warrant instrument on March 18, 2016 (the Pre-Transaction Warrant Instrument) for the offer and issuance of warrants (2016 Warrants) and Ordinary A shares in lieu of 2016 Warrants. The Pre-Transaction Warrant Instrument was amended by Albireo Limited on April 18, 2016.

Pursuant to the terms of the Pre-Transaction Warrant Instrument and prior to completion of the Transaction, the Company issued 110,566 2016 Warrants to employees of, and consultants to, a subsidiary of Albireo Limited with a fair value of $0.67 (€0.58) per warrant. Total cash proceeds received upon issuance was $73,000 (€63,000) for the 2016 Warrants. The 2016 Warrants were immediately exercisable by the holders and Albireo Limited had the right but not the obligation to repurchase the outstanding and unexercised 2016 Warrants if the recipient holder was no longer a qualifying person under the Pre-Transaction Warrant Instrument (Call Option). In September 2016, a warrant holder exercised 5,826 2016 Warrants and received Ordinary A shares for a total payment of $5,000.

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Because the 2016 Warrants were issued at fair value and there were no service conditions, the Company accounted for the 2016 Warrants as equity instruments. The related Call Options were not legally detachable or separately exercisable and therefore were accounted for together with the 2016 Warrants.

The unexercised 2016 Warrants were replaced with options to purchase shares of the Company’s common stock effective as of the date the Transaction was completed. Each replacement option was accounted for as a modification whereby the fair value of the replacement option was compared to the fair value of the original award immediately before the terms were modified, measured based on the market price of the common stock of the Company and other pertinent factors on the date of the modification. The exercise price per share of each replacement option was $1.00. The term of each replacement option was five years from the date of issuance of the corresponding 2016 Warrant, or through April 2021. Of the replacement options, 37,873 were fully vested and exercisable at the time of replacement and the remaining 67,010 vest and become exercisable in equal monthly installments beginning December 1, 2016 and ending July 1, 2019.

13. Long-term debt

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term debt, including current portion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loan Facility</td>
<td>$ 3,075</td>
<td>$ 4,421</td>
</tr>
<tr>
<td>2014 Convertible Loans</td>
<td>—</td>
<td>933</td>
</tr>
<tr>
<td>2015 Convertible Loans</td>
<td>—</td>
<td>2,026</td>
</tr>
<tr>
<td>Total debt</td>
<td>3,075</td>
<td>7,380</td>
</tr>
<tr>
<td>Less: current portion</td>
<td>(3,075)</td>
<td>(2,514)</td>
</tr>
<tr>
<td>Long-term debt</td>
<td>$ —</td>
<td>$ 4,866</td>
</tr>
</tbody>
</table>

**Loan Facility**

The Company (in particular, Albireo Limited) executed a loan agreement (Loan Facility) with Kreos Capital IV (UK) Limited (Kreos UK) in December 2014, at which time the Company borrowed €6.0 million ($7.3 million). The Loan Facility has a term of 36 months with principal and interest payable monthly, with an annual interest rate of 11.5%. In addition, the Company is required to make an end-of-loan payment equal to 1.25% of the amounts lent by Kreos UK. The amount outstanding as of December 31, 2016 is $3.1 million (€2.9 million). The outstanding amount is due and payable in average monthly installments of €245,000 ($258,000, based on the Euro to USD exchange rate at December 31, 2016) and an end of loan payment of €670,000 ($739,000, based on the Euro to USD exchange rate at December 31, 2016) due and payable on December 1, 2017. The Company has paid $552,000 and $761,000 in interest on the Loan Facility for the years ended December 31, 2016 and 2015, respectively.

The debt discount of $393,000 remaining as of December 31, 2016 is being accreted over the remaining 12 months of the loan term. Interest expense included $907,000 and $691,000 of discount accretion for the years ended December 31, 2016 and 2015, respectively.

The Company has the option to redeem all outstanding amounts. Upon the occurrence of a sale or a change of control, the Company shall redeem the principal, accrued interest and other fees, and remaining interest payments calculated until the end of the term, discounted by 5%.

Parent’s subsidiary, Albireo Limited, has pledged its shares in its subsidiary, Albireo AB, and has granted a debenture (incorporating fixed and floating charges) over its assets by way of security for the obligations it owes under the Loan Facility.

The Loan Facility is guaranteed by Parent and two of Parent’s indirect subsidiaries, Elobix AB and Albireo AB, as the principal obligors that have severally agreed to indemnify and keep indemnified Kreos UK in full and on demand from and against all and any losses, costs, claims, liabilities, damages, demands and expenses suffered or incurred by the Kreos UK arising out of, or in connection with, any failure of the Company to perform or discharge any of its obligations or liabilities.

In addition, Parent, Elobix AB and Albireo AB have agreed to pledge the following:
- Parent shares in Albireo Limited
Although the bank accounts of Albireo AB and Elobix AB were pledged, Albireo AB and Elobix AB are not restricted from using the cash for working capital requirements.

The Company also pledged its present and future rights to fees, royalties and other payments due and payable any time under its license agreement with EA Pharma to Kreos UK in support of the Loan Facility.

On February 4, 2016, the Company (in particular, Albireo Limited) entered a Deed of Variation related to the Loan Facility. Under the terms of the Deed of Variation, the timing of principal payments was changed such that €512,000 ($567,000, based on the Euro to USD exchange rate at December 31, 2016) of the payments was deferred to become payable at the end of the loan term. The total principal due under the Loan Facility remained unchanged. In addition, there were no changes to the maturity date or the stated interest rate.

The Company accounted for the amendment to the Loan Facility prospectively in accordance with ASC 470-50, Modifications and Extinguishments, as there were no concessions granted to the Company by the lender and the difference in cash flows between the original and amended loans did not change by more than 10% per lender. As a result of the modification, the transaction costs incurred in connection with the amendment were expensed when incurred and the effective interest rate calculation was updated, resulting in an effective interest rate of 39.3%.

In connection with the Loan Facility, the Company issued to Kreos Capital detachable warrants with a right to acquire shares at €720,000 to purchase certain shares of the Company’s stock under specified circumstances (the Warrants).

In connection with the Transaction, the Warrants were replaced with a warrant to purchase 67,271 shares of the Company’s common stock at an exercise price of $11.78 per share (Replacement Kreos Warrants). The Replacement Kreos Warrants have been fair valued as of December 31, 2016 at $844,000 (€762,000). The exchange was accounted for as a modification whereby the fair value of the Replacement Kreos Warrants was compared to the fair value of the Warrants immediately before the terms were modified, measured based on the market price of the common stock of the Company and other pertinent factors on the date of the modification.

The term of the Replacement Warrants is five years. After the Transaction, the Replacement Kreos Warrants were classified as liabilities because the amount of shares used to settle the Replacement Kreos Warrants is not fixed, as the Replacement Kreos Warrants contain certain price protection clauses. Subsequent to the replacement, fair value of the Replacement Kreos Warrants is remeasured at each reporting period until settled, with any changes in fair value recorded in the Consolidated Statements of Operations.

2015 Convertible Loans

As of December 31, 2015, the Company had convertible debt outstanding with a par value of $3.5 million (2015 Convertible Loans). The carrying value of the debt and its related discount was $2.0 million as of December 31, 2015. The 2015 Convertible Loans had been accounted for in accordance with ASC Subtopic 470-20, “Debt with Conversion and Other Options” (ASC 470-20). The Company had bifurcated the conversion feature of the 2015 Convertible Loans from the debt instrument, classified the conversion feature as a derivative liability and accreted the resulting debt discount as interest expense using the effective interest rate method over the contractual term of the 2015 Convertible Loans. The Company recognized noncash accretion in the amount of $106,000 and $22,000 in Interest expense for the years ended December 31, 2016 and 2015, respectively.

The conversion features had previously been accounted for as a derivative and separately accounted from the 2015 Convertible Loans. The derivative liabilities were recognized as a noncurrent liability. See Note 14 for discussion of Derivatives and Note 2 for discussion of Fair value of financial instruments.
In connection with the Transaction, the 2015 Convertible Loans were converted into 297,372 shares of the Company’s common stock based on a conversion price of $19.50. The carrying value of the debt at the time of conversion was $2.1 million and the fair value of the derivative liabilities was $1.8 million. The fair value of the shares received at conversion was $5.8 million. The difference between the fair value of the shares and the carrying value of the debt plus the fair value of the derivative liabilities was $1.9 million, which was recognized as a loss on conversion and recorded in Other income and expense for the year ended December 31, 2016.

Prior to the conversion, interest accrued at a rate of 8% per annum. Accrued interest in the amount of $306,000 had been accrued through the date of conversion. Subject to completion of the Transaction, the holders of the 2015 Convertible Loans waived their rights to any unpaid interest and discharged the Company from this liability. The $306,000 of accrued interest has been recognized as a gain on debt extinguishment and also recorded in Other income and expense during 2016.

2014 Convertible Loans

As of December 31, 2015, the Company had convertible debt outstanding with a par value of $1.3 million (2014 Convertible Loans). The carrying value of the debt and its related discount was $933,000 as of December 31, 2015. The 2014 Convertible Loans had been accounted for in accordance with ASC 470-20. The Company had bifurcated the conversion feature of the 2014 Convertible Loans from the debt instrument, classified the conversion feature as a derivative liability and accreted the resulting debt discount as interest expense using the effective interest rate method over the contractual term of the 2014 Convertible Loans. The Company had recognized noncash accretion in the amount of $52,000 and $39,000 in Interest expense for the years ended December 31, 2016 and 2015, respectively.

The conversion features had previously been accounted for as a derivative and separately accounted from the 2014 Convertible Loans. The derivative liabilities were recognized as a noncurrent liability. See Note 14 for discussion of Derivatives and Note 2 for discussion of Fair value of financial instruments.

In connection with the Transaction, the 2014 Convertible Loans were converted into 116,883 shares of the Company’s common stock based on a conversion price of $19.50. The carrying value of the debt at the time of conversion was $1.0 million and the fair value of the derivative liabilities was $545,000. The fair value of the shares received at conversion was $2.3 million. The difference between the fair value of the shares and the carrying value of the debt plus the fair value of the derivative liabilities was $732,000, which was recognized as a loss on conversion and recorded in Other income and expense for the year ended December 31, 2016.

Prior to the conversion, interest accrued at a rate of 8% per annum. Accrued interest in the amount of $198,000 had been recorded through the date of conversion. Prior to completion of the Transaction, the holders of the 2014 Convertible Loans waived their rights to any unpaid interest and discharged the Company from this liability. The $198,000 of accrued interest has been recognized as a gain on debt extinguishment and is recorded in Other income and expense for the year ended December 31, 2016.

14. Derivatives

The following disclosures summarize the fair value of derivative instruments not designated as hedging instruments in the Consolidated Balance Sheets and the effects of changes in fair value related to those derivative instruments on the Consolidated Statements of Operations (in thousands):

<table>
<thead>
<tr>
<th>Derivative Instruments Not Designated as Hedging Instruments</th>
<th>Balance Sheet Location</th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derivative liabilities</td>
<td>Noncurrent liabilities</td>
<td>$</td>
<td>$2,047</td>
</tr>
<tr>
<td>Warrants liability</td>
<td>Current liabilities</td>
<td>844</td>
<td>1,163</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effect of Derivative Instruments Not Designated as Hedging Instruments</th>
<th>Location of Gains (Losses) Recognized</th>
<th>December 31, 2016</th>
<th>December 31, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derivative liabilities</td>
<td>Non-operating income</td>
<td>$261</td>
<td>$172</td>
</tr>
<tr>
<td>Warrants liability</td>
<td>Non-operating (expense) income</td>
<td>(294)</td>
<td>148</td>
</tr>
</tbody>
</table>

The derivative liabilities related to the conversion feature embedded in the 2014 Convertible Loans and 2015 Convertible Loans have been separately recognized at their fair value. The Company determined that embedded features met the definition of a derivative and was required to be recorded at fair value at issuance and remeasured for each reporting period thereafter.
15. Subsequent Events

On February 7, 2017, Parent entered into an Office Lease Agreement with SHIGO 10 PO Owner LLC for approximately 5,116 rentable square feet (the New Office) in the building located at 10 Post Office Square, Boston, Massachusetts. The New Office will serve as the Company's executive offices.

The initial term of the lease is 62 months beginning on the later of the date on which the landlord substantially completes certain renovations to the New Office or March 1, 2017. The Company has the option to extend the lease one time for an additional 5-year period.

Following a two-month rent abatement period, the Company will be obligated to make monthly rent payments in an amount beginning at $20,997 and increasing by approximately 2% annually for the term of the lease. In addition, the Company is responsible under the lease for specified costs and charges, including certain operating expenses, utilities, taxes and insurance.

In addition, the lease contains customary events of default that entitle the landlord, among other things, to terminate the lease and recover from the Company all rent payments and other amounts payable as of the date of termination and that would otherwise be payable for the remainder of the term of lease, plus certain additional costs and expenses arising from the termination. The specified events of default include, among others, nonpayment of rent or other amounts due and payable by the Company under the lease, an uncured breach of a covenant under the lease and certain bankruptcy and insolvency events.
<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Exhibit Description</th>
<th>Filed Herewith</th>
<th>Incorporated by Reference herein from Form or Schedule</th>
<th>Filing Date</th>
<th>SEC File/Reg. Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Amended and Restated Share Exchange Agreement, dated as of July 13, 2016, by and among the Registrant (formerly Biodel Inc.), Albireo Limited and the Sellers listed on Schedule I thereto.</td>
<td></td>
<td>8-K (Exhibit 2.1)</td>
<td>7/13/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.1</td>
<td>Restated Certificate of Incorporation of the Registrant, filed with the Secretary of State of the State of Delaware on May 17, 2007.</td>
<td></td>
<td>S-1 (Exhibit 3.1)</td>
<td>2/7/2007</td>
<td>333-140504</td>
</tr>
<tr>
<td>3.1.2</td>
<td>Certificate of Designation of Series A Convertible Preferred Stock of the Registrant, filed with the Secretary of State of the State of Delaware on May 17, 2011.</td>
<td></td>
<td>8-K (Exhibit 4.6)</td>
<td>5/19/2011</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.3</td>
<td>Certificate of Amendment to the Restated Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on June 11, 2012.</td>
<td></td>
<td>8-K (Exhibit 3.1)</td>
<td>6/11/2012</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.4</td>
<td>Certificate of Designation of Series B Convertible Preferred Stock of the Registrant, filed with the Secretary of State of the State of Delaware on June 26, 2012.</td>
<td></td>
<td>8-K (Exhibit 4.8)</td>
<td>6/27/2012</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.5</td>
<td>Certificate of Amendment to the Restated Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on December 20, 2012.</td>
<td></td>
<td>10-K (Exhibit 3.5)</td>
<td>12/21/2012</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.6</td>
<td>Certificate of Amendment to the Restated Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on March 17, 2015.</td>
<td></td>
<td>8-K (Exhibit 3.1)</td>
<td>3/18/2015</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.7</td>
<td>Certificate of Amendment to the Restated Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on November 3, 2016 (Reverse Stock Split).</td>
<td></td>
<td>8-K (Exhibit 3.1)</td>
<td>11/4/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.1.8</td>
<td>Certificate of Amendment to the Restated Certificate of Incorporation, filed with the Secretary of State of the State of Delaware on November 3, 2016 (Name Change).</td>
<td></td>
<td>8-K (Exhibit 3.2)</td>
<td>11/4/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>3.2</td>
<td>Amended and Restated Bylaws of the Registrant.</td>
<td></td>
<td>S-8 (Exhibit 4.2)</td>
<td>7/6/2007</td>
<td>333-144407</td>
</tr>
<tr>
<td>4.1</td>
<td>Form of common stock certificate.</td>
<td></td>
<td>10-K (Exhibit 4.1)</td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>Exhibit Number</td>
<td>Exhibit Description</td>
<td>Filed Herewith</td>
<td>Incorporated by Reference herein from Form or Schedule</td>
<td>Filing Date</td>
<td>SEC File/Reg. Number</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>--------------------------------------------------------</td>
<td>--------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>4.2</td>
<td>Form of Warrant issued in the Registrant’s June 2012 private placement.</td>
<td>8-K (Exhibit 4.9)</td>
<td>6/22/2012</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>4.3</td>
<td>Warrant to Purchase Common Stock of Albireo Pharma, Inc., dated November 4, 2016, issued to Kreos Capital IV (Expert Fund) Limited.</td>
<td>8-K (Exhibit 4.1)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>4.4</td>
<td>Registration Rights Agreement, dated as of July 25, 2014, by and between the Registrant and Lincoln Park Capital Fund, LLC.</td>
<td>8-K (Exhibit 10.2)</td>
<td>7/28/2014</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.1</td>
<td>Supplemental Deed, dated as of May 24, 2016, by and among Kreos Capital IV (UK) Limited, Albireo Limited, Albireo AB and Eloix AB, including as Schedule 1 thereto the Amended and Restated Agreement for the Provision of a Loan Facility of up to €6,000,000, dated as of December 18, 2014, by and among Kreos Capital IV (UK) Limited, Albireo Limited, Albireo AB and Eloix AB.</td>
<td>8-K (Exhibit 10.1)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.2</td>
<td>Guaranty and Security Agreement, dated as of November 4, 2016, by and between Albireo Pharma, Inc. and Kreos Capital IV (UK) Limited.</td>
<td>8-K (Exhibit 10.2)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.3*</td>
<td>Employment Agreement, dated as of July 27, 2015, by and between Albireo, Inc. and Ronald H.W. Cooper.</td>
<td>8-K (Exhibit 10.3)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.4*</td>
<td>Employment Agreement, dated as of February 14, 2008, by and between Albireo AB and Jan P. Mattsson, Ph.D.</td>
<td>8-K (Exhibit 10.4)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.5*</td>
<td>Employment Agreement, dated as of August 4, 2016, by and between Albireo, Inc. and Thomas A. Shea.</td>
<td>8-K (Exhibit 10.5)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.6*</td>
<td>Employment Agreement, dated as of September 6, 2016, by and between Albireo, Inc. and Paresh N. Soni, M.D., Ph.D.</td>
<td>8-K (Exhibit 10.6)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.7*</td>
<td>Employment Agreement, dated as of November 28, 2016, by and between the Registrant and Martha J. Carter.</td>
<td>10-K (Exhibit 10.7)</td>
<td>12/22/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.8*</td>
<td>Employment Agreement, dated as of February 17, 2016, by and between Albireo, Inc. and Peter A. Zorn.</td>
<td>8-K (Exhibit 10.7)</td>
<td>11/4/2016</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>10.9.1*</td>
<td>Employment Agreement, dated August 21, 2014, by and between the Registrant and Gary G. Gemignani.</td>
<td>8-K (Exhibit 10.1)</td>
<td>8/27/2014</td>
<td>001-33451</td>
<td></td>
</tr>
<tr>
<td>Exhibit Number</td>
<td>Exhibit Description</td>
<td>Filed Herewith</td>
<td>Incorporated by Reference herein from Form or Schedule</td>
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</tr>
<tr>
<td>----------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>--------------------------------------------------------</td>
<td>-------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>10.9.2*</td>
<td>Amendment to Executive Employment Agreement, dated April 1, 2016, by and between the Registrant and Gary G. Gemignani.</td>
<td>8-K (Exhibit 10.1)</td>
<td></td>
<td>4/1/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.9.3*</td>
<td>General Release &amp; Waiver Agreement, dated November 18, 2016, by and between the Registrant and Gary G. Gemignani.</td>
<td>10-K (Exhibit 10.9.3)</td>
<td></td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.10.1*</td>
<td>Change of Control Agreement entered into between the Registrant and certain of its former executive officers.</td>
<td>S-1 (Exhibit 10.12)</td>
<td></td>
<td>2/7/2007</td>
<td>333-140504</td>
</tr>
<tr>
<td>10.10.2*</td>
<td>Executive Severance Agreement entered into between the Registrant and certain of its former executive officers.</td>
<td>S-1 (Exhibit 10.13)</td>
<td></td>
<td>2/7/2007</td>
<td>333-140504</td>
</tr>
<tr>
<td>10.10.3*</td>
<td>Amendment to Executive Severance Agreement and Change of Control Agreement, dated April 1, 2016, by and between the Registrant and Paul S. Bavier.</td>
<td>8-K (Exhibit 10.2)</td>
<td></td>
<td>4/1/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.10.4*</td>
<td>General Release &amp; Waiver Agreement, dated November 15, 2016, by and between the Registrant and Paul S. Bavier.</td>
<td>10-K (Exhibit 10.10.4)</td>
<td></td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.11.1*</td>
<td>Employment Agreement, dated March 26, 2010, between the Registrant and Errol B. De Souza.</td>
<td>8-K (Exhibit 10.1)</td>
<td></td>
<td>4/1/2010</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.11.2*</td>
<td>General Release &amp; Waiver Agreement, dated February 26, 2016, by and between the Registrant and Errol B. De Souza.</td>
<td>10-Q (Exhibit 10.1)</td>
<td></td>
<td>5/10/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.12*</td>
<td>Albireo Pharma, Inc. 2016 Equity Incentive Plan.</td>
<td>8-K (Exhibit 10.9)</td>
<td></td>
<td>11/4/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.13*</td>
<td>Form of Stock Option Agreement under the Albireo Pharma, Inc. 2016 Equity Incentive Plan.</td>
<td>10-K (Exhibit 10.13)</td>
<td></td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.14*</td>
<td>Replacement Stock Options granted to Ronald H.W. Cooper in connection with the closing of the Transaction.</td>
<td>10-K (Exhibit 10.14)</td>
<td></td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.15*</td>
<td>Replacement Stock Options granted to Peter A. Zorn in connection with the closing of the Transaction.</td>
<td>10-K (Exhibit 10.15)</td>
<td></td>
<td>12/22/2016</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.16*</td>
<td>2010 Stock Incentive Plan, as amended.</td>
<td>Schedule 14A (Exhibit A)</td>
<td></td>
<td>1/26/2012</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.17*</td>
<td>2010 Incentive Stock Option Agreement.</td>
<td>10-Q (Exhibit 10.2)</td>
<td></td>
<td>5/7/2010</td>
<td>001-33451</td>
</tr>
<tr>
<td>10.18*</td>
<td>2010 Non Statutory Stock Option Agreement.</td>
<td>10-Q (Exhibit 10.3)</td>
<td></td>
<td>5/7/2010</td>
<td>001-33451</td>
</tr>
<tr>
<td>Exhibit Number</td>
<td>Exhibit Description</td>
<td>Filed Herewith</td>
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<td>10.25*</td>
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<td>License Agreement, dated as of April 2, 2012, by and between Elobix AB, as assignee of Albireo AB, and EA Pharma Co., Ltd. (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.).</td>
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<td>10.28.2**</td>
<td>First Amendment to the License Agreement, dated as of January 30, 2015, by and between Elobix AB, as assignee of Albireo AB, and EA Pharma Co., Ltd. (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.).</td>
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<td>Second Amendment to the License Agreement, dated as of April 6, 2016, by and between Elobix AB and EA Pharma Co., Ltd. (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.).</td>
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<td>Incorporated by Reference herein from Form or Schedule</td>
<td>Filing Date</td>
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* Management contract or compensatory plan or arrangement.

** Confidential treatment is being requested with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Exchange Act of 1934, as amended.
LICENSE AGREEMENT

by and between

ALBIREO AB

and

AJINOMOTO PHARMACEUTICALS CO., LTD.

April 2, 2012

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
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Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
LICENSE AGREEMENT

This LICENSE AGREEMENT (the “Agreement”) is entered into on this 2nd day of April, 2012 (the “Effective Date”), by and between Albireo AB, a company organized under the laws of Sweden with its principal place of business at Arvid Wallgrens Backe 20, 413 46 Gothenburg, Sweden (“Albireo”) and Ajinomoto Pharmaceuticals Co., Ltd., a company organized under the laws of Japan with its principal place of business at 1-1, Irfune 2-chome, Chuo-ku, Tokyo 104-0042, Japan (“Ajinomoto”). Albireo and Ajinomoto may each be referred to herein individually as a “Party” and collectively as the “Parties.”

RECITALS

WHEREAS, Albireo owns or otherwise controls certain patents, patent applications, technology, know-how, scientific and technical information and other proprietary rights and information relating to the research, development and manufacture of the Albireo Compound (as defined below);

WHEREAS, Ajinomoto is engaged in the research, development, manufacture and commercialization of pharmaceutical products, and desires to acquire an exclusive license in the Territory (as defined below) under Albireo’s patents, patent applications, technology, know-how, scientific and technical information and other proprietary information relating to the Albireo Compound; and

WHEREAS, subject to the terms of this Agreement, Albireo wishes to grant to Ajinomoto, and Ajinomoto wishes to receive from Albireo, an exclusive license in the Territory to use, research, develop, manufacture and commercialize the Albireo Compound and Products (as defined below) in the Field (as defined below).

AGREEMENT

NOW THEREFORE, in consideration of the mutual promises and covenants set forth below and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. DEFINITIONS.

1.1. “Administrator” has the meaning set forth in Section 12.1.4.

1.2. “Adverse Event” means any adverse medical occurrence in a patient or clinical investigation subject that is administered a pharmaceutical product, as designated in any Applicable Law in the Territory and that is required to be reported to a Regulatory Authority.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
1.3. “Affiliate(s)” means, with respect to a Person, any other Person that controls, is controlled by, or is under common control with such first Person. For purposes of this definition only, “control” means (i) to possess, directly or indirectly, the power to direct the management or policies of an other Person, whether through ownership of voting securities or by contract relating to voting rights or corporate governance; or (ii) to own, directly or indirectly, more than fifty percent (50%) of the outstanding voting securities or other ownership interests of the other Person.

1.4. “Ajinomoto Data” has the meaning set forth in Section 10.3.1(d).

1.5. “Ajinomoto Indemnified Party” has the meaning set forth in Section 11.1.

1.6. “Ajinomoto Know-How” means (i) Know-How that Ajinomoto Controls as of the Effective Date, if any, or that comes into the Control of Ajinomoto during the Term to the extent actually used by Ajinomoto to Develop, Manufacture, or Commercialize the Albireo Compound or Products in the Field, including, without limitation, any method of making the Albireo Compound or Products, any composition or formulations of the Albireo Compound or Products, or any method of using or administering the Albireo Compound or Products; and (ii) Know-How that is conceived, developed and, in the case of patentable Know-How, Invented solely by employees of Ajinomoto or its Affiliates, or Third Parties acting on behalf of Ajinomoto or its Affiliates during the Term in the course of Ajinomoto’s performance under this Agreement. For the avoidance of doubt, neither Joint Know-How nor Know-How which is Albireo Know-How licensed to Ajinomoto pursuant to this Agreement are included in the definition of Ajinomoto Know-How.

1.7. “Ajinomoto Patent Rights” means (i) any Patent Right that Ajinomoto Controls as of the Effective Date, if any, or that comes into the Control of Ajinomoto during the Term to the extent such rights Cover the Albireo Compound or Products in the Field, including, without limitation, any method of making the Albireo Compound or Products, any composition or formulations of the Albireo Compound or Products, or any method of using or administering the Albireo Compound or Products as actually made, used or sold by Ajinomoto; and (ii) any Patent Right that is conceived, developed and Invented solely by employees of Ajinomoto or its Affiliates, or Third Parties acting on behalf of Ajinomoto or its Affiliates during the Term in the course of Ajinomoto’s performance under this Agreement. For the avoidance of doubt, neither Joint Patent Rights nor Patent Rights which are Albireo Patent Rights licensed to Ajinomoto pursuant to this Agreement are included in the definition of Ajinomoto Patent Rights.

1.8. “Ajinomoto Technology” means Ajinomoto’s interest in (i) the Ajinomoto Know-How and (ii) the Ajinomoto Patent Rights, and all other intellectual property rights in any of the foregoing.

1.9. “Albireo Compound” means Albireo’s proprietary compound designated by Albireo on the Effective Date as “A3309” which has the chemical structure set forth in Schedule 1.9, including, without limitation, all [***] thereof.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
1.10. “Albireo Indemnified Party” has the meaning set forth in Section 11.2.

1.11. “Albireo Know-How” means (i) Know-How that Albireo or its Affiliates Control as of the Effective Date or that comes into the Control of Albireo or its Affiliates during the Term to the extent necessary or useful to Manufacture, Develop or Commercialize the Albireo Compound or Products in the Field, including, without limitation, any method of making the Albireo Compound or Products, any composition or formulations of the Albireo Compound or Products, or any method of using or administering the Albireo Compound or Products; (ii) Know-How that is conceived, developed and, in the case of patentable Know-How, Invented solely by employees of Albireo or its Affiliates, or Third Parties acting on behalf of Albireo or its Affiliates during the Term in the course of Albireo’s performance under this Agreement; and (iii) any data or results described in the proviso in Section 1.70. For the avoidance of doubt, Joint Know-How and Know-How which is Ajinomoto Know-How licensed to Albireo pursuant to this Agreement are not included in the definition of Albireo Know-How.

1.12. “Albireo Patent Rights” means any Patent Right that Albireo or its Affiliates Control as of the Effective Date or that comes into the Control of Albireo or its Affiliates during the Term, including, without limitation, any Patent Right that is conceived, developed and Invented solely by employees of Albireo or its Affiliates, or Third Parties acting on behalf of Albireo or its Affiliates, during the Term in the course of Albireo’s performance under this Agreement to the extent such rights are necessary or useful to Manufacture, Develop or Commercialize the Albireo Compound or Products in the Field, including, without limitation, any method of making the Albireo Compound or Products, any composition or formulations of the Albireo Compound or Products, or any method of using or administering the Albireo Compound or Products; provided, however, that “Albireo Patent Rights” shall not include any Patent Rights to the extent that they Cover the use of the Albireo Compound or related products for the treatment of Liver Diseases. For the avoidance of doubt, Joint Patent Rights and Patent Rights which are Ajinomoto Patent Rights licensed to Albireo pursuant to this Agreement are not included in the definition of Albireo Patent Rights. A list of the Albireo Patent Rights is set forth on Schedule 1.12, which Schedule shall be amended on a timely basis during the Term to reflect changes to the list of Albireo Patent Rights, provided that failure to include an Albireo Patent Right or otherwise update Schedule 1.12 shall not limit the scope of the definition of “Albireo Patent Rights.” For the sake of clarity, if a Valid Claim is included within a Patent Right listed on Schedule 1.12, such Valid Claim shall only provide Innovator Protection if such Valid Claim satisfies the requirements of Section 1.66.

1.13. “Albireo Technology” means Albireo’s interest in (i) the Albireo Know-How and (ii) the Albireo Patent Rights, and all other intellectual property rights in any of the foregoing.

1.14. “API Manufacturing” means the manufacture, production and supply of the Albireo Compound for inclusion in a Product Developed and Commercialized in accordance with this Agreement.

1.15. “Applicable Laws” means all applicable statutes, ordinances, regulations, rules, or orders of any kind whatsoever of any regulatory authority.
1.16. “Arbitrators” has the meaning set forth in Section 12.1.4.

1.17. “Audited Party” has the meaning set forth in Section 5.5.6.

1.18. “Auditing Party” has the meaning set forth in Section 5.5.6.

1.19. “BAS” means any compounds or compositions of matter that [***] in the [***] and prevent [***] the same.

1.20. “Bulk Price” means, on a Product-by-Product basis, with respect to any period, the purchase price of the Albireo Compound per dosage unit.

1.21. “Calendar Quarter” means each of the three (3) consecutive month periods ending on March 31, June 30, September 30 and December 31.

1.22. “Change of Control” means, with respect to Albireo or any of its Affiliates, (i) any sale, transfer, assignment, or other disposition, whether by operation of law or otherwise, of the voting stock or other securities, which results in any single Third Party owning directly or indirectly more than a majority of voting stock or other securities; (ii) the sale of substantially all assets in one or a series of transactions to a Third Party buyer; (iii) a merger or consolidation with any Third Party, as a result of which the equity holders of Albireo or any of its Affiliates immediately prior to such event hold less than a majority of the outstanding capital stock of the surviving entity or parent of the surviving entity; or (iv) the acquisition by a Third Party of the right to nominate a controlling majority of members of the board of directors.

1.23. “Chronic Idiopathic Constipation” or “CIC” has the meaning set forth on Schedule 1.23.

1.24. “Claim” has the meaning set forth in Section 12.1.4.

1.25. “Clinical Supply” has the meaning set forth in Section 4.4.1.

1.26. [***] means any pharmaceutical product in finished form that contains an Albireo Compound [***] at least [***] and all [***] thereof, provided that [***] contained in such [***] are [***]. Notwithstanding the foregoing, [***] shall not be deemed to be [***] and [***] in a Product [***] Combination Product.

1.27. “Commercialization” means any and all activities of using, importing, marketing, promoting, distributing, offering for sale or selling a Product in the Territory, including, for example, pre-commercial launch market development activities conducted in anticipation of Regulatory Approval which approves selling and/or marketing a Product, seeking pricing and reimbursement approvals for a Product, if applicable, preparing advertising and promotional materials, sales force training, all interactions and correspondence with a Regulatory Authority regarding Post-Approval Clinical Trials. When used as a verb, “Commercialize” means to engage in Commercialization.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
1.28. “Commercialization Plan” has the meaning set forth in Section 4.5.1.

1.29. “Commercially Reasonable Efforts” means those efforts and resources normally used by [***] for a product or compound owned by it or to which it has rights of the type it has hereunder, which is of [***]. Without limiting the foregoing, Commercially Reasonable Efforts as it applies to the clinical development of the Albireo Compound and Products hereunder means adherence to the activities and timelines set forth in the Territory Development Plan, as may be amended from time to time. “Commercially Reasonable” as used herein shall be interpreted in a corresponding manner.

1.30. “Competing Product” means a product that (i) is offered in the [***] and [***] as a Product or another [***] or [***] that may reasonably be expected to be substituted for a Product by a pharmacy; (ii) is approved for Commercialization by the Regulatory Authority in a country; (iii) contains an Albireo Compound as an active pharmaceutical ingredient; and (iv) is, in whole or in part, approved by such Regulatory Authority, where the Third Party granted such approval has provided the applicable Regulatory Authority with scientific data to substantiate a claim of equivalence to a Product containing the same Albireo Compound as the approved pharmaceutical product.

1.31. “Confidential Information” means, with respect to a Party, all information (and all tangible and intangible embodiments thereof), which is Controlled by such Party, and is disclosed by such Party to the other Party pursuant to this Agreement. Any technical information disclosed at a meeting of the JDC, JCC or any other committee established pursuant to this Agreement shall constitute Confidential Information unless otherwise specified.

1.32. “Control” or “Controlled” means, with respect to any intellectual property of a Party, that the Party or its Affiliates (i) owns, has an interest in, or other than pursuant to this Agreement, has a license to such intellectual property; and (ii) has the ability to grant access, a license or a sublicense to such intellectual property to the other Party as provided in this Agreement without violating an agreement with or other rights of any Third Party, provided that, in the event a Future Acquirer becomes Albireo’s Affiliate or succeeds the position of Albireo as a Party, any intellectual property right controlled by such Future Acquirer shall be excluded from intellectual property Controlled by Albireo for purposes of this Agreement to the extent that, and only to the extent that, such intellectual property right (a) is not actually used by Albireo or its Affiliates or Licensees to develop, manufacture or commercialize the Albireo Compound or Products after the Future Acquirer qualified as such; (b) comes under the control of such Future Acquirer without any reference or access, by such Future Acquirer, to (A) Albireo Technology, Joint Technology, Ajinomoto Technology, Licensee Know-How, or Licensee Patent Rights; (B) Albireo’s Confidential Information or Ajinomoto’s Confidential Information or any other information under this Agreement related to the Albireo Compound or Products, or related to Ajinomoto or its Affiliates or Sublicensees; or (C) any information which such Future Acquirer obtains by being qualified as such; and (c) is not any intellectual property which would have been granted to Ajinomoto but for any occurrence of Change of Control. The Parties agree that, in the event a Future Acquirer becomes Albireo’s Affiliate or succeeds the position of Albireo as a Party, each Party shall, if requested by the other Party, discuss in good faith whether

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maintaining the language of this Section 1.32 as it is should be adequate in order to maintain the relationship of the Parties contemplated herein. For the purpose of this Section 1.32, “control” or “controlled” means, with respect to any intellectual property of a Future Acquirer, that the Future Acquirer (i) owns, has an interest in, or other than pursuant to this Agreement, has a license to such intellectual property; and (ii) has the ability to grant access, a license or a sublicense to such intellectual property to Ajinomoto as provided in this Agreement without violating an agreement with or other rights of any Third Party.

1.33. “Cover” means, with respect to a Patent Right, that (i) making, using, selling, offering for sale, disposing of or importing of a given compound, product, composition or formulation; (ii) using of a given method or use; (iii) making use of given Know-How; or (iv) performance of a given invention.[***].

1.34. “Development” means all activities performed by or on behalf of either Party in the performance of any Territory Development Plan for the Albireo Compound and Products in the Field. Development shall include, without limitation, all activities related to research, preclinical testing, test method development and stability testing, toxicology, formulation, clinical studies, seeking Regulatory Approval and otherwise handling regulatory affairs, statistical analysis and report writing performed pursuant to the Territory Development Plan with respect to Products. Development shall not include Manufacturing or Commercialization. When used as a verb, “Develop” means to engage in Development.

1.35. “Development Costs” means Albireo’s direct costs specifically identifiable or allocable to Development of a Product pursuant to a Territory Development Plan and actually and reasonably incurred by Albireo or its Affiliates, including FTE Costs, costs of supplies and materials and amounts paid to Third Parties performing activities on behalf of Albireo or its Affiliates.

1.36. “Development Milestone” has the meaning set forth in Section 5.2.1.

1.37. “Disclosing Party” has the meaning set forth in Section 6.1.1.

1.38. “Drug Price” means, on a Product-by-Product basis, Japan’s National Health Insurance drug price, per dosage unit, assigned to a given Product by the Ministry of Health, Labour and Welfare of Japan, minus any consumption taxes contained in such drug price.

1.39. “Effective Date” means the date of this Agreement first set forth above.

1.40. “Effective Filing Date” means, with respect to a patent application, the earlier of (i) the filing date of such patent application or (ii) the earliest filing date of any earlier applications, in any jurisdiction, from which such patent application is entitled to claim the benefit of an earlier filing date under the Applicable Law.

1.41. “Elected Patent Rights” has the meaning set forth in Section 8.3.1.

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1.42. “External Factor” means one or more of the following events or circumstances occurred in Development or Manufacturing or regulatory conditions relating to the Albireo Compound or a Product that delays the further Development of a Product or results in delayed achievement of the enrollment of the first human subject in Japan in any clinical trial, including, without limitation, a Phase I clinical trial, by [***], provided that such events or circumstances were not caused by the negligent act or omission of Ajinomoto, its Sublicensees or any of its Affiliates: (i) the clinical trial of the Albireo Compound or Product is [***]; (ii) [***] difficulties, with respect to [***], for which Albireo receives written notice from Ajinomoto within [***] of becoming aware of such difficulty; (iii) [***] difficulties due to (A) incomplete conduct of activities undertaken by Albireo under the Territory Development Plan, for which Albireo receives written notice from Ajinomoto within [***] of becoming aware of such incompleteness, (B) Albireo’s notice pursuant to Section 4.1.4 which delays orwithholds a Territory Study for a period greater than [***], or (C) Albireo’s notice of inadequacy; (iv) Albireo’s receipt of notice from Ajinomoto alerting Albireo to such inadequacy; or (iv) Albireo’s breach of this Agreement, which breach remains uncured for [***] measured from the date written notice of such breach is given to Albireo by Ajinomoto.


1.44. “Field” means all prophylactic and therapeutic uses of a pharmaceutical product in any formulation or dosage form: (i) to treat or prevent Gastrointestinal Diseases, symptoms of constipation of all causes, and postoperative ileus; and (ii) for use in colonoscopy cleansing procedures.

1.45. “Financial Records” has the meaning set forth in Section 5.5.5.

1.46. “First Commercial Sale” means, with respect to a Product and any country of the Territory, the first sale of such Product under this Agreement for use in the Field to a Third Party in such country, after such Product has been granted Regulatory Approval which approves selling and/or marketing such Product for use in the Field by the competent Regulatory Authorities in such country.

1.47. “First Indication” has the meaning set forth in Section 5.2.1.

1.48. “Force Majeure” has the meaning set forth in Section 12.2.

1.49. “FTE” means a full-time scientific or technical person, or in the case of less than a full-time scientific or technical person, a full-time equivalent scientific or technical person year, carried out by an employee of Albireo or its Affiliates.

1.50. “FTE Costs” means the actual FTEs employed by Albireo or its Affiliates in the conduct of Development activities under the Territory Development Plan multiplied by the applicable FTE Rate.
1.51. “FTE Rate” means the rate that is applicable to an FTE. The rate is based on [***] which is demonstrated by [***] and is intended to capture [***].

1.52. “Future Acquirer” means the Third Party to any Change of Control transaction and any of such Third Party’s Affiliates.

1.53. “GAAP” means generally accepted accounting principles in each country in the Territory, as in effect from time to time.

1.54. “Gastrointestinal Diseases” means Functional Gastrointestinal Diseases in humans as defined by the Rome Foundation in “Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders,” which is attached hereto as Exhibit 1.54. “Gastrointestinal Diseases” shall not include any Liver Diseases.

1.55. “Global Development Plan” has the meaning set forth in Section 4.2.1.

1.56. “Good Clinical Practice” or “GCP” means the then current standards for clinical trials for pharmaceuticals, as set forth in Applicable Laws and regulations promulgated thereunder, as amended from time to time.

1.57. “Good Laboratory Practice” or “GLP” means the then current standards for laboratory activities for pharmaceuticals, as set forth in Applicable Laws and regulations promulgated thereunder, as amended from time to time.

1.58. “Good Manufacturing Practice” or “GMP” means the then current standards for manufacturing activities for pharmaceuticals, as set forth in Applicable Laws and regulations promulgated thereunder, as amended from time to time.

1.59. “Government Authority” means any court, agency, department, authority or other instrumentality of any national, state, county, city or other political subdivision.

1.60. “Grace Period” has the meaning set forth in Section 4.1.2.

1.61. “IBS-C” has the meaning set forth in Section 3.4.

1.62. “Indemnified Party” has the meaning set forth in Section 11.3.

1.63. “Indemnifying Party” has the meaning set forth in Section 11.3.

1.64. “Indemnity Cap” has the meaning set forth in Section 11.5.2.

1.65. “Infringement” has the meaning set forth in Section 8.7.1.

1.66. “Innovator Protection” means, with respect to a given Product sold by Ajinomoto, its Affiliates or its Sublicensees in a given country in the Territory, that (i) at least one Valid Claim of an Albireo Patent Right (other than an Albireo Patent Right that is Controlled by Albireo or its Affiliates non-exclusively with respect to such Product in such
country) or a Joint Patent Right in such country Covers [***]; (ii) such [***] in such country; and/or (iii) at least one Valid Claim of an Ajinomoto Patent Right (other than an Ajinomoto Patent Right that is Controlled by Ajinomoto non-exclusively pursuant to a Third Party License with respect to such Product in such country) in such country Covers [***]; provided, however, that any Innovator Protection provided pursuant to clause (iii) of this Section 1.66 shall expire no later than fifteen (15) years after the First Commercial Sale of the first Product sold under this Agreement in such country. For purposes of this Section 1.66 and Section 5.3.2(b), “[***]” means, with respect to a Product, [***] by Ajinomoto, its Affiliates or its Sublicensees, or a Third Party acting on their behalf; and, for purposes of this Section 1.66 and Section 10.3.1(d), “[***]” means, with respect to a Product in a country in the Territory, [***].

1.67. “Invented” means the act of invention by inventors, as determined in accordance with the patent laws of England.

1.68. “JCC” has the meaning set forth in Section 3.2.

1.69. “JDC” has the meaning set forth in Section 3.1.

1.70. “Joint Know-How” means any Know-How that is conceived, developed and/or, in the case of patentable Know-How, Invented jointly by an employee of Albireo or its Affiliates (or a Third Party acting on any of their behalf) and an employee of Ajinomoto or its Affiliates (or a Third Party acting on any of their behalf); provided, however, that, notwithstanding the foregoing, any data or results generated from studies funded, at least in part, by Albireo, shall not constitute “Joint Know-How” under this Agreement.


1.73. “Know-How” means all inventions, discoveries, data, information (including, without limitation, scientific, technical or regulatory information), processes, methods, techniques, materials, technology, results, analyses, laboratory, pre-clinical and clinical data, or other know-how, whether or not patentable, including, without limitation, pharmacology, toxicology, drug stability, manufacturing and formulation methodologies and techniques, clinical and non-clinical safety and efficacy studies, marketing studies, absorption, distribution, metabolism and excretion studies.

1.74. “Legal Action” has the meaning set forth in Section 8.7.2.

1.75. “Liability” has the meaning set forth in Section 11.1.

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1.76. “Licensee” means any Albireo Affiliate or a Third Party (other than Ajinomoto’s Sublicensee) that is granted a license, sublicense, covenant not to sue or other grant of rights directly or indirectly by Albireo with respect to development, manufacture, and/or commercialization of the Albireo Compound and/or Product. “License” means an agreement or arrangement pursuant to which such a license, sublicense, covenant not to sue or other grant of rights has been granted to a Licensee.

1.77. “Licensee Know-How” means Know-How that Licensee controls as of the effective date of the License or that comes into the control of Licensee during the term of the License to the extent actually used by Licensee to develop, manufacture, or commercialize the Albireo Compound or Products, including, without limitation, any method of making the Albireo Compound or Products, any composition or formulations of the Albireo Compound or Products, or any method of using or administering the Albireo Compound or Products.


1.79. “Liver Diseases” means the following diseases, including manifestations, symptoms and signs thereof: (i) cirrhosis/fibrosis; [***].

1.80. “Local Study” has the meaning set forth in Section 4.2.3.

1.81. “Manufacture,” “Manufactured” or “Manufacturing” means all activities involved in the production of the Albireo Compound and Products to be Developed and/or Commercialized under this Agreement, including, without limitation, API Manufacturing and having the Albireo Compound or Products manufactured by a Third Party.

1.82. “Names and Terms” has the meaning set forth in Section 6.1.6.

1.83. “NDA Approval” means the Regulatory Approval of an NDA for the applicable Product in any country or regulatory jurisdiction.

1.84. “NDA Filing” means submission to the applicable Regulatory Authority of the NDA for the applicable Product in any country or regulatory jurisdiction.

1.85. “Net Price” means, on a Product-by-Product basis, with respect to any period, Net Sales of a Product in the Field divided by the corresponding sold units of dosage of the Product.

1.86. “Net Sales” means, on a country-by-country and Product-by-Product basis, with respect to any period for each country in the Territory, the gross amounts invoiced by Ajinomoto, its Sublicensees or its Affiliates, as applicable, to unrelated Third Parties for sales of a Product in the Field in such country, less the following deductions to the extent included in the gross invoiced sales price for such Product or otherwise directly paid or incurred by Ajinomoto, its Sublicensees or its Affiliates with respect to the sale of such Product in such country: (i) any rebates, trade, quantity and cash discounts, and other usual and customary discounts to

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customers; (ii) retroactive price reductions, credits, adjustments and allowances, including, without limitation, reject ions and returns (including, without limitation, recalls, market withdrawals, damaged goods, and other corrective actions), and including, without limitation, allowances and credits related to inventory management or similar agreements with wholesalers; (ii i) compulsory payments, rebates and chargebacks and any payments of similar nature including, without limitation, those for managed health care organizations or federal, state, and local governments, their respective agencies (including, without limitation, Relief System for Sufferers from Adverse Drug Reactions in Japan), purchasers and reimbursers; (i v) sales, excise, turnover, inventory, use, and similar taxes and import/export duties actually due or incurred with respect to the sale of such Product, including, without limitation, value-added taxes and consumption taxes; (v) [***]; and (v i) freight, postage, shipping and insurance charges actually paid for local and international delivery of such Product. Net Sales will be determined in accordance with GAAP. Without limiting the generality of the foregoing, the following shall not be deemed sales: [***].

In the event that a Product is sold as a [***] in a country, Net Sales from the sale of such [***] in such country shall be calculated for each applicable period by multiplying the Net Sales (as determined without reference to this paragraph) of such [***] (in its entirety) in such country by the fraction A/(A+B), where A is the average gross invoice price of the Product containing the same Albireo Compound included in such [***] as the sole active ingredient when sold separately in finished form in such country and B is the average gross invoice price of the product containing the other prophylactically and/or therapeutically active pharmaceutical ingredient(s) included in the [***] when sold separately in finished form in such country each during the applicable period or, if sales of all products did not occur during such period, the most recent such period in which sales of all products occurred in such country. In the event no such separate sales are made by Ajinomoto, its Affiliates or Sublicensees in such country, Net Sales of the [***] in such country shall be calculated by multiplying such Net Sales by a fraction fairly and reasonably reflecting the relative value contributed by the Albireo Compound to the total value of the [***] as determined by the Parties in good faith. In the event that the Parties are unable to mutually agree upon the fair market value of any products for which no sales exist, then the matter shall be resolved pursuant to Section 12.1.3. To be a [***], products must be invoiced as a single product.

1.87. “New Drug Application” or “NDA” means, with respect to a Product in a country or regulatory jurisdiction, an application to obtain Regulatory Approval which approves selling and/or marketing such Product in such country or regulatory jurisdiction.
1.88. “Patent Right” means any and all (i) patent applications filed under Applicable Law in any jurisdiction in the Territory, including, without limitation, all provisional applications, substitutions, continuations, continuations-in-part, divisions, renewals, and all patents granted thereon; (ii) all patents, reissues, reexaminations and extensions or restorations by existing or future extension or restoration mechanisms, including, without limitation, supplementary protection certificates or the equivalent thereof; and (iii) any other form of government-issued right substantially similar to any of the foregoing.

1.89. “Person” means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture, or similar entity or organization, including, without limitation, a government or political subdivision or department or agency of a government.

1.90. “Pharmacovigilance Agreement” has the meaning set forth in Section 4.3.4.

1.91. “Phase I” in reference to a clinical trial means a trial defined in 21 C.F.R. 312.21(a), as may be amended from time to time, or any equivalent thereto in any other jurisdiction in the Territory.

1.92. “Phase III” in reference to a clinical trial means a trial defined in 21 C.F.R. 312.21(c), as may be amended from time to time, or any equivalent thereto in any jurisdiction in the Territory.

1.93. “Phase IV” in reference to a clinical trial means a trial conducted after a product achieves Regulatory Approval which approves selling and/or marketing such product, carried out for purposes of conducting safety surveillance and ongoing technical support of the product.

1.94. “Post-Approval Clinical Trial” means any clinical trial for use of a Product in an indication, other than a Phase III or Phase IV clinical trial, to be conducted after a Regulatory Approval which approves selling and/or marketing such Product for such indication.

1.95. “Product” means any pharmaceutical product in finished form that contains the Albireo Compound, either as the sole active ingredient [***], and all present and future formulations, dosages and dosage forms thereof.

1.96. “Quality Agreement” has the meaning set forth in Section 4.4.1.

1.97. “Receiving Party” has the meaning set forth in Section 6.1.1.

1.98. “Recipients” has the meaning set forth in Section 6.1.1.

1.99. “Regulatory Approval” means the approval and authorization of a Regulatory Authority in a country or regulatory jurisdiction necessary to develop, manufacture, distribute, sell or market a Product in that country or regulatory jurisdiction, including pricing and reimbursement approval, where required.

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1.100. “Regulatory Authority” means any national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity in each country of the world involved in the granting of regulatory approval for a pharmaceutical product.

1.101. “Regulatory Exclusivity” means any rights or protections which are recognized, afforded or granted by any Regulatory Authority in any country or region of the Territory in association with the Regulatory Approval of a Product in the Field, providing such Product: (i) a period of marketing exclusivity during which a Regulatory Authority that recognizes, affords or grants such marketing exclusivity shall refrain from either reviewing or approving a marketing authorization application or similar regulatory submission submitted by a Third Party seeking to market a Competing Product; or (ii) a period of data exclusivity during which a Third Party seeking to market a Competing Product is precluded from either referencing or relying on previous Regulatory Authority findings of safety or effectiveness with respect to such Product to support the submission, review or approval of a marketing authorization application or similar regulatory submission before the applicable Regulatory Authority.

1.102. “Regulatory Submissions” means applications for Regulatory Approval, notifications and other submissions made to or with a Regulatory Authority that are necessary to Develop, Manufacture or Commercialize a Product in the Field in a particular country, whether obtained before or after a Regulatory Approval in the country. Regulatory Submissions include, without limitation, investigational new drug applications and NDAs, and amendments and supplements to any of the foregoing and their foreign counterparts, applications for pricing and reimbursement approvals, and all proposed labels, labeling, package inserts, monographs and packaging for a Product in a particular country.

1.103. “Relevant Countries” has the meaning set forth in Section 10.3.1.

1.104. “Restricted Product” has the meaning set forth in Section 6.3.1.

1.105. “Right of Reference” means the authority to rely upon, and otherwise use, an investigation for the purpose of obtaining approval of an application to a Regulatory Authority, including, without limitation, the ability to make available the underlying raw data from the investigation for audit by such Regulatory Authority, if necessary.

1.106. “Royalty Period” means, on a country-by-country and Product-by-Product basis, the period of time commencing on the date of First Commercial Sale of a Product in a country and extending until the date on which [***].

1.107. “Sales Milestone” has the meaning set forth in Section 5.2.2.

1.108. “Sublicense” means, with respect to a Party, an Affiliate of such Party or a Third Party that is granted a license, sublicense, covenant not to sue or other grant of rights under this Agreement by such Party pursuant to Section 2.5.1 or 2.5.2 of this Agreement, as the case may be. “Sublicense” means an agreement or arrangement pursuant to which such a license, sublicense, covenant not to sue or other grant of rights under this Agreement has been granted.

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granted by such Party to a Sublicensee pursuant to Section 2.5.1 or 2.5.2. For the sake of clarification, an Affiliate of Albireo or a Third Party shall become a Sublicensee on the effective date of the relevant Sublicense between Albireo and such Affiliate or Third Party, regardless of whether any Ajinomoto Technology or Joint Technology exists on the effective date of such Sublicense.

1.109. “Sublicensee Material Breach” has the meaning set forth in Section 2.5.4.

1.110. “Sued Party” has the meaning set forth in Section 8.8.2.

1.111. “Supply Agreement” has the meaning set forth in Section 4.4.1.


1.113. “Term” has the meaning set forth in Section 10.1.

1.114. “Territory” means Japan, the Kingdom of Thailand, the Republic of Korea, the Republic of Indonesia, the Socialist Republic of Vietnam and Taiwan.

1.115. “Territory Development Plan” means the plan for the Development of the Albireo Compound and Products for Regulatory Approval in the Field in the Territory approved by the JDC and as amended or updated from time to time, but in no event less frequently than once a year, in accordance with this Agreement. The initial Territory Development Plan as of the date hereof is attached hereto as Exhibit 1.115.

1.116. “Territory Study” has the meaning set forth in Section 3.1.2(e).


1.118. “Third Party License” means a license, sublicense, covenant not to sue or other grant of rights directly or indirectly to either Party by a Third Party, including, without limitation, a Licensee.

1.119. “Trademark” has the meaning set forth in Section 8.6.1.

1.120. “Valid Claim” means any claim of (i) any issued and unexpired Patent Right in the Territory that has not been (A) revoked or held unenforceable, unpatentable or invalid by a Government Authority of competent jurisdiction in a decision that is not appealable or that has not been appealed within the time allowed for appeal or (B) abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise; or (ii) any patent application in the Territory that has not been (A) cancelled, withdrawn or abandoned or (B) finally rejected by an administrative agency or Government Authority of competent jurisdiction in a decision that is not appealable or that has not been appealed within the time allowed for appeal, provided that, on a country-by-country basis, a Valid Claim shall exclude any [***] claim of such patent application that (x) has not been

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granted within [***] from the Effective Filing Date of the patent application unless and until a patent issues from such application or (y) does not have a reasonable *bona fide* basis for patentability and enforceability.

1.121. “Year” means each twelve (12) month period ending December 31st.

2. GRANT OF LICENSES.

2.1. **License to Ajinomoto.** Subject to the terms and conditions of this Agreement, Albireo hereby grants to Ajinomoto, effective on the Effective Date, a royalty-bearing, exclusive license (even as to Albireo), with the right to sublicense as set forth in Section 2.5, under the Albireo Technology and Albireo’s interest in the Joint Technology to (i) Develop, Manufacture and Commercialize the Albireo Compound and Products in the Field in the Territory; and (ii) conduct pre-clinical Development and Manufacture of the Albireo Compound and Products in any country in the world for Commercialization in the Field in the Territory. For the sake of clarity, neither Ajinomoto nor any of its Sublicensees or Affiliates shall conduct clinical Development activities related to the Albireo Compound or Products outside of the Territory.

2.2. **License to Albireo.** Subject to the terms and conditions of this Agreement, Ajinomoto hereby grants to Albireo (i) a royalty-free, non-exclusive license, with the right to sublicense as set forth in Section 2.5, under the Ajinomoto Technology and Ajinomoto’s interest in the Joint Technology to the extent necessary for Albireo to exercise its rights and perform its obligations under this Agreement; (ii) a royalty-free, non-exclusive license, with the right to sublicense as set forth in Section 2.5, under the Ajinomoto Technology to conduct development and manufacture of the Albireo Compound and Products in any field in any country in the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term) and to commercialize the Albireo Compound and Products in any field outside of the Territory; and (iii) a royalty-free, exclusive license, with the right to sublicense as set forth in Section 2.5, under Ajinomoto’s interest in the Joint Technology to conduct development and manufacture of the Albireo Compound and Products in any field in any country in the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term) and to commercialize the Albireo Compound and Products in any field outside of the Territory, provided that Ajinomoto reserves the right under its interest in the Joint Technology to, and to have Third Parties acting on Ajinomoto’s behalf, conduct pre-clinical Development and Manufacture of the Albireo Compound and Products in any country in the world for Commercialization in the Field in the Territory. Neither Albireo nor its Affiliates shall directly or indirectly (through Licensees or otherwise) commercialize a Product outside the Field in the Territory during the Term of this Agreement. Ajinomoto acknowledges and confirms that Albireo or its Affiliates may commercialize a product other than the Product, outside the Field in the Territory during the Term and that such commercialization is not prohibited by the immediately preceding sentence or this Agreement.
2.3. Restrictions. Except as permitted by this Agreement, Albireo will not exercise or otherwise exploit the Ajinomoto Technology for any purpose other than to commercialize the Albireo Compound and Products in the Field outside the Territory. Except as permitted by this Agreement, Ajinomoto will not exercise or otherwise exploit the Albireo Technology to commercialize the Albireo Compound and Products (i) in the Field outside of the Territory; or (ii) outside the Field. Neither Albireo nor its Affiliates shall, directly or indirectly, through Licensees or otherwise, commercialize the Albireo Compound and/or a Product as a pharmaceutical product to treat or prevent Liver Diseases. Neither Albireo nor its Affiliates shall directly sell or distribute for sale any Product through channels that are intended to permit importation of a Product into the Territory, other than pursuant to the rights granted to Ajinomoto under this Agreement, and Albireo shall ensure that each License contains a provision prohibiting the relevant Licensee from undertaking any such sales or distribution. Likewise, neither Ajinomoto nor its Affiliates shall directly sell or distribute for sale any Product through channels that are intended to permit importation of a Product outside the Territory, other than pursuant to the rights granted to Albireo under this Agreement, and Ajinomoto shall ensure that each Sublicense to which it is a party contains a provision prohibiting the relevant Sublicensee from undertaking any such sales or distribution.

2.4. Joint Technology. Except as otherwise granted by each Party to the other pursuant to Section 2.1 and Section 2.2, each Party hereby grants the other Party a world-wide, non-exclusive, perpetual, royalty-free, fully paid up, freely sublicensable right and license to exploit the Joint Technology in any manner without compensating or accounting to the other Party.

2.5. Sublicensing.

2.5.1. Ajinomoto Right to Sublicense. Ajinomoto shall have the right to grant sublicenses under the rights granted to Ajinomoto in Section 2.1 to its Affiliates and to [***] for the Development, Manufacture and Commercialization of the Albireo Compound and Products in the Field in any country in the Territory and for the pre-clinical Development and Manufacture of the Albireo Compound and Products in any country in the world, provided that Ajinomoto shall obtain the prior written consent of Albireo prior to granting any sublicense under this Section 2.5.1, such consent not to be unreasonably withheld and, further provided that Ajinomoto shall remain responsible for its obligations under this Agreement, including the obligations to make payments to Albireo hereunder. Ajinomoto shall be responsible for the performance of each Sublicensee and shall ensure that each Sublicensee complies with all relevant provisions of this Agreement.

2.5.2. Albireo Right to Sublicense. Albireo shall have the right to grant sublicenses under the rights granted to Albireo in Section 2.2 to its Affiliates and to Third Parties (i) to the extent necessary for Albireo, to exercise its rights and perform its obligations under this Agreement, (ii) to develop and manufacture the Albireo Compound and Products in any field in any country in
the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term), and (iii) to commercialize the Albireo Compound and Products in any field outside of the Territory, provided that Albireo shall remain responsible for its obligations under this Agreement. Albireo shall be responsible for the performance of each Sublicensee and shall ensure that each Sublicensee complies with all relevant provisions of this Agreement. Albireo shall not grant a sublicense of the rights described in clauses (ii) and (iii) of this Section 2.5.2 unless the potential Sublicensee is a Licensee who has agreed to (a) grant to Albireo a license to Licensee Know-How and Licensee Patent Rights with respect to such Licensee, with, at least, the right to grant a sublicense to Ajinomoto with the right to further sublicense or (b) assign such Licensee Know-How and Licensee Patent Rights to Albireo. Albireo hereby confirms that the Licensee Know-How and Licensee Patent Rights so granted or assigned to Albireo are included in Albireo Know-How and Albireo Patent Rights.

2.5.3. Sublicense Requirements. Each Sublicense of a Party (i) shall be subject and subordinate to, and consistent with, the terms and conditions of this Agreement; (ii) shall not diminish, reduce or eliminate any of such Party’s obligations under this Agreement; (iii) shall require the Sublicensee(s) to comply with all applicable terms of this Agreement; (iv) shall require that the Sublicensee(s) of such Party grant to the other Party a Right of Reference to the same extent of the Right of Reference granted to such other Party pursuant to Section 2.6; (v) shall include an irrevocable commitment to make available any data controlled by such Sublicensee(s) arising out of such Sublicensee(s)’ development activities under the Global Development Plan or the Territory Development Plan, or Local Studies performed by such Sublicensee(s), (including, without limitation, by granting to the sublicensing Party a sublicenseable license under such data) to the non-sublicensing Party and its Sublicensees to the extent necessary for the non-sublicensing Party and its Sublicensees to exploit the rights granted under Sections 2.1 and 2.2, as applicable; and (vi) shall prohibit further sublicensing on terms which are not consistent with the other terms for Sublicense under this Section 2.5. Each Party shall provide the other Party with a complete (excepting financial terms) copy of each Sublicense within thirty (30) days after execution thereof.

2.5.4. Breach of Sublicense. In the event of an uncured material breach by any Sublicensee under a Sublicense that would constitute a material breach of such Party’s obligations under this Agreement (a “Sublicensee Material Breach”), such Party shall provide prompt written notice of such Sublicensee Material Breach to the other Party and shall use Commercially Reasonable Efforts to remedy such Sublicensee Material Breach; provided, however, that if such Party is unable to cure such Sublicensee Material Breach in accordance with Section 10.2.1 of this Agreement, such Sublicensee Material Breach shall be deemed to be an uncured material breach by such Party under this Agreement.

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2.6. Right of Reference. Each Party hereby grants to the other Party and its Sublicensees a Right of Reference to all data included in the regulatory submissions and Regulatory Approvals Controlled by such Party (including, without limitation, Regulatory Submissions and Regulatory Approvals assigned by Ajinomoto to Albireo pursuant to clause (i) of Section 10.3.1(c)), and to all data Controlled by such Party included in Regulatory Submissions and Regulatory Approvals Controlled by such other Party, relating to Products to the extent necessary or useful for such other Party to (i) in the case of Ajinomoto, (A) Develop, Manufacture and Commercialize the Albireo Compound and Products in the Field in the Territory and (B) conduct pre-clinical Development and Manufacture of the Albireo Compound and Products outside of the Territory, and (ii) in the case of Albireo, (A) develop and manufacture the Albireo Compound and Products in any field in any country in the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term) and (B) commercialize the Albireo Compound and Products in any field outside of the Territory. Each Party shall provide a signed statement to the other Party that such other Party may rely on, in support of the approval of such other Party’s Regulatory Submissions, and provide the applicable Regulatory Authority access to, the underlying raw data included in such regulatory submissions and Regulatory Approvals Controlled by such Party and the underlying raw data Controlled by such Party included in such Regulatory Submissions and Regulatory Approvals Controlled by such other Party. Any Right of Reference granted pursuant to this Section 2.6 shall be effective during the Term; provided, however, that with respect to any data included in a Regulatory Approval granted during the Term which approves selling and/or marketing a Product and the relevant Regulatory Submissions (including Regulatory Submissions filed after such Regulatory Approval that are required by the competent Regulatory Authority and/or Applicable Law), the Right of Reference to such data shall extend until the later of (a) the [***] the Term or (b) [***] after the grant of such Regulatory Approval. Each Party shall maintain, at its expense, during the Term, all data, and the underlying raw data thereof, Controlled by such Party included or to be included in Regulatory Submissions and Regulatory Approvals Controlled by the other Party to the extent necessary or useful for such other Party to maintain and/or file the Regulatory Submissions for and to maintain Regulatory Approvals of Products; provided, however, that with respect to any data, and the underlying raw data thereof, included in a Regulatory Approval granted during the Term which approves selling and/or marketing a Product and the relevant Regulatory Submissions (including Regulatory Submissions filed after such Regulatory Approval that are required by the competent Regulatory Authority and/or Applicable Law) that is Controlled by such other Party, such Party shall maintain such data until the later of (x) the [***] the Term or (y) [***] after the grant of such Regulatory Approval.

2.7. Technology Transfer. Within thirty (30) days after the Effective Date, Albireo shall use Commercially Reasonable Efforts to make available all Albireo Know-How to Ajinomoto, at Ajinomoto’s expense. With respect to any data, study results, and other information relating to the Albireo Compound and Products presented by Albireo to Ajinomoto prior to the Effective Date or during the Term, Albireo shall promptly notify Ajinomoto if Albireo should become aware of any material incompleteness and/or material inaccuracy of such data, study results, and other information.
2.8. No Other Rights. No rights, other than those expressly set forth in this Agreement are granted to either Party hereunder, and no additional rights shall be deemed granted to either Party by implication, estoppel or otherwise. All rights not expressly granted by either Party to the other hereunder are reserved.

3. DECISION MAKING AND DISPUTE RESOLUTION.

3.1. Joint Development Committee. Within thirty (30) days of the Effective Date, the Parties shall establish a joint development committee (the “JDC”) that will be responsible for overseeing the Development of Products in the Field in the Territory, and will serve as a forum for exchanging data, information and Development strategy regarding the Products. In addition, the JDC will serve as a forum for sharing and discussing material data and information regarding development of Products by Albireo or its Licensees for commercialization outside of the Territory. Within sixty (60) days of the Effective Date, the JDC shall adopt a charter consistent with the terms of this Agreement.

3.1.1. Membership. The JDC will consist of three (3) senior representatives from each Party. Albireo and Ajinomoto will each designate a co-chair for the JDC. The co-chairs will be responsible for calling meetings and setting the agenda (which shall include a list of all participants expected at a meeting) and circulating such agenda at least [***] prior to each meeting and distributing minutes of the meetings within [***] following such meeting, but will not otherwise have any greater power or authority than any other member of the JDC. JDC members shall have such expertise as appropriate to the activities of the JDC from time to time and the JDC may invite personnel of the Parties having formulation, manufacturing, commercial, marketing and other expertise to participate in discussions of the JDC from time to time as appropriate to assist in the activities of the JDC. The JDC may appoint additional committees as desired.

3.1.2. Responsibilities. The JDC’s responsibilities will include, among others:

(a) reviewing and approving amendments to the Territory Development Plan;

(b) establishing target product profiles for Products in the Territory (including indications for which Products will be Developed and Commercialized in the Territory, key labeling claims required for commercial success of Products given the competitive environment, and any other key product features and benefits which will be used to Develop or support a promotional message or reimbursement status for Products);

(c) reviewing and evaluating progress under the Territory Development Plan on a quarterly basis;

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(d) allocating and assigning Development activities in the Territory Development Plan between the Parties;

(e) reviewing protocols (including their modification) for pre-clinical or clinical studies relating to the Products in the Territory (each, a “Territory Study”);

(f) monitoring progress of Territory Studies and proposing additional studies for Products;

(g) recommending whether to jointly Develop a Product in the Territory for new indications or new formulations;

(h) reviewing and commenting on Regulatory Submissions in the Territory relating to Products;

(i) facilitating the exchange of all data, information, material or results relating to Development of Products;

(j) establishing procedures regarding the collection, sharing and reporting of Adverse Event information related to Products consistent with the Pharmacovigilance Agreement to be entered into in accordance with Section 4.3.4;

(k) arranging for each Party to discuss and agree upon the appropriate [***] for the [***] in the [***] activities under the [***] and to [***]; and

(l) receiving and discussing all material data, information, material or results relating to development of Products by Albireo or Licensees for commercialization outside of the Territory.

3.1.3. Meetings. During Development, the JDC will meet at such frequency as shall be established by the Parties (but not less frequently than four (4) times per Year). Meetings of the JDC shall alternate between the offices of the Parties, unless otherwise agreed upon by the members of the JDC, or may be held telephonically or by video conference. Meetings of the JDC shall be effective only if at least one (1) representative of each Party is in attendance or participating in the meeting. Members of the JDC shall have the right to participate in and vote at meetings by telephone. Each Party shall be responsible for expenses incurred by its employees and its members of the JDC in attending or otherwise participating in JDC meetings. Each Party shall use reasonable efforts to cause its representatives to attend the meetings of the JDC. If a representative of a Party is unable to attend a meeting, such Party may designate an alternate to attend such meeting in place of the absent representative.

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3.1.4. Minutes and Agendas. The minutes of each JDC meeting shall provide a description in reasonable detail of the discussions held at the meeting and a list of any actions, decisions or determinations approved by the JDC. Minutes of each JDC meeting shall be approved or disapproved, and revised as necessary, at the next meeting.

3.2. Joint Commercialization Committee. No later than the dosing of the first patient in the first Phase III clinical trial for the Product in the Territory, the Parties will establish a joint commercialization committee (“JCC”) that will oversee the Commercialization of the Product in the Field in the Territory. The JCC will coordinate selling and marketing efforts under the Commercialization Plan and will serve as a forum regarding Product Commercialization in the Field in the Territory. In addition, the JCC will serve as a forum for sharing and discussing material data and information regarding commercialization of Products by Albireo or Licensees outside of the Territory. No later than sixty (60) days after the JCC is established, the JCC shall adopt a charter consistent with the terms of this Agreement.

3.2.1. Membership. The JCC will consist of three (3) senior representatives from each Party. Albireo and Ajinomoto will each designate a co-chair for the JCC. The co-chairs will be responsible for calling meetings and setting the agenda for and distributing minutes of the meetings, but will not otherwise have any greater power or authority than any other member of the JCC. JCC members shall have such expertise as appropriate to the activities of the JCC from time to time and the JCC may invite personnel of the Parties having development, formulation, manufacturing, financial and other expertise to participate in discussions of the JCC from time to time as appropriate to assist in the activities of the JCC.

3.2.2. Responsibilities. The JCC’s responsibilities will be limited to the following:

(a) reviewing the strategy for the Commercialization of Products in the Field in the Territory;

(b) reviewing the Commercialization Plan for Products in the Field in the Territory, as well as updating the Commercialization Plan on an annual basis to reflect materially changed circumstances, and amending the Commercialization Plan from time to time as appropriate;

(c) overseeing the implementation of the strategy for Commercializing Products in the Field in the Territory (including strategies related to Regulatory Approvals, reimbursement, publications, advertising and promotion, brand integrity, sales, and launch sequence as set forth in the Commercialization Plan);

(d) providing input to the JDC regarding the target product profile for Products and making recommendations regarding changes to the same;
3.2.3. Meetings. The JCC will meet at such frequency as shall be established by the Parties (but not less frequently than two (2) times per Year commencing twelve (12) months prior to the anticipated final Regulatory Approval necessary for the First Commercial Sale of the initial Product in the Territory and during the first five (5) years of Commercialization). Meetings of the JCC shall alternate between the offices of the Parties, unless otherwise agreed upon by the members of the JCC, or may be held telephonically or by video conference. Meetings of the JCC shall be effective only if at least one (1) representative of each Party is in attendance or participating in the meeting. Members of the JCC shall have the right to participate in and vote at meetings by telephone. Each Party shall be responsible for expenses incurred by its employees and its members of the JCC in attending or otherwise participating in JCC meetings.

3.2.4. Minutes and Agendas. The minutes of each JCC meeting shall provide a description in reasonable detail of the discussions held at the meeting and a list of any actions, decisions or determinations approved by the JCC. Minutes of each JCC meeting shall be approved or disapproved, and revised as necessary, at the next meeting.

3.3. Other Committees. The Parties may establish other committees or sub-committees as the Parties deem appropriate.

3.4. Elevation and Dispute Resolution. Each Party’s representatives on any committee will collectively have one vote on all matters that are within the responsibility of such committee. The members of each committee will use reasonable efforts to reach consensus on all decisions. In the event that the members of the JDC or JCC are unable to agree on a particular issue within [***] days of such issue being first presented to such committee, such issue shall be referred to [***] of each Party or their designees for resolution and, in the event such individuals are unable to resolve such issue within [***] days, [***], provided that [***] shall reasonably consider [***] hereunder and shall [***] consistent with the goal of obtaining Regulatory Approval for Products as soon as practicable and to commercialize the Products where all Regulatory Approval necessary for marketing and distribution is obtained and, provided further, that no amendment to the Territory Development Plan that allocates responsibilities or activities to Albireo may be approved by [***]. For the avoidance of doubt, no decision of the JDC, JCC or [***] may be made that would (i) reduce the obligations of the Parties under this Agreement; or (ii) reasonably be expected to have a material adverse effect on

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the Global Development Plan or commercialization of the Albireo Compound in China, the US and/or the EU. Notwithstanding clause (ii) of this Section 3.4, the JDC, JCC and [***] may decide to undertake any activity required pursuant to Applicable Law and/or written instructions from the competent Regulatory Authority in a country in the Territory to obtain Regulatory Approval of a Product for CIC or Constipation-Predominant Irritable Bowel Syndrome (“IBS-C”) in such country, provided that, [***] and shall use Commercially Reasonable Efforts to [***] to avoid or minimize the adverse effects of such activity.

4. DEVELOPMENT, REGULATORY, COMMERCIALIZATION.

4.1. Development

4.1.1. Territory Development Plan. The initial Territory Development Plan for the initial Product in the Field is set forth in Exhibit 1.115. Ajinomoto will direct, coordinate and manage the Development of the initial Product in the Field in the Territory in accordance with the Territory Development Plan. The Territory Development Plan will include, among other things, the indications in the Field for which each Product is to be Developed and other exploratory indications in the Field for which a Product may be developed, critical activities to be undertaken, timelines, Go/No Go decision points and relevant decision criteria and allocations of responsibilities between the Parties for the various activities to be undertaken under the Territory Development Plan. During the Term, Ajinomoto will amend the Territory Development Plan on an ongoing basis as necessary, any amendments (other than amendments required to comply with Applicable Laws or written requirements imposed by Regulatory Authorities) being subject to review by the JDC, and any amendments required to comply with Applicable Laws or written requirements imposed by Regulatory Authorities being subject to report to the JDC, provided that the Territory Development Plan will at all times contain terms that reflect the use of Commercially Reasonable Efforts to Develop the Product to obtain Regulatory Approval in the Field in Japan and, after the first patient is dosed in a Phase III trial of the Product in Japan, in the other countries throughout the Territory as soon as practicable and provided further that Ajinomoto will not assign any Development activities to Albireo beyond those set forth in the initial Territory Development Plan without Albireo’s prior consent, such consent not to be unreasonably withheld.

4.1.2. Development Activities. Except for the specific responsibilities allocated to Albireo as set forth in the Territory Development Plan or assigned to Albireo by Ajinomoto after receiving Albireo’s prior consent and subject to Section 4.1.4, Ajinomoto will be responsible for all aspects of Development of Products, including conducting all clinical trials for Products and payment of all costs associated with the Development activities undertaken by Albireo in accordance with the Territory Development Plan; provided, however, that if such activities undertaken by Albireo or its Affiliate are also a

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part of the Global Development Plan, Albireo shall be responsible for all costs associated with such activities, unless such activities are also (i) specific to or primarily related to obtaining Regulatory Approval in the Territory and (ii) specifically requested by Ajinomoto, in which case Ajinomoto shall be responsible for all costs associated with such activities. Ajinomoto shall use Commercially Reasonable Efforts to implement, conduct and complete the Development activities under the Territory Development Plan, and, to the extent the Territory Development Plan contemplates activities by Albireo, to cooperate with and provide reasonable support to Albireo in Albireo’s conduct of activities under the Territory Development Plan. Without limiting the foregoing, Ajinomoto shall use Commercially Reasonable Efforts to enroll the first human subject in Japan in any clinical trial for the purpose of Regulatory Approval of a Product, including, without limitation, a Phase I clinical trial, by the [***] of the Effective Date. In the event Ajinomoto fails to enroll such human subject in Japan by the [***], this Agreement shall automatically terminate on the [***] following such [***]; provided, however, that Ajinomoto may maintain this Agreement if, within [***] after such [***], Ajinomoto (a) enrolls the first human subject in a clinical trial in Japan or (b) pays the first milestone payment set forth in Section 5.2.1 to Albireo; and provided, further, that if Ajinomoto’s failure to enroll the first human subject in a clinical trial in Japan by [***] is attributable to an External Factor, the Parties shall promptly meet to discuss in good faith an appropriate grace period beyond such [***] period (such grace period, the “Grace Period”). Once the Grace Period is agreed upon by the Parties, such [***] period shall be extended by such Grace Period. Payment of the first milestone pursuant to this Section 4.1.2 shall terminate any obligation to pay such milestone upon actual enrollment of the first human subject in any clinical trial in Japan. Each Party will undertake its Development activities in accordance with all Applicable Laws, GCP, GLP and GMP.

4.1.3. Reports of Development Activities. Each Party shall report on Development activities undertaken by such Party or its Sublicensees in accordance with the Territory Development Plan, including, without limitation, by providing a reasonably detailed summary of all results, data and material inventions, if any, obtained from such activities. Such reports shall be provided by each Party to the other at least [***] prior to each meeting of the JDC, but not less frequently than quarterly. In addition, each Party shall, upon the other party’s request and at the other party’s expense, make appropriate scientific and regulatory personnel available to the other Party, either by telephone or in person as the Parties may mutually agree, as reasonably required to keep the other Party informed of Development activities.

4.1.4. Territory Studies. Ajinomoto, its Affiliates, and/or its Sublicensees may conduct Territory Studies if the following conditions have been met: (i) such Territory Study is included in an approved Territory Development Plan; and (ii) Ajinomoto has provided written notice to Albireo of
its (or its Affiliates’ or Sublicensees’) intent to commence any such Territory Study, which notice shall include a copy of the Territory Study protocol, and Albireo has not, within [***] of receipt of such notice, notified Ajinomoto that it has made a good faith determination that the conduct of such Territory Study will adversely affect the development or commercialization of the Product by Albireo, its Licensees or its Sublicensees in [***], the US and/or the EU. In the event Albireo provides the notice to Ajinomoto described in the prior sentence, Ajinomoto shall consult with Albireo and shall use Commercially Reasonable Efforts to implement all reasonable requests of Albireo made to avoid or minimize the adverse effects of such Territory Study prior to conducting such Territory Study. If Albireo determines, in its sole discretion, that the adverse effects of a Territory Study cannot be mitigated through the requested changes agreed to be implemented by Ajinomoto, Ajinomoto, its Affiliates and/or its Sublicensees shall not commence such Territory Study; provided, however, that Ajinomoto, its Affiliates and/or Sublicensees may commence such Territory Study if such Territory Study is required to obtain Regulatory Approval of a Product for CIC or IBS-C in a country in the Territory pursuant to Applicable Laws or written instruction from the competent Regulatory Authority in such country. Albireo may share the protocol, data and results of any Territory Study with Licensees, provided that such Licensee shall be subject to a confidential disclosure agreement that is at least as protective of such information as the confidentiality restrictions in this Agreement and provided further that Albireo shall have the right to share with Ajinomoto, its Affiliates, and its Sublicensees and shall provide promptly, at least, to Ajinomoto any of such Licensee’s similar protocols, data and study results. Each Party and its Sublicensee will undertake its Territory Studies activities in accordance with all Applicable Laws, GCP, GLP and GMP.

4.1.5. Regulatory Diligence Obligations. Ajinomoto shall use Commercially Reasonable Efforts to apply for and obtain Regulatory Approval throughout the Territory as soon as practicable.

4.2. Global Development Plan and Local Studies.

4.2.1. Global Development Plan. A summary of Albireo’s Global Development Plan is set forth in Exhibit 4.2.1 (the “Global Development Plan”). The Global Development Plan will include, among other things, Phase III clinical studies, pre-clinical studies and CMC (chemistry, manufacturing, and controls) for obtaining Regulatory Approval in the US and the EU. Albireo shall use Commercially Reasonable Efforts to implement and conduct the development activities identified under the Global Development Plan. Albireo shall be responsible for all aspects of the Global Development Plan and payment of all costs associated with the development activities undertaken by Albireo in accordance with the Global Development Plan; provided, however, that if such activities are also the Development activities undertaken by Albireo or its

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Affiliate in accordance with the Territory Development Plan and further are also (i) specific to or primarily related to obtaining Regulatory Approval in the Territory and (ii) specifically requested by Ajinomoto. Ajinomoto shall be responsible for all costs associated with such activities. Ajinomoto acknowledges that the Global Development Plan is subject to change (including, without limitation, the inclusion of additional studies) at any time by Albireo or its Licensees, in Albireo’s or such Licensee’s reasonable discretion; provided, however, that Albireo shall provide Ajinomoto with [***] prior written notice of such changes and provided further that in the event that Ajinomoto notifies Albireo that it has made a good faith determination that such changes proposed to the revised Global Development Plan will adversely affect Development, Manufacture or Commercialization of the Albireo Compound and/or Product by Ajinomoto or its Sublicensees, Albireo shall consult with Ajinomoto and shall use Commercially Reasonable Efforts to implement all reasonable requests of Ajinomoto made to avoid or minimize the adverse effects of such changes proposed to the revised Global Development Plan. Albireo will conduct its development activities under the Global Development Plan in accordance with all Applicable Laws, GCP, GLP and GMP.

4.2.2. Reports of Development Activities. Albireo shall report on development activities undertaken by Albireo in accordance with Global Development Plan, including, without limitation, by providing a reasonably detailed summary of all results, data and, material inventions, if any, obtained from such activities. Albireo shall report on development activities of each of its Licensees, including, without limitation, by providing a reasonably detailed summary of all results, data and, to the extent such Licensee is a Sublicensee of Albireo pursuant to clause (ii) or (iii) of Section 2.5.2, Licensee Know-How and Licensee Patent Rights, if any, obtained from such activities; provided, however, that Albireo’s reporting obligations with respect to each Licensee’s activities under this Section 4.2.2 shall exist if, and only to the extent that, Ajinomoto agrees in writing to permit Albireo to report to such Licensee on Ajinomoto’s development activities on terms substantially similar to this Section 4.2.2. Albireo shall provide reports of its and its Licensees development activities to Ajinomoto [***]. Additionally, at least [***] prior to each meeting of the JDC, Albireo shall provide Ajinomoto with updates of such development activities to the previous meeting of the JDC. In addition, Albireo shall, upon Ajinomoto’s request and at Ajinomoto’s expense, make appropriate scientific and regulatory personnel available to Ajinomoto, either by telephone or in person as the Parties may mutually agree, as reasonably required to keep Ajinomoto informed of development activities under the Global Development Plan.

4.2.3. Local Studies. Albireo or its Licensee may conduct pre-clinical and clinical studies relating to Products outside of the Global Development Plan but not in the Territory (each, a “Local Study”) if the following conditions have been met: (i) Albireo has provided written notice to
Ajinomoto of its or its Licensee’s intent to commence any such Local Study, which notice shall include a copy of synopsis of the Local Study protocol; and (ii) Ajinomoto has not, within [***] of receipt of such notice, notified Albireo that [***]. In the event Ajinomoto provides the notice to Albireo described in the prior sentence, Albireo shall consult with Ajinomoto and shall use Commercially Reasonable Efforts to implement all reasonable requests of Ajinomoto made to avoid or minimize such adverse effects of such Local Study prior to conducting such Local Study. Albireo will conduct its Local Studies in accordance with all Applicable Laws, GCP, GLP and GMP.

4.2.4. Reports of Local Studies. Albireo shall report on development activities undertaken by it relating to any Local Study, including, without limitation, by providing any protocol, a reasonably detailed summary of all results, data, and material inventions, if any, obtained from such activities. Albireo shall report on development activities undertaken by each of its Licensees relating to any Local Study, including, without limitation, by providing any protocol, a reasonably detailed summary of all results, data, and, to the extent such Licensee is a Sublicensee of Albireo pursuant to clause (ii) or (iii) of Section 2.5.2, Licensee Know-How and Licensee Patent Rights, if any, obtained from such activities; provided, however, that Albireo’s reporting obligations with respect to each Licensee’s activities under this Section 4.2.4 shall exist if, and only to the extent that, Ajinomoto agrees in writing to permit Albireo to report to such Licensee on Ajinomoto’s development activities on terms substantially similar to this Section. Such reports shall be provided by Albireo to Ajinomoto in the same manner as the reports and updates pursuant to Section 4.2.2. Also, Albireo shall, upon Ajinomoto’s request and at Ajinomoto’s expense, make appropriate scientific and regulatory personnel available to Ajinomoto, either by telephone or in person as the Parties may mutually agree, for the purpose to keep Ajinomoto informed of development activities and results obtained under the Local Studies.

4.3. Regulatory Matters.

4.3.1. Responsibility For Regulatory Interactions. Ajinomoto shall be responsible for all regulatory matters relating to Products in the Field in the Territory, including payment of all costs associated with obtaining Regulatory Approvals for Products in the Field in the Territory. Ajinomoto shall have sole authority in the Territory with respect to (i) obtaining Regulatory Approvals for Products in the Field and subsequently maintaining such Regulatory Approvals; (ii) communicating with Regulatory Authorities about Products in the Field; and (iii) preparing and submitting supplements, communications, annual reports, adverse event reports, manufacturing changes, supplier designations and other related regulatory filings and Regulatory Submissions. Ajinomoto shall keep Albireo reasonably (but at least on a [***] basis) informed regarding the status and progress of such activity, including,

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without limitation, providing Albireo with as much advance notice as possible of all meetings scheduled with a Regulatory Authority involved in such Regulatory Submission, providing Albireo with a copy, and English abstract of, all written correspondence from a Regulatory Authority involved in such Regulatory Submission, and providing Albireo with an abstract of oral correspondence from a Regulatory Authority involved in such Regulatory Submission. Ajinomoto shall provide Albireo with any data controlled by Ajinomoto necessary to comply with requirements from Regulatory Authorities outside the Territory, with respect to the Product in the Field, and if reasonably requested by Albireo, English translations of all pre-clinical and clinical study reports related to such data.

4.3.2. Regulatory Cooperation. The Parties shall, each at their own expense, provide the other Party with reasonable access to and copies of any documents or other materials Controlled by such Party that are useful for regulatory filings and correspondence and maintenance of Regulatory Approvals for Products in the Field in such other Party’s territory and will otherwise cooperate with the other Party’s efforts to obtain and maintain Regulatory Approvals for Products in the applicable field and territory. Albireo shall keep Ajinomoto reasonably (but at least on a [***] basis) informed regarding the status and progress of all regulatory matters relating to Products outside of the Territory by providing Ajinomoto with a copy and English abstract of any regulatory submission made to a Regulatory Authority and all written correspondence and abstracts of all material oral correspondence involved in such regulatory submission, in each case to the extent Controlled by Albireo. Albireo shall provide Ajinomoto with any data Controlled by Albireo necessary to comply with requirements from Regulatory Authorities in the Territory, with respect to the Product in the Field, such as annual reports, PSUR and CCDS required by Regulatory Authorities.

4.3.3. Regulatory Audits. If a Party receives a notice that a Regulatory Authority desires to conduct an inspection or audit of its or the other Party’s facility, or a facility under contract with it or the other Party, with regard to the Albireo Compound and a Product, then the Party who has received such notice shall promptly notify the other Party of such inspection or audit. The Party who is to be inspected or audited, or is under contract with a facility to be inspected or audited, shall permit such inspection or audit, or obtain consent by such contracted facility on such inspection or audit, and cooperate for such inspection and audit. Following receipt of the inspection or audit observations of such Regulatory Authority (a copy of which the audited Party will immediately provide to the other Party), the Party who is in charge of the correspondence with the Regulatory Authority shall prepare the response to any such observations and shall provide a copy of such response to the other Party.
4.3.4. **Adverse Events.** Within [***] after the Effective Date, the Parties will enter into a pharmacovigilance agreement, which upon such execution will be attached as an exhibit hereto and hereby incorporated into this Agreement by reference (the “Pharmacovigilance Agreement”). The Parties shall comply with the provisions of such agreement. Albireo shall maintain and will be the recognized holder of a global safety database for Adverse Event reports related to the Albireo Compound and Products received by either Party. Ajinomoto will respond to safety inquiries regarding Products in the Field in the Territory.

4.4. **Manufacture.**

4.4.1. **Clinical Supply.** Ajinomoto may, at any time, Manufacture and/or have Manufactured any necessary amount of the Albireo Compound and/or Products by exercising its rights granted pursuant to Section 2.1. Without prejudice to the generality of the foregoing, unless and until otherwise agreed upon between the Parties, Albireo shall be responsible for API Manufacturing and for the Manufacture of Products for pre-clinical and clinical supply, to the extent required for Ajinomoto or its Sublicensees to perform the Development activities set forth in this Agreement and the Territory Development Plan (such supply of the Albireo Compound and/or Products, the “Clinical Supply”). The Parties shall use good faith efforts to execute a supply agreement (the “Supply Agreement”) and a quality agreement (the “Quality Agreement”) for the Clinical Supply within ninety (90) days after the Effective Date, which Supply Agreement and Quality Agreement shall be on terms consistent with those set forth in this Section 4.4.1, and shall contain terms and conditions customary to the supply of pharmaceutical products similar to the Albireo Compound and the Products. Albireo shall Manufacture and deliver the Clinical Supply to Ajinomoto (or to such Third Parties designated by Ajinomoto) sufficiently in advance for Ajinomoto or its Sublicensees to perform the Development activities as contemplated by the Territory Development Plan. Albireo shall invoice Ajinomoto upon [***] pursuant to this Section 4.4.1 and/or the Supply Agreement for the [***], including, but not limited to, [***]. Ajinomoto shall pay all such invoices received from Albireo within [***] of [***]. The Supply Agreement shall contain terms and conditions of record keeping and audit, similar to [***]. All Manufacturing activities performed pursuant to this Section 4.4.1 and/or the Supply Agreement shall be performed in accordance with Applicable Law and in accordance with GCP, GLP and GMP. All Albireo Compound or Product delivered pursuant to this Section 4.4.1 and/or the Supply Agreement shall conform to any applicable specifications mutually agreed upon by the Parties.

4.4.2. **Commercial Supply.** Ajinomoto shall be responsible for API Manufacturing and Manufacturing of Products for Ajinomoto’s commercial distribution and sale in the Territory in accordance with this Agreement.

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4.5. Commercialization in the Territory. Ajinomoto shall use Commercially Reasonable Efforts to Commercialize a Product/Products in the Field in the Territory in accordance with the Commercialization Plan as follows:

4.5.1. Commercialization Plan. The JCC shall review a strategic commercialization plan for the Products in the Field in the Territory (the “Commercialization Plan”) which sets forth, among other things, [***] all other activities to be conducted by Ajinomoto in connection with the Commercialization of Products in the Field in the Territory. The Commercialization Plan will be updated at least once per year.

4.5.2. Commercialization Activities. Ajinomoto shall have sole responsibility for all aspects of Commercialization of Products in the Field in the Territory and shall use Commercially Reasonable Efforts to implement and conduct the Commercialization activities set forth in the Commercialization Plan. Ajinomoto shall undertake the Commercialization activities set forth in the Commercialization Plan in accordance with all Applicable Laws and applicable industry professional standards.

4.5.3. Reports of Commercialization Activities. Ajinomoto shall report on its performance of the Commercialization activities set forth in the Commercialization Plan at each meeting of the JCC. In addition, Ajinomoto shall, at Albireo’s expense, make appropriate scientific and regulatory personnel available to Albireo, either by telephone or in person as Albireo may reasonably request, as reasonably required to keep Albireo informed of the Commercialization activities, including Ajinomoto’s efforts to achieve the diligence obligations set forth in Section 4.5.4.

4.5.4. Diligence Obligations. Ajinomoto shall use Commercially Reasonable Efforts to Commercialize a Product/Products in the Field in Japan and, after the first patient is dosed in a Phase III trial of the Product in Japan, other countries throughout the Territory. Upon the grant of all Regulatory Approvals necessary for marketing and distribution of a Product in a country, Ajinomoto shall use Commercially Reasonable Efforts to complete a First Commercial Sale of such Product in such country within [***] after obtaining such Regulatory Approval, provided that Ajinomoto [***].

4.6. Publication Strategy. The Parties shall coordinate worldwide publication strategy involving Products and activities involving Products related to scientific conferences inside and outside the Territory. Each Party shall be afforded the opportunity to review and approve any scientific paper or presentation with respect to any Product proposed for publication, presentation or distribution by the other Party or its Affiliates, licensees or Sublicensees and shall have [***] days to complete such review and approval (or such shorter period as may reasonably be required by applicable publication deadlines promptly communicated to such Party). The Party proposing publication or presentation shall (i) not unreasonably reject comments furnished by the other Party; (ii) comply with the other Party’s 30

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5. CONSIDERATION. In consideration for the rights granted to Ajinomoto under this Agreement, including, without limitation, the (i) exclusive license under Albireo Technology; (ii) reports and data provided by Albireo; and (iii) Right of Reference, Ajinomoto will pay to Albireo, pursuant to Section 5.1, 5.2, and 5.3 as follows:

5.1. Upfront Payments. Ajinomoto shall pay to Albireo [***] Euros (€[***]) no later than [***] days after the Effective Date, as an upfront, non-creditable, non-refundable fee; provided, however, that Ajinomoto shall undertake every possible effort, and Albireo shall cooperate with such efforts, to make such payment as soon as possible after the Effective Date.

5.2. Milestones.

5.2.1. Development Milestones. As additional consideration for the rights granted to Ajinomoto under this Agreement, Ajinomoto will pay Albireo the following non-creditable, non-refundable amounts within [***] days after the first occurrence of each of the following events (each, a “Development Milestone”):

<table>
<thead>
<tr>
<th>EVENT</th>
<th>MILESTONE PAYMENT</th>
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<tbody>
<tr>
<td>[***]</td>
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</table>

For the avoidance of doubt, in the event Ajinomoto provides notice of termination of this Agreement to Albireo pursuant to Section 10.2.2 prior to the occurrence of any Development Milestone, Ajinomoto shall remain obligated to make any such or subsequent Development Milestone payment that occurs prior to the effectiveness of such termination.
5.2.2. **Sales Milestones**. Ajinomoto will pay Albireo the following non-creditable, non-refundable amounts within [***] days after the first occurrence of the following events (each, a “Sales Milestone”):

<table>
<thead>
<tr>
<th>EVENT</th>
<th>MILESTONE PAYMENT</th>
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<tr>
<td>[***]</td>
<td>[<em><strong>] Yen (¥[</strong></em>])</td>
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<td>[<em><strong>] Yen (¥[</strong></em>])</td>
</tr>
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</table>

5.2.3. **Milestone Payments**. For the avoidance of doubt, each milestone payment under Section 5.2 shall be owed only once. Once Ajinomoto has made any particular milestone payment, Ajinomoto will not be obligated to make any payment with respect to the subsequent occurrence of the same or a similar milestone event anywhere in the Territory and with respect to any Product.

5.3. **Royalties**. In addition to the payments under Sections 5.1 and 5.2, Ajinomoto shall pay to Albireo the royalty payments set forth in this Section 5.3.

5.3.1. **Royalty Rates**. Subject to Section 5.3.2, Ajinomoto shall pay to Albireo, with respect to sales of each Product sold by Ajinomoto, its Affiliates or its Sublicensees in the Field in the Territory [***], an amount equal to:

- [***] percent ([***]%) of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof below or equal to [***] Yen (¥[***]); plus
- [***] percent ([***]%) of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof greater than [***] Yen (¥[***]) and less than or equal to [***] Yen (¥15,000,000,000); plus
- [***] percent ([***]%) of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof greater than [***] Yen (¥[***]) and less than or equal to [***] Yen (¥[***]); plus
- [***] percent ([***]%) of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof greater than [***] Billion Yen (¥[***]).

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
For the purpose of clarification, if Ajinomoto receives ¥[***] of aggregate Net Sales of all Products in each Calendar Quarter in a given Year, then Ajinomoto will pay a royalty of ( [***] % of ¥[***] ) in each of the first two (2) Calendar Quarters, a royalty of ( [***] % of ¥[***] ) plus ( [***] % of ¥[***] ) in the third Calendar Quarter, and a royalty of ( [***] % of ¥[***] ) in the fourth Calendar Quarter.

For the purpose of further clarification, if the Royalty Period of a Product is expired or does not exist in a country, the sales of such Product in such country shall not be counted as Net Sales under this Agreement and, thereby, in no way will such sales be counted in determining whether a Sales Milestone has been achieved under Section 5.2.2 or determining the applicable royalty tier pursuant to this Section 5.3.

5.3.2. Adjustments in Royalty Rates.

(a) Competing Products. Subject to Section 5.3.2(b), on a country-by-country and Product-by-Product basis, if one or more Competing Products is being sold in such country and the sales of all such Competing Products during a Calendar Quarter (based on data from a mutually agreed Third Party source) are greater than [***] percent ([***]% of the aggregate of all such sales combined with the sales of the applicable Product in such country in such Calendar Quarter, then Ajinomoto shall pay to Albireo for each such Calendar Quarter [***] applicable to such Product, a reduced royalty rate on Net Sales of such Product in such country equal to [***] percent ([***]% of the royalty rate applicable under Section 5.3.1, but only for so long as such Competing Products are being sold in such country at such level.

(b) Competing Products and [***]. On a country-by-country and Product-by-Product basis, if (i) a Competing Product is being sold in such country and (ii) [***], then Ajinomoto shall [***] royalties on Net Sales of such Product in such country during the applicable Royalty Period, but only for so long as such Competing Product is being sold in such country. For the sake of clarity, if such Competing Product ceases to be sold in such country and no other Competing Products are being sold in such country, Net Sales of such Product in such country shall thereafter be subject to [***] applicable under Section 5.3.1, subject to Sections 5.3.2(c) and 5.3.2(d), for the duration of the applicable Royalty Period.

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(c) **Bulk Price**. On a Product-by-Product basis, in Japan, in the event Ajinomoto, its Affiliates, or Sublicensees purchases the Albireo Compound as the active pharmaceutical ingredient for such Product and the Bulk Price provided by Albireo or on Albireo’s behalf [***], the royalty rate applicable under Section 5.3.1 [***] shall be [***] by the following [***] :

\[
\frac{(Bulk \ Price) - [***](Drug \ Price)}{Net \ Price} \times 100 \times 0.50
\]

By way of example, if the [***].

With respect to each of [***] other than [***] in the [***], the Parties shall discuss in good faith whether [***] based on [***] should apply to such country. Such discussion will be held as soon as practicable after the [***].

(d) **Licenses from Third Parties**. If Ajinomoto enters into an agreement with a Third Party to obtain a license under a Patent Right or other right in the absence of which Ajinomoto, its Affiliates, or Sublicensees could not legally (including, without infringing any Third Party Patent Rights) Develop, Manufacture or Commercialize the Albireo Compound and/or a Product in the Field in the Territory, Ajinomoto may subtract from the royalties set forth in Section 5.3 [***] percent ( [***]%) of the amount that Ajinomoto paid to such Third Party pursuant to such agreement; provided, however, that the royalties shall not be reduced to less than [***] percent ( [***]%) of the amount that would otherwise be due under Section 5.3.1.

Notwithstanding the foregoing, under no circumstances shall the aggregate royalty rate so calculated under Sections 5.3.2(c) and 5.3.2(d) be reduced to [***] of the amount that would otherwise be due under Section 5.3.1.

5.3.3. **Fully Paid-Up, Royalty Free License**. Following the expiration of the Royalty Period for any Product in a given country in the Territory, no further royalties shall be payable in respect of sales of such Product in such country and, thereafter, the license granted to Ajinomoto under Section 2.1 with respect to such Product in such country shall automatically become a fully paid-up, perpetual, irrevocable, royalty-free license.

5.4. **Payment of Albireo Territory Development Costs and Expert Costs**.

5.4.1. **Development Cost Report**. Within [***] after the end of each Calendar Quarter during which Albireo has performed Development activities pursuant to the Territory Development Plan and/or provided regulatory assistance pursuant to Section 4.3 or 4.2.2, Albireo shall deliver to Ajinomoto an invoice of Development Costs during such Calendar Quarter, which invoice shall set forth the [***] during such Calendar Quarter and the amount of other costs reasonably included in such Development Costs, including costs incurred under

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5.4.2. Payment of Development Costs. Ajinomoto shall pay any invoice delivered by Albireo pursuant to Section 5.4.1 within [***] days of receipt of any such invoice.

5.4.3. Expert Cost Report and Payment. Within [***] after the end of each Calendar Quarter during which either Party has made appropriate personnel available to the other Party pursuant to Section 4.1.3, 4.2.2, or 4.2.4, such Party shall deliver to the other Party an invoice of expenses [***]. The other Party shall pay any invoice delivered by such Party pursuant to this Section 5.4.3 within [***] of receipt of any such invoice.

5.5. Reports and Payments.

5.5.1. Royalty Reports. Within [***] ([***]) days [***] after the end of each Calendar Quarter beginning with the Calendar Quarter in which the First Commercial Sale is made in a country following receipt of Regulatory Approval in such country, Ajinomoto shall deliver to Albireo a report setting forth for the previous Calendar Quarter the following information on a Product-by-Product basis: (i) the gross sales and Net Sales of each Product in the Field in each country of the Territory; (ii) the number of units sold by Ajinomoto, its Affiliates or its Sublicensees; (iii) the basis for any adjustments to the royalty payable for the sale of each Product; (iv) the royalty due hereunder for the sales of each Product; and (v) the applicable exchange rate as determined in accordance with this Agreement. The total royalty due for the sale of Products during such Calendar Quarter shall be remitted at the time such report is made.

5.5.2. Taxes and Withholding. The Parties agree to cooperate with one another and use reasonable efforts, to the extent permitted under applicable law, to minimize obligations for any and all income or other taxes required by applicable law to be withheld or deducted from any royalties, milestone payments, expert cost payments, or other payments made by a Party to the other Party under this Agreement, including by completing all procedural steps, and taking all reasonable measures, to ensure that any withholding tax is reduced or eliminated to the extent permitted under applicable law, including income tax treaty provisions and related procedures for claiming treaty relief. To the extent that a Party is required to deduct and withhold taxes on any payment to the other Party, the paying Party shall deduct and withhold such taxes and pay the amounts of such taxes on behalf of the receiving Party to the proper Government Authority in a timely manner and promptly submit to the receiving Party an official tax certificate or other evidence of such withholding sufficient to enable the receiving Party to claim such payment of taxes. The paying Party shall render the receiving Party reasonable assistance in order to allow the

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receiving Party to recover, as permitted by applicable law, withholding taxes, value added taxes or similar obligations resulting from payments made hereunder or to obtain the benefit of any present or future treaty against double taxation which may apply to such payments. Notwithstanding the foregoing, if a payment made by a Party to the other Party hereunder is subject to a deduction of tax or withholding tax that arises as a result of the paying Party’s failure to comply with this Section 5.5.2 or, if the paying Party is Ajinomoto, Ajinomoto’s failure to make such payment from Japan (other than at the request of Albireo), then such payment shall be increased to the amount that the receiving Party would have received if the paying Party had not failed to take such action. In no case will any obligation of a Party to make a payment to the other Party under this Agreement be reduced as a result of any income or other taxes imposed on any payments between the paying Party and other Persons (other than the receiving Party), including, without limitation, any withholding or other taxes imposed on payments made by a Sublicensee pursuant to a Sublicense.

5.5.3. **Currency.** All amounts payable hereunder shall be in Euros. Currency translation into Euros shall be made by using the simple arithmetic average of the telegraphic transfer selling (TTS) rates on the last business day of each calendar month of the relevant Calendar Quarter quoted by Bank of Tokyo-Mitsubishi UFJ. If, due to restrictions or prohibitions imposed by a national or international authority, payments cannot be made as provided in this Section 5, the Parties shall consult with a view to finding a prompt and acceptable solution, and the paying Party shall deal with such payments as the other Party may lawfully direct at no additional out-of-pocket expense to the paying Party.

5.5.4. **Method of Payment.** Except as permitted pursuant to Section 5.5.3, each payment hereunder shall be made by wire transfer to the bank account designed by the Party receiving payments under this Section 5 in writing to the paying Party at least [***] before the payment is due.

5.5.5. **Record Keeping.** Ajinomoto shall keep, and shall causes its Affiliates and Sublicensees to keep, books and accounts of record in connection with the sale of Products, including records of gross invoiced sales, Net Sales, exchange rates and royalty payments (collectively, the “Financial Records”), in accordance with GAAP and in sufficient detail to permit accurate determination of all figures necessary for verification of royalties and Sales Milestone payments to be made by Ajinomoto under this Section 5. Albireo shall keep, and shall causes its Affiliates and Sublicensees to keep, books and accounts of record in connection with the Development Costs in accordance with GAAP and in sufficient detail to permit accurate determination of all figures necessary for verification of Development Costs payments to be made by Ajinomoto under this Section 5; furthermore, in the event this Agreement is [***] shall [***]. Each Party and its Affiliates, Sublicensees, and Licensees shall keep such records for a period of at least [***] after the end of the Calendar Quarter in which they are generated.

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5.5.6. Audits. Upon thirty (30) days prior written notice from the other Party (the “Auditing Party”), the Party required to keep such books and accounts of record as set forth in Section 5.5.5 (as applicable, the “Audited Party”) shall permit an independent certified public accounting firm of internationally recognized standing, selected by the Auditing Party and reasonably acceptable to the Audited Party, to examine the relevant books and records of the Audited Party and its Affiliates, as may be reasonably necessary to verify the royalty reports submitted by Ajinomoto in accordance with Section 5.5.1, Development Costs reports submitted by Albireo in accordance with Section 5.4.1 and Section 10.3.1(d). An examination by the Auditing Party under this Section will occur not more than [***] and will be limited to the pertinent books and records for any Year ending not more than [***] before the date of the request. The accounting firm will be provided access to such books and records at the Audited Party’s facility or facilities where such books and records are normally kept and such examination will be conducted during the Audited Party’s normal business hours. The Audited Party may require the accounting firm to sign a standard non-disclosure agreement before providing the accounting firm access to its facilities or records. Upon completion of the audit, the accounting firm will provide both the Auditing Party and the Audited Party a written report disclosing whether the royalty reports submitted by Ajinomoto, the Development Costs reports submitted by Albireo, or royalty reports submitted by Albireo are correct or incorrect and the specific details concerning any discrepancies. No other information will be provided to the Auditing Party. If the report submitted by the Audited Party resulted in an underpayment or overpayment, the Party owing underpaid or overpaid amount will promptly pay such amount to the other Party. If, as a result of such inaccurate reports, such underpayment to the Auditing Party or such overpayment to the Audited Party [***] of the total amount owed for the Year then being audited, the Audited Party will reimburse the Auditing Party for the reasonable expense incurred by the Auditing Party in connection with the audit. Any information provided by the Audited Party to the accounting firm and the written report of the accounting firm shall be the Confidential Information of the Audited Party.

5.5.7. Interest. Any payment of any undisputed sums properly due and payable to the receiving Party under this Agreement that is [***] past due shall be subject to interest at an annual percentage rate of then-current base rate of [***] if the paying Party does not make payment within [***] of its receipt of notice that such amount is past due. Likewise, any overpayment for which notice is given that is not refunded within [***] after the date upon which notice of such overpayment was received or made shall, after such date, be subject to interest at an annual percentage rate of then-current base rate of [***]; provided, however, that if the overpayment is due to errors in reports provided by the overpaid Party, such interest shall accrue from the date the overpayment was made. Notwithstanding the preceding, if a Party contests any amounts due.

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hereunder in good faith and promptly notifies the other Party of such dispute, interest shall not accrue as to amounts being so contested until [***] days following the presentation of such notice to the other Party. This Section shall not be construed as prejudicing the receiving Party’s right to receive payment within the relevant period and shall not apply to the extent and for the period that a Force Majeure prevents payment.

6. MUTUAL COVENANTS.


6.1.1. Confidential Information. Except to the extent expressly permitted by this Agreement and subject to the provisions of Sections 6.1.2 and 6.1.3, at all times during the Term and for [***] following the expiration or termination hereof, each Party (the “Receiving Party”) receiving any Confidential Information of the other Party (the “Disclosing Party”) in connection with this Agreement shall: (i) keep completely confidential and shall not publish or otherwise disclose any Confidential Information furnished to it by the Disclosing Party, except to those of the Receiving Party’s employees, Affiliates, sublicensees, consultants, contractors, agents, medical institutes or personnel, or representatives who have a need to know such information (collectively, “Recipients”) to perform such Party’s obligations or exercise its rights hereunder, provided that each such Recipient has a written confidentiality obligation no less strict than the confidentiality provisions herein; and (ii) not use Confidential Information of the Disclosing Party directly or indirectly for any purpose other than performing its obligations or exercising its rights hereunder. The Receiving Party shall be liable for any breach by any of its Recipients of the restrictions set forth in this Agreement, including, without limitation, those set forth in Section 6.1.6.

6.1.2. Exceptions to Confidentiality. The Receiving Party’s obligations set forth in this Agreement shall not extend to any Confidential Information of the Disclosing Party or the Names and Terms:

(a) that is or hereafter becomes part of the public domain through no wrongful act, fault or negligence on the part of a Receiving Party or its Recipients;

(b) that is received from a Third Party without restriction and without breach of any agreement or fiduciary duty between such Third Party and the Disclosing Party;

(c) that the Receiving Party can demonstrate by competent evidence was already in its possession without any limitation or restriction on use or disclosure prior to its receipt from the Disclosing Party;

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(d) that is generally made available to Third Parties by the Disclosing Party without any restriction imposed by the Disclosing Party on disclosure, whether such restriction is by contract, fiduciary duty or by operation of law; or

(e) that the Receiving Party can demonstrate by competent evidence was independently developed by the Receiving Party without any reference to Confidential Information.

6.1.3. Authorized Disclosure.

(a) Notwithstanding the provisions of Section 6.1.1, the Receiving Party and its Recipients may disclose Confidential Information belonging to the Disclosing Party, and the Names and Terms, to the extent that such disclosure is reasonably necessary to:

(i) prosecute or defend litigation;

(ii) comply with applicable governmental laws and regulations (including, without limitation, Applicable Law, rule or regulation or the requirements of a national securities exchange or another similar regulatory body); or

(iii) respond to a valid order, inquiry, or request of, or make filings and submissions to, or correspond or communicate with, any Government Authority.

In the event that the Receiving Party or its Recipients, as applicable, deem it reasonably necessary to disclose Confidential Information belonging to the Disclosing Party pursuant to this Section 6.1.3(a), the Receiving Party shall, to the extent possible, provide the Disclosing Party with reasonable advance notice of such disclosure and take reasonable measures to ensure confidential treatment of such information.

(b) Notwithstanding the provisions of Section 6.1.1, the Receiving Party may disclose Confidential Information belonging to the Disclosing Party to any Third Party who is performing diligence in connection with a transaction with the Receiving Party (including, without limitation, potential Sublicensees and Licensees), provided that each such Third Party has signed a written confidentiality agreement with the Receiving Party no less strict than the terms hereof.

6.1.4. Notification. The Receiving Party shall notify the Disclosing Party immediately, and cooperate with the Disclosing Party as the Disclosing Party may reasonably request, upon the Receiving Party’s discovery of any loss or compromise of the Disclosing Party’s Confidential Information.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
6.1.5. Destruction of Confidential Information. Upon the expiration or earlier termination of this Agreement, the Receiving Party shall (i) destroy all tangible embodiments of Confidential Information of the Disclosing Party, including, without limitation, any and all copies thereof, and those portions of any documents, memoranda, notes, studies and analyses prepared by the Receiving Party or its Recipients that contain or incorporate such Confidential Information and provide written certification of such destruction to the Disclosing Party in a form reasonably acceptable to the Disclosing Party, provided that the legal department of the Receiving Party shall have the right to retain one copy of any such tangible embodiments for archival purposes (provided that such copy shall continue to be maintained on a confidential basis subject to the terms of this Agreement); and (ii) immediately cease, and shall cause its Recipients to cease, use of such Confidential Information as well as any information or materials that contain or incorporate such Confidential Information. Notwithstanding the foregoing, the Receiving Party may keep and use any Confidential Information of the Disclosing Party solely to the extent necessary or useful to exercise its rights and/or perform its obligations that survive such expiration or termination of this Agreement.

6.1.6. Use of Name and Disclosure of Terms. Each Party shall keep the existence of, the terms of and the transactions covered by this Agreement (collectively the “Names and Terms”) confidential and shall not disclose such information to any Third Party through a press release or otherwise, or mention or otherwise use the name, insignia, symbol, trademark, trade name or logotype of the other Party or its Affiliates in any manner without the prior written consent of the other Party in each instance (which may be withheld at the other Party’s discretion); provided, however, that each Party shall be permitted to disclose the Names and Terms without the prior consent of the other Party to its Recipients to perform such Party’s obligations or exercise its rights hereunder, provided that each such Recipient has a written confidentiality obligations no less strict than the confidentiality provisions in this Agreement. The restrictions imposed by this Section shall not prohibit either Party from making any disclosure that is required by Applicable Law, rule or regulation or the requirements of a national securities exchange, tax agency, or another similar regulatory body including, without limitation, disclosing such information in any clinical trial database maintained by or on behalf of a Party. Further, the restrictions imposed on each Party under this Section 6.1.6 are not intended, and shall not be construed, to prohibit a Party from identifying the other Party in its internal business communications, provided that any Names and Terms in such communications remains subject to the confidentiality obligation of this Section 6.1.6. Notwithstanding the foregoing, the Parties acknowledge that they each may engage in financing, licensing and merger and acquisition transactions after the Effective Date and that in such event, the Parties may disclose the existence of this Agreement, including its terms and subject matter, under terms of confidentiality no less strict than those contained in this Agreement, to parties or potential parties in such transaction.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
6.1.7. Remedies. The Parties acknowledge and agree that the restrictions set forth in Section 6.1 are reasonable and necessary to protect the legitimate interests of the Parties and that neither Party would have entered into this Agreement in the absence of such restrictions, and that any breach or threatened breach of any provision of Section 6.1 will result in irreparable injury to the other Party for which there will be no adequate remedy at law. Notwithstanding anything to the contrary in this Agreement, in the event of a breach or threatened breach of any provision of Section 6.1 by a Party, the other Party shall be authorized and entitled to obtain from any court of competent jurisdiction injunctive relief, whether preliminary or permanent, specific performance and an equitable accounting of all earnings, profits and other benefits arising from such breach, which rights shall be cumulative and in addition to any other rights or remedies to which such Party may be entitled in law or equity. The breaching Party agrees to waive any requirement that the non-breaching Party (i) post a bond or other security as a condition for obtaining any such relief; and (ii) show irreparable harm, balancing of harms, consideration of the public interest or inadequacy of monetary damages as a remedy. Nothing in this Section 6.1.7 is intended, or shall be construed, to limit the Parties’ rights to equitable relief or any other remedy for a breach of any provision of this Agreement.

6.2. Compliance with Law. Each Party hereby covenants and agrees to comply with all Applicable Laws related to its activities connected with the Development, Manufacture and Commercialization (as applicable) of the Albireo Compound and Products. Without limiting the generality of the foregoing:

6.2.1. Patient Information. Each Party agrees to abide by all laws, rules, regulations, and orders of all applicable supranational, national, federal, state, provincial, and local governmental entities concerning the confidentiality or protection of patient identifiable information and/or patients’ protected health information in the course of their performance under this Agreement.

6.2.2. Export Controls. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States or other countries which may be imposed upon or related to Albireo or Ajinomoto from time to time. Each Party agrees that it shall not export, directly or indirectly, any technical information acquired from the other Party pursuant to this Agreement or any Products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency or other governmental entity.

6.2.3. Debarment. Each Party agrees that it shall not use, in any capacity, in connection with any of its obligations to be performed under this Agreement any individual who has been debarred under the FD&C Act or the Generic Drug Enforcement Act or similar Applicable Law in any jurisdiction in the Territory.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
6.3. Non-Competition.

6.3.1. Non-Competition by Ajinomoto. After First Commercial Sale of a Product [***] in a country in the Territory [***], neither Ajinomoto nor any of its Affiliates shall, directly or indirectly, or in collaboration with any Third Party, license or otherwise authorize any Third Party to distribute for sale and sell commercially in such country any pharmaceutical products for the treatment of CIC or IBS-C (each such product, a “Restricted Product”), other than the Albireo Compound and Products, without complying with this Section 6.3.1; [***]. Ajinomoto shall not be deemed to be in breach of this Section 6.3.1 if Ajinomoto or any of its Affiliates acquires a Restricted Product through an acquisition of or a merger with the whole or substantially the whole of the business or assets of another entity, so long as Ajinomoto (or its Affiliate) enters into a definitive agreement with a Third Party to divest such Restricted Product within twelve (12) months after the closing of such acquisition or merger. For the sake of clarity, a pharmaceutical product for any of the following indications shall not constitute a Restricted Product so long as such product is not also indicated for the treatment of CIC or IBS-C: (i) the prophylaxis and treatment of Opioid-Induced Constipation; (ii) the prophylaxis and treatment of symptoms of constipation; (iii) use in postoperative ileus (prophylaxis and treatment); and (iv) colonoscopy cleansing procedures; neither Ajinomoto nor any of its Affiliates shall be restricted by this Section 6.3.1 with respect to such non-Restricted Product.

6.3.2. Non-Competition by Albireo. After First Commercial Sale of a Product [***] in a country in the Territory until [***], neither Albireo nor any of its Affiliates shall, directly or indirectly, or in collaboration with any Third Party, license or otherwise authorize any Third Party to, distribute for sale and sell commercially any Restricted Product in such country in the Field without complying with this Section 6.3.2; provided, however, that the prohibitions set forth in this Section 6.3.2 shall not apply to any products that (i) are being commercialized by Albireo as of the Effective Date or (ii), in the event Albireo or any of its Affiliates undergoes a Change of Control, are products under development or being commercialized by the Third Party entity(ies) involved in the Change of Control, as of the effective date of such Change of Control or is subsequently developed or commercialized by such Third Party or its Affiliates (other than Albireo) without use of the Albireo Technology and/or Joint Technology.

6.4. Non-Solicitation. During the Term, neither Party nor any of its Affiliates shall, directly or indirectly, anywhere in the world employ, solicit for employment, or recommend for employment any person engaged in the development, manufacture or commercialization of the Albireo Compound or Products employed by the other Party or any of its Affiliates, during the period such person is so employed or for [***] after termination of such person’s employment with the other Party (or any of its Affiliates).

42 Portions of this Exhibit, indicated by the mark “[***]”, were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
7. REPRESENTATIONS AND WARRANTIES.

7.1. Representations and Warranties of Each Party. As of the Effective Date, each of Ajinomoto and Albireo hereby represents and warrants to the other Party hereto as follows:

(a) it is a corporation or entity duly organized and validly existing under the laws of the state or other jurisdiction of its incorporation or formation;

(b) the execution, delivery and performance of this Agreement by such Party has been duly authorized by all requisite corporate action and does not require any shareholder action or approval;

(c) it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder;

(d) the execution, delivery and performance by such Party of this Agreement and its compliance with the terms and provisions does not and shall not conflict with or result in a breach of any of the terms and provisions of or constitute a default under (i) a loan agreement, guaranty, financing agreement, agreement affecting a product or other agreement or instrument binding or affecting it or its property; (ii) the provisions of its charter or operative documents or bylaws; or (iii) any order, writ, injunction or decree of any court or governmental authority entered against it or by which any of its property is bound; and

(e) it has the full right, power and authority to grant all of the right, title and interest in the licenses granted to the other Party under this Agreement.

7.2. Additional Representations and Warranties of Albireo. Albireo hereby represents and warrants to Ajinomoto that as of the Effective Date:

(a) Albireo solely owns the Albireo Patent Rights listed in Schedule 1.12 attached to this Agreement, and Albireo, together with its Affiliates, has timely paid all maintenance fees, annuities, and the like due or payable with respect to such Albireo Patent Rights (for the avoidance of doubt, such timely payment includes payment of any maintenance fees for which the fee is payable, even if the surcharge date or final deadline for payment of such fee would be in the future);

(b) Albireo Patent Rights includes no Patent Rights that are Controlled by Albireo pursuant to a Third Party License, and any and all Albireo Patent Rights are listed in Schedule 1.12 attached to this Agreement;

(c) Albireo, together with its Affiliates, has the rights with respect to all Albireo Technology that it purports to grant to Ajinomoto hereunder;

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
(d) No Albireo Patent Rights are subject to, or were developed pursuant to, any funding agreement with any government or government agency;

(e) To its actual knowledge, without having made any inquiry other than freedom-to-operate analysis with respect to the Albireo Patent Rights, the manufacture anywhere in the world, use, sale, offer for sale and import in the Field in the Territory of the Albireo Compound and/or a Product does not infringe any Patent Rights of a Third Party;

(f) Albireo has not received any written or oral claim of ownership, inventorship or patent infringement from any Third Party (including, without limitation, by current or former officers, directors, employees, consultants, or personnel of Albireo or any predecessor) with respect to the Albireo Technology, and Albireo is not aware of any reasonable basis for any such claim;

(g) Albireo is not subject to any agreement with a Third Party that includes a royalty or similar payment obligation to, or other restriction or limitation in favor of, such Third Party (including, without limitation, current or former officers, directors, employees, consultants or personnel of Albireo or any predecessor) with respect to its rights to practice the Albireo Technology in the Territory and its right and ability to perform its obligations under this Agreement;

(h) Albireo is not in breach of any material provisions of any agreements with Third Parties relating to the Albireo Patent Rights, if any, and the execution of this Agreement and Albireo’s performance of its obligations hereunder and the consummation of the transactions contemplated herein will not result in any such breach;

(i) There are no challenges, oppositions, interferences, or other proceedings pending or, to Albireo’s best knowledge, threatened with respect to the Albireo Technology;

(j) Albireo has not brought any claim against any Third Party relating to the infringement, misappropriation, or other violation of any Albireo Technology; and

(k) To Albireo’s best knowledge all data, study results, and other information relating to the Albireo Compound and the Product presented by Albireo to Ajinomoto prior to the Effective Date, as of the time such data, study results, and other information were presented to Ajinomoto, were complete in all material respects and accurate.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
7.3. Representation by Legal Counsel. Each Party hereto represents that it has had the opportunity to consult with legal counsel in connection with reviewing and drafting this Agreement. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption shall exist or be implied against the Party which drafted such terms and provisions.

7.4. No Inconsistent Agreements. Neither Party has in effect, and after the Effective Date neither Party shall, enter into any oral or written agreement or arrangement that would be inconsistent with its obligations under this Agreement or limit the ability of either Party to grant the licenses set forth in Section 2 of this Agreement.

7.5. Disclaimer. THE FOREGOING WARRANTIES OF EACH PARTY ARE IN LIEU OF ANY OTHER WARRANTIES, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTIES OF NONINFRINGEMENT, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR ANY IMPLIED WARRANTIES OF FITNESS FOR A PARTICULAR PURPOSE, ALL OF WHICH ARE HEREBY SPECIFICALLY EXCLUDED AND DISCLAIMED. EACH PARTY HEREBY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE DEVELOPMENT, MANUFACTURE OR COMMERCIALIZATION OF ANY PRODUCT UNDER THIS AGREEMENT WILL BE SUCCESSFUL.

8. INTELLECTUAL PROPERTY.

8.1. Disclosure. During the Term, the Parties shall promptly disclose to one another all Know-How (whether patentable or not) arising out of each Party’s performance of activities under this Agreement.

8.2. Ownership.

8.2.1. Ownership of Technology. As between the Parties, each Party shall own any Patent Right or Know-How solely conceived and reduced to practice by employees of it or its Affiliates, or Third Parties acting on behalf of it or its Affiliates during the Term in the course of its performance under this Agreement, and the Parties shall jointly own any Patent Right or Know-How jointly conceived and/or reduced to practice by an employee of Albireo or its Affiliates (or a Third Party acting on any of their behalf) and an employee of Ajinomoto or its Affiliates (or a Third Party acting on any of their behalf). Notwithstanding the foregoing, all data and results generated from studies funded at least in part by Albireo shall be excluded from such jointly owned Patent Right or Know-How, and such excluded data and results shall be solely and exclusively owned by Albireo. Subject to the license grants under Section 2 of this Agreement, as between the Parties, Albireo shall own all Albireo Technology and Ajinomoto shall own all Ajinomoto Technology. [***]. In the event inventorship and ownership of any Technology cannot be resolved by the Parties with advice of their respective intellectual property counsel, such dispute shall be resolved through arbitration pursuant to Section 12.1.4, provided that such arbitration panel shall include at least one (1) arbitrator who is a specialist in English patent law and in chemical and pharmaceutical patents.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
8.2.2. Employee Assignment. To the extent permissible under applicable laws, each Party will cause each employee and contractor conducting work on such Party’s behalf under this Agreement to be bound by an obligation that (i) compels prompt disclosure to the Party of all Albireo Technology, Ajinomoto Technology, and Joint Technology, as applicable, conceived or reduced to practice by such employee or contractor during any performance under this Agreement; (ii) automatically assigns to the Party all title and interest in and to all such Technology and all Patent Rights disclosing or claiming such Technology; and (iii) obligates such persons to similar obligations of confidentiality as set forth in this Agreement. Each Party will require each employee and contractor conducting work on such Party’s behalf under this Agreement to maintain records in sufficient detail and in a good scientific manner appropriate for patent purposes to properly reflect all work done.


8.3.1. Albireo Patent Rights and Joint Patent Rights in the Territory. Ajinomoto shall have the first right, at its sole discretion, to file, prosecute and maintain the Albireo Patent Rights in the Territory in Albireo’s name and Joint Patent Rights in the Territory in the joint names of Albireo and Ajinomoto or its Affiliate, using patent counsel selected by Ajinomoto and reasonably acceptable to Albireo, and shall be responsible for the payment of all such patent prosecution and maintenance costs. Albireo shall cooperate and render all assistance reasonably requested by Ajinomoto in connection with such efforts. Ajinomoto agrees to keep Albireo fully informed of the course of patent prosecution or other proceedings relating to any such Patent Rights, including, without limitation, by providing Albireo with copies of office actions and other material correspondence between Ajinomoto and the patent offices throughout the Territory concerning such Patent Rights. If Ajinomoto elects not to file, prosecute or maintain any of such Albireo Patent Rights and/or the Joint Patent Rights in the Territory, Ajinomoto shall provide Albireo with no less than [***] written advance notice sufficient to avoid any loss or forfeiture, and Albireo shall have the right, but not the obligation, at Albireo’s sole expense, to file, prosecute or maintain such Albireo Patent Rights and such Joint Patent Rights in the joint names of Albireo and Ajinomoto or its Affiliate. For any such Albireo Patent Rights and Joint Patent Rights that Albireo elects to file, prosecute or maintain at its sole expense (the “Elected Patent Rights”), Albireo agrees to keep Ajinomoto informed of material developments in the course of patent prosecution or other proceedings relating to any such Elected Patent Rights, including, without limitation, by providing Ajinomoto with copies of office actions and other material correspondence between Albireo and the patent offices throughout the Territory concerning such Elected Patent Rights.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
8.3.2. Patent Term Extensions. At Ajinomoto’s reasonable request, Albireo shall supply Ajinomoto as for Albireo Patent Rights and Joint Patent Rights, with any information in its possession or control pertaining to, or desirable for, gaining patent term extensions in the Territory, including, without limitation, supplementary protection certificates and any other extensions that are now or become available in the future wherever applicable to the Albireo Patent Rights and Joint Patent Rights that are applicable to the Products in the Territory. Albireo shall supply Ajinomoto in a timely manner with any supporting affidavits or documents required in connection with any such extensions of the Albireo Patent Rights and Joint Patent Rights. Neither Albireo nor its Affiliates shall take any action the consequence of which is to preclude Ajinomoto from obtaining any extension of the term of any Albireo Patent Rights or Joint Patent Rights. Final decisions and elections with respect to obtaining such extension or supplemental protection certificates shall be made [***]. Notwithstanding the foregoing, Albireo’s obligations under this Section 8.3.2 with respect to Albireo Patent Rights that are Controlled by Albireo pursuant to a Third Party License shall be subject to the terms of such Third Party License.

8.4. Ajinomoto Patent Rights. Ajinomoto shall have the right, in its sole discretion, to prepare, file, prosecute and maintain the Ajinomoto Patent Rights.

8.5. Joint Patent Rights outside the Territory. The Parties will consult with each other for the purpose of determining the jurisdictions outside the Territory in which to file Joint Patent Rights. Albireo will undertake filing, prosecution and maintenance of the Joint Patent Rights in the determined jurisdictions in the joint names of Albireo and Ajinomoto or its Affiliate, using patent counsel selected by Albireo and reasonably acceptable to Ajinomoto. The Parties will be equally responsible for the payment of all such patent prosecution and maintenance costs, including reasonable attorneys’ fees. Albireo agrees to keep Ajinomoto fully informed of the course of patent prosecution or other proceedings relating to any such Joint Patent Rights outside the Territory, including, without limitation, by providing Ajinomoto with copies of office actions and other material correspondence between Albireo and the patent offices outside the Territory concerning such Joint Patent Rights. Albireo shall consider Ajinomoto’s reasonable comments on the filing, prosecution or other proceedings relating to any such Joint Patent Rights outside the Territory. If either Party intends to abandon all or a part of its share in the Joint Patent Rights outside the Territory, such Party will notify the other Party of such intention, and such other Party will have the right to acquire the aforesaid share in such Joint Patent Rights without compensation, and the abandoning Party shall be free from any obligations as provided in this Section 8.5 with regard to such Joint Patent Rights thereafter. Notwithstanding the first sentence in this Section 8.5, in case either Ajinomoto or Albireo has no intention to file Joint Patent Rights in certain country(ies) outside the Territory, the other Party may have sole rights to file, prosecute and maintain the Joint Patent Rights in such country(ies) at its sole cost and will have the exclusive right therefrom.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
8.6. Trademarks.

8.6.1. Product Trademarks. Ajinomoto shall select, Control and, as between the Parties, own any trademark which is identified as a trademark or brand name for a Product in its application for Regulatory Approval for such Product in the Territory (each such trademark, a “Trademark”). Ajinomoto shall be solely responsible for applying for and maintaining the registrations for the Trademarks in the Territory (including payment of all costs associated therewith), and all goodwill associated therewith will inure to the benefit of Ajinomoto. Ajinomoto shall assume full responsibility, at its sole costs and expense, for any infringement by Ajinomoto, its Affiliates or its Sublicensees of the rights of Third Party by the use of the Trademark in connection with the Product in the Field in the Territory and will defend and indemnify Albireo for and against any such claims of such infringement in accordance with Section 11.2.

8.6.2. Trademark License. Ajinomoto hereby grants to Albireo, effective on the Effective Date, an exclusive, royalty-free, irrevocable license, with the right to freely sublicense, to use the Trademarks for the Commercialization of Products outside of the Territory. This provision shall not be construed as imposing on Ajinomoto any obligation or responsibility relating to the Trademarks outside the Territory, including, without limitation, applying for and maintaining the registrations for the Trademark outside the Territory. Albireo shall assume full responsibility, at its sole costs and expense, for any infringement by Albireo or its sublicensees of the rights of Third Party by the use of the Trademark and will defend and indemnify Ajinomoto and its Affiliates for and against any claims of such infringement in accordance with Section 11.1.

8.6.3. Use of Trademark. The manner of use of the Trademarks outside of the Territory will be subject to periodic review by Ajinomoto. Neither Albireo nor its sublicensee will use the Trademarks in a way that is inconsistent with the usage rules reviewed by the JCC and decided on by Ajinomoto.

8.7. Enforcement of Technology Rights.

8.7.1. Notice. Each Party shall promptly notify the other Party when such Party becomes aware of any actual, potential or suspected infringement or misappropriation of the Albireo Technology, Ajinomoto Technology, or the Joint Technology by any Third Party in the Territory (an “Infringement”), including, without limitation, a Third Party’s application for Regulatory Approval of a Competing Product in the Territory.

8.7.2. Enforcement. With regard to any actual or threatened legal actions relating to the Albireo Technology, Ajinomoto Technology, or the Joint Technology (including, without limitation, any legal action for Infringement by a Third Party in the Territory, or any defense of a declaratory judgment action brought by a Third Party, or any other action or proceeding by a Third Party that
may affect any of such Technologies, including, without limitation, any reexamination, revocation or other similar proceeding) anywhere within the Territory (each a “Legal Action”), Ajinomoto shall have the first right, in its sole discretion, to initiate, enforce and/or defend any such Legal Action, with Albireo’s option to participate, at its own expense, in such Legal Action; provided, however, that such first right of Ajinomoto, with respect to Albireo Technology that is Controlled by Albireo pursuant to a Third Party License, shall be subject to any rights to initiate, enforce and/or defend Legal Actions relating to such Albireo Technology that are reserved by the Third Party licensor under such Third Party License, in which case Albireo shall, upon Ajinomoto’s request, and to the extent permitted under such Third Party License, request that such Third Party licensor exercise such reserved rights to the extent that Ajinomoto could have exercised such rights pursuant to this Section 8.7.2 if such rights were not reserved by such Third Party licensor, provided further, with respect to any Albireo Patent Right (other than an Albireo Patent Right that is Controlled by Albireo or its Affiliates non-exclusively with respect to Products), if such Albireo Patent Right is Controlled by Albireo pursuant to a Third Party License, Albireo shall notify Ajinomoto promptly after the execution of such Third Party License whether the Third Party licensor reserves, under such Third Party License, any rights to initiate, enforce and/or defend Legal Actions relating to such Albireo Patent Right. Albireo shall render, at Ajinomoto’s expense, all assistance reasonably requested by Ajinomoto in connection with any such Legal Action, or in connection with any other action to prevent infringement. In the event Ajinomoto elects not to initiate, enforce and/or defend any such Legal Action, or does not initiate any legal action within *** days from the discovery by Ajinomoto of the facts forming the basis for any such Legal Action, then Albireo shall have the sole right, at its expense, to initiate, enforce and/or defend the action, subject to Ajinomoto’s prior written approval. The Party who initiates, enforces and/or defends a Legal Action pursuant to this Section shall be responsible for the costs of such action (including attorneys’ fees), and the Parties hereto shall equally share the costs if the Parties otherwise agree to initiate, enforce and/or defend such Legal Action. Any recoveries received in such a Legal Action shall be allocated in the following manner.

1) Firstly, reimburse the [***] for its [***];

2) Secondly, reimburse the [***] for its [***];

3) The remaining portion shall belong to [***]; provided, however, that in case [***] is [***], such remaining shall be considered [***] for the purposes of [***] under this Agreement, [***] and in case [***] is [***], the amount of any recovery remaining then shall be allocated [***].

Portions of this Exhibit, indicated by the mark “[***].” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
8.8. Third Party Claims.

8.8.1. Third Party Claims - Course of Action. If (i) the Development, Commercialization or Manufacture of the Albireo Compound or a Product under this Agreement; or (ii) any development, manufacture, or commercialization of the Albireo Compound or a Product by Albireo or Licensees is alleged by a Third Party to infringe a Third Party’s patent right(s) or misappropriate a Third Party’s trade secret, the Party becoming aware of such allegation shall promptly notify the other Party thereof, in writing, reasonably detailing the claim.

8.8.2. Third Party Suit. If a Third Party sues a Party (the “Sued Party”) alleging that the Sued Party’s, or its Sublicensee’s Development, Manufacture, or Commercialization of the Albireo Compound or any Product in the Field in the Territory infringes or shall infringe said Third Party’s patent right(s) or misappropriates said Third Party’s trade secret, Ajinomoto shall have the first right to defend such Third Party suit on behalf of both of the Parties and any expenses or costs incurred by Ajinomoto in connection with such suit, and [***]. Albireo shall render, at Ajinomoto’s expense, all assistance reasonably requested by Ajinomoto in connection with any such suit. For such suit as Ajinomoto is unable to defend hereunder solely or jointly in its own name, Albireo will join such suit voluntarily at the expense of Ajinomoto. Ajinomoto shall not admit the invalidity of any patent within the Albireo Patent Rights or the Joint Patent Rights, without written consent of Albireo, such consent not to be unreasonably withheld.

If Ajinomoto does not exercise its right to defend Third Party suit granted pursuant to this Section 8.8.2 in a particular jurisdiction within [***] from the date when the relevant suit becomes known to Ajinomoto, then Albireo shall be entitled to defend such suit at its own cost and expense in such jurisdiction subject to Ajinomoto’s prior written approval and any recovery in such suit shall be retained by Albireo in full, subject to the other applicable terms of this Agreement, if any. Albireo shall keep Ajinomoto reasonably informed on a monthly basis, in person or by telephone, prior to and during the pendency of any such suit. Albireo shall not admit the invalidity of any patent within the Ajinomoto Patent Rights or the Joint Patent Rights without written consent of Ajinomoto, such consent not to be unreasonably withheld.

8.9. Patent Marking. Each Party agrees to mark and have its Affiliates, and all Licensees and Sublicensees mark all Products (or their containers or labels) as required by the applicable statutes or regulations, if any, in the country or countries of sale thereof.

8.10. No Implied Licenses. Except as expressly set forth in this Agreement, no right or license under any Albireo Technology or Ajinomoto Technology is granted or shall be granted by implication as a result of the respective rights of the Parties under this Agreement. All such rights or licenses are or shall be granted only as expressly provided in this Agreement.
8.11. Privileged Communications. In furtherance of this Agreement, it is possible that Ajinomoto and Albireo should disclose to one another privileged communications with counsel, including opinions, memoranda, letters and other written, electronic and verbal communications. Such disclosures will be made with the understanding that they shall remain confidential, they will not be deemed to waive any applicable attorney-client privilege and that they are made in connection with the shared community of legal interests existing between Albireo and Ajinomoto. Including the community of legal interests in avoiding infringement of any valid, enforceable patents of Third Parties and maintaining the validity of Albireo Patent Rights, Ajinomoto Patent Rights and Joint Patent Rights.

8.12. Recordation of License. The Parties agree and acknowledge that notwithstanding anything in Section 6.1.6, Ajinomoto shall have the right to record or file a summary of the terms of this Agreement disclosing such amount of the terms as is necessary to effect such recordation or filing with any patent office or similar authority in the Territory if Ajinomoto reasonably determines that such recordation is beneficial or required to give effect to or protect its rights under this Agreement. For clarity, such recordation includes, without limitation, registrations of patent licenses in the Japanese patent office and any equivalents or similar registrations or filings thereto in any other jurisdiction in the Territory and, to the extent permitted under Section 8.3.2, filings of requests for patent term extensions in the Japanese patent office and any equivalents or similar registrations or filings thereto in any other jurisdiction in the Territory. Albireo shall provide all such cooperation and assistance, and perform all such acts and execute and deliver all such documents, as Ajinomoto may reasonably request in connection with such recordation or filing. Ajinomoto shall provide Albireo with an English translation of any such summary for prior review and comment at least [***] days before making any recordation or filing and will not unreasonably reject comments provided by Albireo.

9. GOVERNMENT APPROVALS. Ajinomoto and Albireo shall cooperate and use respectively all reasonable efforts to make all registrations, filings and applications, to give all notices and to obtain as soon as practicable all governmental or other consents, transfers, approvals, orders, qualifications, authorizations, permits and waivers, if any, and to do all other things necessary or desirable for the consummation of the transactions as contemplated hereby.

10. TERM AND TERMINATION.

10.1. Term. The term of this Agreement shall commence on the Effective Date and, unless earlier terminated as provided in this Section 10, shall continue in full force and effect until the expiration of the last-to-expire Royalty Period for any Product in any country in the Territory (the “Term”).

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
10.2. Rights of Termination.

10.2.1. Termination for Material Breach. This Agreement may be terminated effective immediately on a country-by-country basis or in its entirety by written notice by either Party at any time during the Term if the other Party materially breaches this Agreement, which breach remains uncured for [***] days measured from the date that written notice of such breach is given to the breaching Party, which notice shall specify the nature of the breach and demand its cure. Notwithstanding the foregoing, if a Party is alleged to be in material breach and disputes such termination through the dispute resolution procedures set forth in this Agreement, then the other Party’s right to terminate this Agreement shall be suspended for so long as such dispute resolution procedures are being pursued by the Party in good faith and if it is finally and conclusively determined that the Party is in material breach, then prior to any termination becoming effective or any remedies being enforced, such Party shall have the right to cure such material breach after such determination within the cure period provided above in this Section 10.2.1.

10.2.2. Ajinomoto Right of Termination; Automatic Termination for Failure to Commence Clinical Trials. Prior to its expiration, this Agreement may be terminated in its entirety, or country-by-country (except for Japan), at any time by Ajinomoto effective upon at least one hundred and eighty (180) days prior written notice to Albireo for any reason. In addition, this Agreement shall be terminated in its entirety to the extent provided in Section 4.1.2.

10.2.3. Bankruptcy. This Agreement may be terminated by written notice by either Party at any time during the Term if the other Party shall file in any court or agency, pursuant to any statute or regulation of any state or country, a petition in bankruptcy or insolvency, or a petition for reorganization, or a petition for an arrangement or for the appointment of a receiver or trustee of that Party or of its assets, or if the other Party proposes a written agreement of composition or extension of its debts, or if the other Party shall be served with an involuntary petition against it, filed in any insolvency proceeding, and such petition shall not be dismissed within [***] days after the filing thereof, or if the other Party shall propose or be a party to any dissolution or liquidation, or if the other Party shall make an assignment for the benefit of its creditors. The Parties agree that, in case of bankruptcy or insolvency of Albireo without termination of this Agreement by Ajinomoto pursuant to this Section 10.2.3, all rights and licenses granted by Albireo under this Agreement shall remain intact after such bankruptcy or insolvency, and Ajinomoto, as a licensee of such rights and licenses, shall be entitled to retain and may fully exercise all of its rights and elections to the maximum extent available to it under the applicable laws.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
10.3. Effects of Termination or Expiration.

10.3.1. Effects of Termination by Ajinomoto without Cause or by Albireo with Cause. If this Agreement is terminated automatically or by Ajinomoto pursuant to Section 10.2.2, or by Albireo pursuant to Section 10.2.1 or 10.2.3, then the following provisions shall be effective, but only for the country or countries for which such termination is effective (the “Relevant Countries”), upon such termination:

(a) All licenses granted by Albireo to Ajinomoto hereunder shall automatically terminate;

(b) All licenses granted by Ajinomoto to Albireo shall become fully paid up, irrevocable, perpetual, royalty-free licenses;

(c) Ajinomoto shall assign to Albireo all right, title and interest in and to: (i) all Regulatory Submissions and Regulatory Approvals Controlled by Ajinomoto pertaining to the Albireo Compound or Products and all data generated in clinical trials undertaken by Ajinomoto, its Affiliates or Sublicensees hereunder, provided that Ajinomoto and its Sublicensees retain the licenses and Right of Reference granted under Section 2 to such Regulatory Submissions, Regulatory Approvals, and data for the countries in the Territory that are not Relevant Countries; (ii) all of Ajinomoto’s interest in any Trademark (including, without limitation, the goodwill symbolized by such Trademark) used to brand the Product; and (iii) all of Ajinomoto’s interest in any copyrights of works exclusively used for the Product to the extent necessary or useful for Commercializing the Product;

(d) Ajinomoto shall grant, and hereby grants, to Albireo, a worldwide, exclusive (even as to Ajinomoto), royalty-free (except as set forth in this subsection (d)) and fully sublicensable license to practice any invention Covered by the Ajinomoto Patent Rights or Joint Patent Rights, and to practice the Ajinomoto Know-How and Joint Know-How, for purposes of Development and Commercialization of any Albireo Compound or Products in the Field. Notwithstanding the foregoing, in the event this Agreement is terminated by Ajinomoto without cause pursuant to Section 10.2.2, then, with respect to sales of any Royalty-Bearing Product by Albireo or its Licensees in the Relevant Countries in the Territory after such termination, Albireo shall deliver to Ajinomoto a report similar to the report set forth in Section 5.5.1 and pay to Ajinomoto a royalty of [***] percent ([***]%) of net sales (calculated by applying the definition of Net Sales in Section 1.86 mutatis mutandis to sales of Royalty-Bearing Products by Albireo or its Licensees) of such Royalty-Bearing Product by Albireo or its Licensees in the Relevant Countries. For purposes of this Section 10.3.1, “Royalty-Bearing Product” means a Product, (i) which is Covered by or the use of which is Covered by an Ajinomoto Patent Right or a Joint Patent Right, or which makes use of Ajinomoto Know-How or Joint Know-

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
How; or (ii) for which Regulatory Approval is based substantially on data generated in any activities undertaken by Ajinomoto, its Affiliates or Sublicensees ("Ajinomoto Data"). Any royalty owed pursuant to this Section 10.3.1(d) shall only be owed on a country-by-country and Royalty-Bearing Product-by-Royalty-Bearing Product basis until the later of (A) the expiration of the last Valid Claim of an Ajinomoto Patent Right or a Joint Patent Right Covering such Royalty-Bearing Product (including its composition and/or formulation) in such country or an Indication (as defined in Section 1.66) of such Royalty-Bearing Product in such country and (B) the expiration of Regulatory Exclusivity of the Ajinomoto Data used to obtain Regulatory Approval of such Royalty-Bearing Product in such country;

(e) Ajinomoto shall furnish Albireo with reasonable cooperation to assure a smooth transition of any clinical or other studies in progress related to the Albireo Compound or Products which Albireo determines to continue in compliance with Applicable Laws and ethical guidelines applicable to the transfer or termination of any such studies. In the event that Albireo informs Ajinomoto that it does not intend to continue specific development activities then in progress, costs incurred in closing out such activities shall be borne by Ajinomoto. In addition, Ajinomoto will return all Albireo Confidential Information to Albireo; and

(f) Until termination is effective, the Parties shall continue to perform their obligations under this Agreement, including, without limitation, the Territory Development Plan and Commercialization Plan then in effect and pay all costs allocated for each Party to pay in accordance with any budgets then in effect, except with respect to activities that Albireo elects to discontinue with respect to the Territory Development Plan and Commercialization Plan then in effect, including all payment obligations accrued through the effective date of termination.

Subsection (a) above will be effective upon any such termination, and subsections (b), (c), (d), (e) and (f) above shall be effective upon termination, or if such termination is by Ajinomoto pursuant to Section 10.2.2, upon the earlier of such termination or Albireo’s earlier election.

Notwithstanding the foregoing, subsections (a), (c), (d) and (e) above shall not be applicable for any Product in the Relevant Countries with respect to which the license granted to Ajinomoto under Section 2.1 becomes a fully paid-up license pursuant to Section 5.3.3, except in the event this Agreement is terminated by Albireo pursuant to Section 10.2.1.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
10.3.2. Effects of Termination by Ajinomoto with Cause. If this Agreement is terminated in its entirety by Ajinomoto pursuant to Section 10.2.1 or 10.2.3, (i) all licenses granted by Albireo to Ajinomoto shall automatically terminate; (ii) all licenses granted by Ajinomoto to Albireo shall automatically terminate; and (iii) Albireo shall return all Ajinomoto Confidential Information to Ajinomoto.

10.3.3. Survival of Certain Obligations. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing before such expiration or termination. The provisions of this Agreement that must, by their nature or terms, survive expiration or termination of this Agreement to give effect to their intention, shall so survive. Such provisions include, without limitation, Sections 2.4 (Joint Technology), 2.6 (Right of Reference) (for the time period set forth therein), 5.3.3 (Fully Paid-Up, Royalty Free License), 5.4 (Payment of Albireo Territory Development Costs and Expert Costs) (to the extent necessary to reimburse costs incurred during the Term), 5.5.1 (Royalty Reports) (to the extent necessary to determine and remit royalty payments on Net Sales earned during the Term), 5.5.2 (Taxes and Withholding) (with respect to payments made after the Term), 5.5.3 (Currency) (with respect to payments made after the Term), 5.5.4 (Method of Payment) (with respect to payments made after the Term), 5.5.5 (Record Keeping) (for the time period set forth therein), 5.5.6 (Audits) (for the time period set forth in Section 5.5.5), 5.5.7 (Interest) (with respect to payments that become overdue during or after the Term), 6.1 (Confidentiality) (for the time period set forth therein), 7.3 (Representation by Legal Counsel), 7.5 (Disclaimer), 8.2 (Ownership), 8.4 (Ajinomoto Patent Rights), 8.5 (Joint Patent Rights outside the Territory) (with respect to Joint Patent Rights filed before the expiration or termination of this Agreement), 8.10 (No Implied Licenses), 8.11 (Privileged Communications), 10.3 (Effects of Termination or Expiration), 11 (Product Liability, Indemnification and Insurance), 12.1 (Governing Law, Jurisdiction; Dispute Resolution), 12.3 (Waiver and Non-Exclusion of Remedies), 12.4 (Notices), 12.5 (Entire Agreement), 12.8 (No Benefit to Others), 12.12 (Publicity), 12.13 (Relationship of the Parties) and 12.14 (Headings), as well as any other Sections or defined terms referred to in such Sections or necessary to give them effect. Furthermore, any other provisions required to interpret the Parties’ rights and obligations under this Agreement shall survive to the extent required. Any expiration or early termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement before termination.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
11. PRODUCT LIABILITY, INDEMNIFICATION AND INSURANCE.

11.1. Indemnification by Albireo. Albireo shall indemnify, defend and hold harmless Ajinomoto, its Affiliates and Sublicensees, and each of its and their respective employees, officers, directors and agents (each, a “Ajinomoto Indemnified Party”) from and against any and all losses, damages, liabilities, settlements, penalties, fines and expenses (including, without limitation, reasonable attorneys’ fees and expenses) (collectively, “Liability”) that the Ajinomoto Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

(a) any Albireo representation or warranty set forth herein being untrue in any material respect when made or any material breach by Albireo of any of its covenants or obligations hereunder; or

(b) the gross negligence or willful misconduct by or of Albireo, its Affiliates, Sublicensees and Licensees, and their respective employees, officers, directors, and agents; or

(c) any claims arising from or related to Albireo’s development, manufacture or commercialization of the Albireo Compound or Products;

except in each case, to the extent caused by the gross negligence or willful misconduct of Ajinomoto or any Ajinomoto Indemnified Party, or by breach of this Agreement by Ajinomoto.

11.2. Indemnification by Ajinomoto. Ajinomoto shall indemnify, defend and hold harmless Albireo, its Affiliates and Sublicensees, and each of its and their respective employees, officers, directors and agents (each, a “Albireo Indemnified Party”) from and against any and all Liabilities that the Albireo Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

(a) any Ajinomoto representation or warranty set forth herein being untrue in any material respect when made or a material breach by Ajinomoto of any of its covenants or obligations hereunder; or

(b) the gross negligence or willful misconduct by or of Ajinomoto, its Affiliates and Sublicensees, and their respective employees, officers, directors and agents; or

(c) any claims arising from or related to Ajinomoto’s development, manufacture or commercialization of the Albireo Compound or Products;

except in each case, to the extent caused by the gross negligence or willful misconduct of Albireo or any Albireo Indemnified Party, or by breach of this Agreement by Albireo.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
11.3. Procedure. Each Party shall notify the other in the event it becomes aware of a claim for which indemnification may be sought hereunder or for which Liability is shared pursuant to this Section 11. In case any proceeding (including, without limitation, any governmental investigation) shall be instituted involving any Party in respect of which indemnity may be sought pursuant to this Section 11, such Party (the “Indemnified Party”) shall promptly notify the other Party (the “Indemnifying Party”) in writing and the Indemnifying Party and Indemnified Party shall meet to discuss how to respond to any claims that are the subject matter of such proceeding. The Indemnifying Party, upon request of the Indemnified Party, shall retain counsel reasonably satisfactory to the Indemnified Party to represent the Indemnified Party and shall pay the fees and expenses of such counsel related to such proceeding. In any such proceeding, the Indemnifying Party shall have the right to retain its own counsel, but the fees and expenses of such counsel shall be at the expense of the Indemnified Party unless (i) the Indemnifying Party and the Indemnified Party shall have mutually agreed to the retention of such counsel or (ii) the named parties to any such proceeding (including any impleaded parties) include both the Indemnifying Party and the Indemnified Party and representation of both Parties by the same counsel would be inappropriate due to actual or potential differing interests between them. All such fees and expenses incurred pursuant to Section 11.1 or 11.2 shall be reimbursed as they are incurred. The Indemnifying Party shall not be liable for any settlement of any proceeding unless effected with its written consent. The Indemnifying Party shall not, without the written consent of the Indemnified Party, effect any settlement of any pending or threatened proceeding in respect of which the Indemnified Party is, or arising out of the same set of facts could have been, a party and indemnity could have been sought hereunder by the Indemnified Party, unless such settlement includes an unconditional release of the Indemnified Party from all liability on claims to which the indemnity relates that are the subject matter of such proceeding.

11.4. Insurance. Each Party further agrees to obtain and maintain, during the term of this Agreement, Commercial General Liability Insurance, Products Liability Insurance and Product Recall Insurance with reputable and financially secure insurance carriers to cover its indemnification obligations under Sections 11.1 or 11.2, as applicable, with limits of not less than [***] U.S. Dollars ($[***]) per occurrence and [***] U.S. Dollars ($[***]) in the aggregate, which shall be raised to [***] U.S. Dollars ($[***]) per occurrence and [***] U.S. Dollars ($[***]) in the aggregate from and after the First Commercial Sale of any Product in any country in the Territory.

11.5. Liability Limitations.

11.5.1. No Consequential Damages. NOTWITHSTANDING THE FOREGOING, IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER FOR ANY CONSEQUENTIAL, INCIDENTAL, INDIRECT, SPECIAL, PUNITIVE OR EXEMPLARY DAMAGES UNDER THIS AGREEMENT, EXCEPT TO THE EXTENT THE DAMAGES RESULT FROM A PARTY’S WILLFUL MISCONDUCT OR ARISE FROM A PARTY’S INDEMNIFICATION OBLIGATIONS UNDER THIS SECTION 11.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
11.5.2. Scope of Albireo’s Liability. The maximum aggregate amount that Albireo shall be required to pay for indemnification arising under Section 11.1 in respect of all claims by all Ajinomoto Indemnified Parties shall be equal to the total amount of payments actually received by Albireo pursuant to Section 5 of this Agreement (the “Indemnity Cap”); provided, however, that such Indemnity Cap shall not apply to Liabilities based on or arising out of the gross negligence or willful misconduct of Albireo.

12. MISCELLANEOUS.

12.1. Governing Law, Jurisdiction; Dispute Resolution.

12.1.1. Governing Law. The interpretation and construction of this Agreement shall be governed by the laws of England, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction.

12.1.2. Jurisdiction. With respect to actions for equitable relief brought pursuant to Section 6.1.7 or 12.1.4(e), each Party (i) irrevocably submits to the exclusive jurisdiction of the courts sitting in England, with respect to actions or proceedings arising in whole or in part out of, related to, based upon or in connection with this Agreement or the subject matter hereof; (ii) agrees that all claims in respect of such actions or proceedings may be heard and determined only in any such court; and (iii) agrees not to bring any action or proceeding arising out of or relating to this Agreement in any other court (except to the extent required to enforce an order, judgment or ruling for equitable relief in an action brought pursuant to Section 6.1.7 or 12.1.4(e) issued by a court sitting in England). Each Party waives any defense of inconvenient forum to the maintenance of any action or proceeding so brought and waives any bond, surety or other security that might be required of the other Party with respect thereto.

12.1.3. Dispute Resolution. In the event of a dispute arising out of or relating to this Agreement either Party shall provide written notice of the dispute to the other, in which event the dispute shall be referred to the executive officers designated below or their successors, for attempted resolution by good faith negotiations within [***] business days after such notice is received. Said designated officers are, as of the Effective Date, as follows:

For Albireo: [***] or his designate
For Ajinomoto: [***] or his designate

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
In the event the designated executive officers do not resolve such dispute within the allotted [***] business days, either Party may, after the expiration of the [***] business day period, seek to resolve the dispute through arbitration in accordance with Section 12.1.4. Notwithstanding the preceding, the Parties acknowledge that the failure of the JCC or JDC to reach consensus as to any matter, which failure does not involve a breach by a Party of its obligations hereunder, shall not be deemed a dispute which may be referred for resolution by arbitration hereunder.

12.1.4. Arbitration.

(a) Claims. Any claim, dispute, or controversy of whatever nature arising between the Parties out of or relating to this Agreement that is not resolved under Section 12.1.3 within the required thirty (30) business days time period, or for which a Party is entitled to seek equitable relief under Section 6.1.7 or 12.1.4(e), including, without limitation, any action or claim based on tort, contract, or statute, or concerning the interpretation, effect, termination, validity, performance and/or breach of this Agreement (“Claim”), will be resolved by final and binding arbitration before a panel of three (3) experts with relevant industry experience (the “Arbitrators”). One (1) Arbitrator will be chosen by Albireo and one (1) Arbitrator will be chosen by Ajinomoto within fifteen (15) business days from the notice of initiation of arbitration. The third Arbitrator will be chosen by mutual agreement of the Arbitrator chosen by Albireo and the Arbitrator chosen by Ajinomoto within fifteen (15) business days of the date that the last of such Arbitrators were appointed. The Arbitrators will be administered by the International Chamber of Commerce (the “Administrator”) in accordance with its then existing arbitration rules or procedures regarding commercial or business disputes. The arbitration will be held in [***]. The Arbitrators will be instructed by the Parties to complete the arbitration within ninety (90) business days after selection of the final Arbitrator.

(b) Arbitrators’ Award. The Arbitrators will, within fifteen (15) calendar days after the conclusion of the arbitration hearing, issue a written award and statement of decision describing the essential findings and conclusions on which the award is based, including, without limitation, the calculation of any damages awarded. The decision or award rendered by the Arbitrators will be final and non-appealable, and judgment may be entered upon it in accordance with applicable law in England or any other court of competent jurisdiction. The Arbitrators will be authorized to award compensatory damages, but will NOT be authorized (i) to award non-economic damages, such as for emotional distress, pain and suffering or loss of consortium; (ii) to award punitive damages; or (iii) to reform, modify or materially change this Agreement or any other agreements contemplated hereunder; provided, however, that the damage limitations described in parts (i) and (ii) of this sentence will not apply if such damages are statutorily imposed.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
(c) Costs. Each Party will bear [***], and [***] arising out of the arbitration and the costs of the [***], and will pay [***] of the fees and costs of [***]; provided, however, that the Arbitrators will be authorized to determine whether a Party is the prevailing Party, and if so, to award to the prevailing Party reimbursement for its reasonable attorneys’ fees, costs and disbursements (including, for example, expert witness fees and expenses, photocopy charges, travel expenses, etc.), and/or the fees and costs of the Administrator and the Arbitrators.

(d) Compliance with this Agreement. Unless the Parties otherwise agree in writing, during the period of time that any arbitration proceeding is pending under this Agreement, the Parties will continue to comply with all those terms and provisions of this Agreement that are not the subject of the pending arbitration proceeding.

(e) Injunctive or Other Equity Relief. Nothing contained in this Agreement will deny any Party the right to seek injunctive or other equitable relief from a court of competent jurisdiction in the context of a bona fide emergency or prospective irreparable harm, and such an action may be filed and maintained notwithstanding any ongoing arbitration proceeding.

12.2. Force Majeure. No liability shall result from, and no right to terminate shall arise, in whole or in part, based upon any delay in performance or non-performance, in whole or in part, by either of the Parties to this Agreement to the extent that such delay or non-performance is caused by an event of Force Majeure. “Force Majeure” means an event that is beyond a non-performing Party’s reasonable control, including, without limitation, an act of God, act of the other Party, strike, lock-out or other industrial/labor dispute, power failure, war, riot, civil commotion, terrorist act, malicious damage, epidemic, quarantine, fire, flood, storm, natural disaster or compliance with any law or governmental order, rule, regulation or direction, whether or not it is later held to be invalid or inapplicable. The Force Majeure Party shall within ten (10) days of the occurrence of the Force Majeure event, give written notice to the other Party stating the nature of the Force Majeure event, its anticipated duration and any action being taken to avoid or minimize its effect. Any suspension of performance shall be of no greater scope and of no longer duration than is reasonably required and the Force Majeure Party shall use reasonable efforts to remedy its inability to perform; provided, however, if the suspension of performance continues or is anticipated to continue for thirty (30) days after the date of the occurrence, the unaffected Party shall have the right but not the obligation to perform on behalf of the Force Majeure Party for the duration of such Force Majeure and such additional period as may be reasonably required to assure a smooth and uninterrupted transition of such activities. If such failure to perform would constitute a material breach of this Agreement in the absence of such event of Force Majeure, and continues for one (1) year from the date of the occurrence and the Parties are not able to agree on appropriate amendments within such period, such other Party shall have the right, notwithstanding the first sentence of this Section 12.2, to terminate this Agreement immediately by written notice to the Force Majeure Party, in which case neither Party shall have any liability to the other except for those rights and liabilities that they agreed to provide for in this Agreement.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
accrued prior to the date of termination and the consequences of termination pursuant to Sections 10.3.1 or 10.3.2, as applicable, as if such termination was a termination as to which such consequences applied.

12.3. Waiver and Non-Exclusion of Remedies. A Party’s failure to enforce, at any time or for any period of time, any provision of this Agreement, or to exercise any right or remedy shall not constitute a waiver of that provision, right or remedy or prevent such Party from enforcing any or all provisions of this Agreement and exercising any rights or remedies. To be effective any waiver must be in writing. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by law or otherwise available except as expressly set forth herein.

12.4. Notices.

12.4.1. Notice Requirements. Any notice, request, demand, waiver, consent, approval or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be deemed given only if delivered by hand or sent by facsimile transmission (with transmission confirmed) or by internationally recognized courier service that maintains records of delivery, addressed to the Parties at their respective addresses specified in Section 12.4.2 or to such other address as the Party to whom notice is to be given may have provided to the other Party in accordance with this Section 12.4.1. Such Notice shall be deemed to have been given as of the date delivered by hand or transmitted by facsimile (with transmission confirmed) or on the second business day (at the place of delivery) after deposit with an internationally recognized courier service. This Section is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

12.4.2. Address for Notice.

Albireo:

Albireo AB
Arvid Wallgrens Backe 20
413 46 Gothenburg
Sweden
Fax number: +46-31-7411480
Tel number: +46-31-820223

Attention: Jan P. Mattsson, PhD, Chief Operating Officer

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
With a copy of any notices pursuant to Sections 2.5.4, 6.1.3(a), 6.1.4, 8.7.1, 8.8.1, 10.2, 11.3, 12.1.3, 12.1.4(a), 12.2, 12.3 and/or 12.7:

Ropes & Gray LLP
Prudential Tower
800 Boylston Street
Boston, MA 02199-3600
U.S.A.
Fax number: +1-(617) 235-0706
Tel number: +1-(617) 951-7826
Attention: Marc A. Rubenstein

Ajinomoto:

[***]

Attention: [***]

With a copy of any notices pursuant to Sections 2.5.4, 6.1.3(a), 6.1.4, 8.7.1, 8.8.1, 10.2, 11.3, 12.1.3, 12.1.4(a), 12.2, 12.3 and/or 12.7:

Ajinomoto Co., Inc.
15-1, Kyobashi 1-chome, Chuo-ku
Tokyo, 104-8315 Japan
Fax number: +81-(0)3-5250-8347
Tel number: +81-(0)3-5250-8178
Attention: Intellectual Property Dept.

12.5. Entire Agreement. This Agreement constitutes the entire agreement between the Parties with respect to the subject matter of this Agreement. This Agreement supersedes all prior agreements, whether written or oral, with respect to the subject matter hereof. Each Party confirms that it is not relying on any representations, warranties or covenants of the other Party except as specifically set out in this Agreement. Nothing in this Agreement is intended to limit or exclude any liability for fraud. All Schedules or Exhibits referred to in this Agreement are intended to be and are hereby specifically incorporated into and made a part of this Agreement. In the event of any inconsistency between any such Schedules or Exhibits and this Agreement, the terms of this Agreement shall govern.

12.6. Amendment. Any amendment or modification of this Agreement must be in writing and signed by authorized representatives of both Parties.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
12.7. Assignment. Neither Party may assign its rights or delegate its obligations under this Agreement, in whole or in part without the prior written consent of the other Party, except that each Party shall always have the right, without such consent, (i) to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any of its Affiliates; and (ii) on written notice to the other Party, assign any or all of its rights and delegate or subcontract any or all of its obligations hereunder to (A) any of its Affiliates or (B) a successor of all or substantially all of the business of such Party or of the portion of such business to which this Agreement relates, whether by way of merger, sale of stock, sale of assets or other transaction (or series of transactions). Notwithstanding the foregoing, each Party shall remain responsible for any failure to perform on the part of any such Affiliates. Any attempted assignment or delegation in violation of this Section shall be void.

12.8. No Benefit to Others. The provisions of this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights in any other persons except as otherwise expressly provided in this Agreement.

12.9. Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same instrument. An executed signature page of this Agreement delivered by facsimile transmission shall be as effective as an original executed signature page.

12.10. Severability. To the fullest extent permitted by applicable law, the Parties waive any provision of law that would render any provision in this Agreement invalid, illegal or unenforceable in any respect. If any provision of this Agreement is held to be invalid, illegal or unenforceable, in any respect, then such provision will be given no effect by the Parties and shall not form part of this Agreement. To the fullest extent permitted by applicable law and if the rights or obligations of any Party will not be materially and adversely affected, all other provisions of this Agreement shall remain in full force and effect and the Parties will use their best efforts to negotiate a provision in replacement of the provision held invalid, illegal or unenforceable that is consistent with applicable law and achieves, as nearly as possible, the original intention of the Parties.

12.11. Further Assurance. Each Party shall perform all further acts and things and execute and deliver such further documents as may be necessary or as the other Party may reasonably require to implement or give effect to this Agreement.

12.12. Publicity. Notwithstanding Section 6.1.6, it is understood that the Parties will issue a press release announcing the execution of this Agreement in such form as the Parties shall mutually agree. The Parties agree to consult with each other reasonably and in good faith with respect to the text and timing of any subsequent press releases relating to this Agreement or the activity hereunder prior to the issuance thereof, provided that a Party may not unreasonably withhold consent to such releases, and that either Party may issue such press releases as it determines, based on advice of counsel, are reasonably necessary to comply with laws or regulations or for appropriate market disclosure or as are consistent with information disclosed in prior releases properly made hereunder following prior notice to the other Party as much in advance as possible.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
12.13. Relationship of the Parties. The status of a Party under this Agreement shall be that of an independent contractor. Nothing contained in this Agreement shall be construed as creating a partnership, joint venture, or agency relationship between the Parties or, except as otherwise expressly provided in this Agreement, as granting either Party the authority to bind or contract any obligation in the name of or on the account of the other Party or to make any statements, representations, warranties, or commitments on behalf of the other Party. All Persons employed by a Party or any of its Affiliates shall be employees of such Party or its Affiliates and not of the other Party or such other Party’s Affiliates and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party or its Affiliates, as applicable.

12.14. Headings. The titles, and section and subsection headings, herein are for convenience of reference only and shall not affect the construction of this Agreement.
IN WITNESS WHEREOF, duly authorized representatives of the Parties have duly executed this Agreement to be effective as of the Effective Date.

AJINOMOTO PHARMACEUTICALS CO., LTD. 

By /s/ T. Toyoda
Name: Tomoyasu Toyoda 
Title: President & CEO

ALBIREO AB

By /s/ Jan Mattsson
Name: Jan Mattsson 
Title: COO

By /s/ D. J. Chiswell
Name: D. J. Chiswell 
Title: Chairman

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
Albireo name: A3309 (previously known as AZD7806)

International Non-proprietary Name (INN): Eloixibat.

Systematic name: \( N - [(2\, R) - 2 - \{ \{(3,3\text{-dibutyl}-7\text{-methylthio})-1,1\text{-dioxido}-5\text{-phenyl}-2,3,4,5\text{-tetrahydro}-1,5\text{-benzothiazepin}-8\text{-yl}\text{oxy}}\text{acetyl} \text{amino} \} \text{phenylethanol}\} \text{glycine}

Structural formula:

![Structural formula image]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
The headings are: Reference; Country Name (using standard WIPO two-letter codes); Status (I = inactive; F = filed/pending; G = granted); Application Number; Registration No. = Patent No.

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Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
I. Definition of Chronic Idiopathic Constipation

A diagnosis of Chronic Idiopathic Constipation (“CIC”) (synonymous with functional constipation and chronic constipation) can be based on clinical symptoms, a physician’s opinion, the Rome I, II or III diagnostic criteria (1-3), WGO (4) or ACG (5) guidelines. It is characterized by unsatisfactory defecation that results from infrequent stools, difficult stool passage, or both. The pathophysiology is multi-factorial and may include dysfunction of intestinal motility, visceral sensitivity, ano-rectal musculature and the enteric nervous system. The term chronic implies that the symptom duration is more than three (3) months.

II. References


Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
EXHIBIT 1.54

Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders

[See attached.]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
EXHIBIT 1.115

Territory Development Plan

[***]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
EXHIBIT 4.2.1

Global Development Plan

[See attached.]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
EXHIBIT 6.3.1

[***]

[***]

[***]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
FIRST AMENDMENT TO THE LICENSE AGREEMENT

THIS FIRST AMENDMENT (the “First Amendment”) to the License Agreement, dated as of April 2, 2012 (the “Agreement”), by and between Albireo AB (“Albireo”) and Ajinomoto Pharmaceuticals Co, Ltd. (“Ajinomoto”) is entered into on January 30, 2015.

WITNESSETH:

WHEREAS, Albireo and Ajinomoto previously entered into the Agreement;

WHEREAS, Section 12.6 of the Agreement states that any amendment or modification of the Agreement must be in writing and signed by authorized representatives of both Parties; and

WHEREAS, Albireo and Ajinomoto desire to amend Section 6.3.1 of the Agreement to exclude Sublicensees of Ajinomoto from the non-competition restrictions set forth therein.

NOW THEREFORE, in consideration of the mutual promises and covenants set forth herein and in the Agreement, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. Definitions. Capitalized terms used in this First Amendment and not defined herein shall have the meanings assigned thereto in the Agreement.

2. Amendments.

2.1. Section 6.3.1 of the Agreement is hereby amended, superseded and replaced in its entirety to read as follows:

“6.3.1. Non-Competition by Ajinomoto.

(a) After First Commercial Sale of a Product [***] in a country in the Territory [***], neither Ajinomoto nor any of its Affiliates shall, directly or indirectly, or in collaboration with any Third Party, license or otherwise authorize any Third Party to distribute for sale and sell commercially in such country any pharmaceutical products for the treatment of CIC or IBS-C (each such product, a “Restricted Product”), other than the Albireo Compound and Products, without complying with this Section 6.3.1; [***]; or (ii) the distribution or sale of a Restricted Product in such country by Ajinomoto’s Sublicensee in such country, provided that (x) Albireo has consented to such Sublicensee in accordance with Section 2.5.1, (y) the applicable Sublicense requires such Sublicensee to use Commercially Reasonable Efforts to distribute and/or sell the Product(s) in such country and (z) Ajinomoto has the right to terminate such Sublicense in the event that such Sublicensee is in breach of its obligation to use Commercially Reasonable Efforts.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
to distribute and/or sell the Product(s) and fails to cure such breach within a reasonable cure period. In the event that either Party becomes aware that any such Sublicensee is in breach of such obligation, such Party shall so notify the other Party and Albireo shall have the right to demand that Ajinomoto cure such breach. The Parties acknowledge and agree that such breach shall be deemed to be a breach of Ajinomoto’s obligations under this Agreement and, if such breach is material and Ajinomoto is unable to cure such material breach in accordance with Sections 2.5.4 and 10.2.1 of this Agreement, then such breach shall be deemed to be an uncured material breach by Ajinomoto under this Agreement. For the sake of clarity, a pharmaceutical product for any of the following indications shall not constitute a Restricted Product so long as such product is not also indicated for the treatment of CIC or IBS-C: (i) the prophylaxis and treatment of Opioid-Induced-Constipation; (ii) the prophylaxis and treatment of symptoms of constipation; (iii) use in postoperative ileus (prophylaxis and treatment); and (iv) colonoscopy cleansing procedures; neither Ajinomoto nor any of its Sublicensees shall be restricted by this Section 6.3.1 with respect to such non-Restricted Product.

(b) Ajinomoto shall not be deemed to be in breach of Section 6.3.1(a) if Ajinomoto or any of its Affiliates (or any of its Sublicensees that are not permitted to distribute or sell Restricted Products without fulfilling items (x), (y) and (z) of clause (ii) of Section 6.3.1(a)) acquires a Restricted Product through an acquisition of or a merger with the whole or substantially the whole of the business or assets of another entity, so long as Ajinomoto (or its Affiliate or Sublicensee) enters into a definitive agreement with a Third Party to divest such Restricted Product within twelve (12) months after the closing of such acquisition or merger.”

3. **Effect.** The amendments to the Agreement set forth in Section 2 of this First Amendment shall take effect on and as of the date of this First Amendment.

4. **No Other Amendments.** This First Amendment shall be deemed to be part of and incorporated into the Agreement. Except as expressly set forth in this First Amendment, all of the terms and conditions of the Agreement shall remain unchanged and are ratified, confirmed in all respects, and remain in full force and effect.

5. **Counterparts.** This First Amendment may be executed in counterparts, each of which shall constitute an original and both of which, when taken together, shall constitute one and the same agreement. An executed signature page to this First Amendment delivered by facsimile transmission shall be as effective as an original executed signature page.

[THE REMAINDER OF THE PAGE INTENTIONALLY LEFT BLANK]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
IN WITNESS WHEREOF, each of the parties has caused this First Amendment to be executed on its behalf by their respective officers thereunto duly authorized all as of the date first written above.

ALBIREO AB

By: /s/ Jan Mattsson

Name: Jan Mattsson, Ph.D.
Title: Chief Operating Officer

AJINOMOTO PHARMACEUTICALS CO., LTD.

By: /s/ T. Ishiguro

Name: Tsuneo Ishiguro (Ph.D.)
Title: Vice President
General Manager
Business Development

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
SECOND AMENDMENT TO THE LICENSE AGREEMENT

THIS SECOND AMENDMENT (the “Second Amendment”) to the License Agreement, dated as of April 2, 2012 (the “Original License Agreement”), as amended on January 30, 2015, (the “Agreement”), by and between Elobix AB (“Elobix”) and EA Pharma Co., Ltd. (formerly known as Ajinomoto Pharmaceuticals Co., Ltd., “EA”) is entered into on April 6, 2016. Elobix and EA may each be referred to herein individually as a “Party” and collectively as the “Parties.”

WITNESSETH:

WHEREAS, Alibireo AB, an affiliate of Elobix, and EA previously entered into the Original License Agreement and that certain First Amendment to the Original License Agreement on January 30, 2015 (the “First Amendment”);

WHEREAS, Alibireo AB has previously transferred all of its rights and obligations under the Agreement to Elobix;

WHEREAS, Section 12.6 of the Agreement states that any amendment or modification of the Agreement must be in writing and signed by authorized representatives of both Parties; and

WHEREAS, Elobix and EA desire to amend the Agreement as provided herein.

NOW THEREFORE, in consideration of the mutual promises and covenants set forth herein and in the Agreement, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. Definitions; Confirmation.

1.1. Capitalized terms used in this Second Amendment and not defined herein shall have the meanings assigned thereto in the Agreement.

1.2. Although the First Amendment was executed after the transfer of rights and obligations under the Agreement from Alibireo AB to Elobix and the party thereto (other than EA) was not Elobix but instead Alibireo AB, the Parties hereby confirm that the First Amendment was intended to be executed between Elobix and EA and deem that the First Amendment is and was effective, ab initio, between Elobix and EA.

2. Amendments.

2.1. The following definitions shall be added to Section 1 of the Agreement.

“1.11(A). Alibireo Liver Disease” means each (i) Potential Alibireo Liver Disease for which there has been [***], if any, or (ii) Liver Disease for which an Alibireo Liver Disease Approval is granted, if any.”

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
1.11(B). “Albireo Liver Disease Approval” means the written approval by Albireo for Ajinomoto or its Affiliate to conduct an [***].

1.11(C). “Albireo Liver Disease Milestone” has the meaning set forth in Section 5.2.4.

1.11(D). “Albireo Liver Disease Patent Rights” means any Patent Right that Albireo or its Affiliates Control as of the Second Amendment Date or that comes into the Control of Albireo or its Affiliates thereafter during the Term, including, without limitation, any Patent Right that is conceived, developed and Invented solely by employees of Albireo or its Affiliates, or Third Parties acting on behalf of Albireo or its Affiliates, thereafter during the Term in the course of Albireo’s performance under this Agreement to the extent such rights are necessary or useful to Manufacture, Develop or Commercialize the Albireo Compound or Products for the treatment of an Albireo Liver Disease. For the avoidance of doubt, (A) Joint Patent Rights and Patent Rights which are Ajinomoto Patent Rights licensed to Albireo pursuant to this Agreement are not included in the definition of Albireo Liver Disease Patent Rights and (B) Albireo Liver Disease Patent Rights are not Albireo Patent Rights, unless and except to the extent that a particular Albireo Liver Disease Patent Right would be an Albireo Patent Right if the definition of “Field” in this Agreement did not include clause (iii) thereof (referring to any Albireo Liver Disease). For the sake of clarity, (1) if a Valid Claim is included within an Albireo Liver Disease Patent Right, such Valid Claim shall only provide Innovator Protection if such Valid Claim satisfies the requirements of Section 1.66, and (2) the word “treatment” in this Section 1.11(D) and Section 1.12 below shall be deemed to include, in the alternative, prevention.

1.73(A). “[***]” means a clinical trial of the Albireo Compound and/or a Product relating to the treatment or prevention of [***].

1.94(A). “Potential Albireo Liver Disease” means each [***], if any, for which Albireo, its Affiliate or a Licensee conducts a [***] as part of a development plan for the Albireo Compound and/or such Product to seek Regulatory Approval to treat or prevent such [***]. Albireo shall provide Ajinomoto with written notice within [***] days after (i) Albireo or its Affiliate determines by its official internal procedure, or Albireo or its Affiliate receives notice that a Licensee has determined by its official internal procedure, to conduct an [***], or (ii) the first subject is dosed in such [***], if any, identifying the [***]; provided that Albireo shall not be required to provide such notice more than once for such [***].

1.107(A). “Second Amendment Date” means April 6, 2016.

1.109(A). “[***]” means, with respect to each Potential Albireo Liver Disease, that [***] to (i) conduct a subsequent [***] for the treatment or prevention of such Potential Albireo Liver Disease or (ii) [***] with respect to a [***] such Potential Albireo Liver
2.2. Section 1.44 (the definition of “Field”) is hereby amended and restated in its entirety as follows:

“1.44 ‘Field’ means all prophylactic and therapeutic uses of a pharmaceutical product in any formulation or dosage form: (i) for Gastrointestinal Diseases, symptoms of constipation of all causes, or postoperative ileus; (ii) in colonoscopy cleansing procedures or (iii) from and after the Second Amendment Date, for any Albireo Liver Disease.”

2.3. Section 1.86 of the Agreement is hereby amended by adding the following to the end thereof:

“Notwithstanding the foregoing, Net Sales in Japan of Ajinomoto’s Sublicensee Mochida Pharmaceutical Co., Ltd. or its Affiliates for any particular period shall instead be calculated on a Product-by-Product basis in accordance with X times Y, where:

\[ X = \text{[***]}; \]

\[ Y = \text{[***]} \text{ of the Drug Price for such Product [***]} \]

(for the avoidance of doubt, in the case that Mochida or any of its Affiliates sells to Third Parties (other than Mochida and its Affiliates) Product purchased from Ajinomoto, (1) Net Sales in respect of such Product shall be calculated as Mochida Net Sales and (2) such sales of Product from Ajinomoto to Mochida shall not be included in Net Sales).

In addition, in the event that a Product is sold as a [***] by Mochida in Japan, in determining Mochida Net Sales, (i) the reference to “average gross invoice price” as applied to ‘A’ (in respect of the fraction A/(A+B)) above in this Section 1.86 shall be deemed instead a reference to “Drug Price” and (ii) the reference to “average gross invoice price” as applied to ‘B’ (in respect of the fraction A/(A+B)) above in this Section 1.86 shall be deemed instead a reference to “Japan’s National Health Insurance drug price, per dosage unit, assigned to the product containing the other prophylactically and/or therapeutically active pharmaceutical ingredient(s) included in the [***]”

2.4. Section 2.1 of the Agreement is hereby amended and restated in its entirety as follows:

“2.1 License to Ajinomoto. Subject to the terms and conditions of this Agreement, Albireo hereby grants to Ajinomoto, a royalty-bearing, exclusive license (even as to Albireo), with the right to sublicense as set forth in Section 2.5, (x) effective on the Effective Date, under the Albireo Technology and Albireo’s interest in the Joint Technology, and (y) effective upon the occurrence of the first Albireo Liver Disease, if any, under the Albireo Liver Disease Patent Rights, to (i) Develop, Manufacture and Commercialize the Albireo Compound and Products in the Field in the Territory; and (ii)
conduct pre-clinical Development and Manufacture of the Albireo Compound and Products in any country in the world for Commercialization in the Field in the Territory; provided, however, that Ajinomoto shall not be permitted to conduct any clinical trials for any Albireo Liver Disease [***] or [***] unless Albireo has first requested and thereafter received prior written consent for Albireo or its Affiliates to [***], as the case may be, pursuant to Section 2.3. For the sake of clarity, neither Ajinomoto nor any of its Sublicensees or Affiliates shall conduct clinical Development activities related to the Albireo Compound or Products outside of the Territory.

2.5. Section 2.2 of the Agreement is hereby amended and restated in its entirety as follows:

“ 2.2 License to Albireo. Subject to the terms and conditions of this Agreement, Ajinomoto hereby grants to Albireo (i) a royalty-free, non-exclusive license, with the right to sublicense as set forth in Section 2.5, under the Ajinomoto Technology and Ajinomoto’s interest in the Joint Technology to the extent necessary for Albireo to exercise its rights and perform its obligations under this Agreement; (ii) a royalty-free, non-exclusive license, with the right to sublicense as set forth in Section 2.5, under the Ajinomoto Technology to conduct development and manufacture of the Albireo Compound and Products in any field in any country in the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term) and to commercialize the Albireo Compound and Products in any field outside of the Territory; and (iii) a royalty-free, exclusive license, with the right to sublicense as set forth in Section 2.5, under Ajinomoto’s interest in the Joint Technology to conduct development and manufacture of the Albireo Compound and Products in any field in any country in the world (except to conduct clinical development of the Albireo Compound and Products in the Territory during the Term) and to commercialize the Albireo Compound and Products in any field outside of the Territory, provided that Ajinomoto reserves the right under its interest in the Joint Technology to, and to have Third Parties acting on Ajinomoto’s behalf, conduct pre-clinical Development and Manufacture of the Albireo Compound and Products in any country in the world for Commercialization in the Field in the Territory. Neither Albireo nor its Affiliates shall directly or indirectly (through Licensees or otherwise) commercialize a Product outside the Field in the Territory during the Term. Ajinomoto acknowledges and confirms that Albireo or its Affiliates may commercialize one or more products other than the Product outside the Field in the Territory during the Term, and that such commercialization is not prohibited by the immediately preceding sentence or otherwise by this Agreement.”

2.6. Section 2.3 of the Agreement is hereby amended and restated in its entirety as follows:

“ 2.3 Restrictions. Except as permitted by this Agreement, Albireo will not exercise or otherwise exploit the Ajinomoto Technology for any purpose other than to commercialize the Albireo Compound and Products in the Field outside the Territory. Except as permitted by this Agreement, Ajinomoto will not exercise or otherwise exploit the Albireo Technology to commercialize the Albireo Compound and Products (i) in the Field outside of the Territory; or (ii) outside the Field. Without the prior written consent of Ajinomoto, neither Albireo nor its Affiliates shall, directly or indirectly, through

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
Llicensees or otherwise, (A) commonmercialize the Albireo Compound and/or a Product as a pharmaceutical product to treat or prevent Liver Diseases in the Territory or (B) conduct any clinical trial of the Albireo Compound and/or a Product to treat or prevent any Liver Disease in or outside the Territory, where [***] such clinical trial (1) [***] or (2) [***]; provided that, for clarity [***], Albireo and its Affiliates shall be expressly permitted, directly or indirectly, through Licensees or otherwise, to research, develop, manufacture or commercialize the Albireo Compound and/or a Product to treat or prevent any Liver Disease s outside the Territory. Neither Albireo nor its Affiliates shall directly sell or distribute for sale any Product through channels that are intended to permit importation of a Product into the Territory, other than pursuant to the rights granted to Ajinomoto under this Agreement, and Albireo shall ensure that each License contains a provision prohibiting the relevant Licensee from undertaking any such sales or distribution. Likewise, neither Ajinomoto nor its Affiliates shall directly sell or distribute for sale any Product through channels that are intended to permit importation of a Product outside the Territory, other than pursuant to the rights granted to Albireo under this Agreement, and Ajinomoto shall ensure that each Sublicense to which it is a party contains a provision prohibiting the relevant Sublicensee from undertaking any such sales or distribution.”

2.7. Section 3.1.2(l) of the Agreement is hereby amended and restated in its entirety as follows:

“(l) receiving and discussing all material data, information, material or results relating to development of Products by Albireo or Licensees for commercialization outside of the Territory, including for clarity for use to treat or prevent any Albireo Liver Disease or Potential Albireo Liver Disease. For clarity, neither the JDC nor JCC shall have any decision making authority with respect to Albireo’s development or commercialization of Products outside the Territory; provided that Albireo shall reasonably consider the comments of Ajinomoto’s representative at the JDC or JCC regarding matters relating to the development of Products outside the Territory for use to treat or prevent any Albireo Liver Disease or Potential Albireo Liver Disease.”

2.8. Section 3.2.2(g) of the Agreement is hereby amended and restated in its entirety as follows:

“(g) receiving and discussing material data and information regarding commercialization of Products by Albireo or Licensees outside the Territory, including for clarity for use to treat or prevent any Albireo Liver Disease or Potential Albireo Liver Disease.”

2.9. Section 4.3.2 of the Agreement is hereby amended and restated in its entirety as follows:

“4.3.2 Regulatory Cooperation. The Parties shall, each at its own expense, provide the other Party with reasonable access to and copies of any documents or other materials Controlled by such Party that are useful for regulatory filings and correspondence and maintenance of Regulatory Approvals for Products in the Field in

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
such other Party’s territory and will otherwise cooperate with the other Party’s efforts to obtain and maintain Regulatory Approvals for Products in the applicable field and territory; provided, however, that in no event shall either Party be required to provide access to and copies of any documents or other materials relating to any compound other than the Albireo Compound or any product other than Products. Albireo shall keep Ajinomoto reasonably (but at least on a quarterly basis) informed regarding the status and progress of all regulatory matters relating to Products outside of the Territory by providing Ajinomoto with a copy and English abstract of any regulatory submission made to a Regulatory Authority and all written correspondence and abstracts of all material oral correspondence involved in such regulatory submission, in each case to the extent Controlled by Albireo. Albireo shall provide Ajinomoto with any data Controlled by Albireo necessary to comply with requirements from Regulatory Authorities in the Territory, with respect to the Product in the Field, such as annual reports, PSUR and CCDS required by Regulatory Authorities."

2.10. The Agreement shall be amended by adding a new Section 4.7 to read as follows:

“4.7 Ajinomoto Request for Albireo Liver Disease Approval. In the event Ajinomoto requests that Albireo or its Affiliate grant an Albireo Liver Disease Approval for a particular Liver Disease, Albireo or its Affiliate shall consider and discuss such request with Ajinomoto in good faith.”

2.11. The table in Section 5.2.1 of the Agreement is hereby amended as follows:

(i) The fourth row of the table (covering the “EVENT” of [***]) is hereby deleted in its entirety;

(ii) After the third row of the table (covering the “EVENT” of [***]), the following two (2) rows are inserted; and

<table>
<thead>
<tr>
<th>The Second Amendment Date</th>
<th>Eight million U.S. Dollars ($8,000,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[***]</td>
<td>[***]</td>
</tr>
</tbody>
</table>

(iii) The [***] in the sixth row of the table (after giving effect to the amendments above) (covering the “EVENT” of [***]) is replaced with [***].”

2.12. The Agreement shall be amended by adding a new Section 5.2.4 to read as follows:

“5.2.4. Milestone Payment to Ajinomoto. Albireo will pay to Ajinomoto a non-creditable, non-refundable amount of [***] within [***] days after the first occurrence of NDA Approval granted to Albireo, its Affiliates or Licensees outside the Territory for the use of a Product for the treatment or prevention of any Liver Disease (the “Albireo Liver Disease Milestone”). For the avoidance of doubt, in the event that this Agreement is terminated in its entirety by Albireo pursuant to Section 10.2.1 or by Ajinomoto pursuant to Section 10.2.2 prior to the occurrence of the Albireo Liver Disease portations of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
2.13. Section 5.3.1 of the Agreement is hereby amended and restated in its entirety as follows:

“5.3.1. Royalty Rates. Subject to Section 5.3.2, Ajinomoto shall pay to Albireo, with respect to sales of each Product sold by Ajinomoto, its Affiliates or its Sublicensees in the Field in the Territory during the Royalty Period for each Product, an amount equal to:

[***] of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof [***]; plus

[***] of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof [***]; plus

[***] of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof [***]; plus

[***] of aggregate Net Sales of all Products in a Year in the Territory for the portion thereof [***].

For the purpose of clarification, if there are [***] of aggregate Net Sales of all Products in each Calendar Quarter in a given Year, then Ajinomoto will pay a royalty of [***] in the first Calendar Quarter, a royalty of [***] in the second Calendar Quarter, a royalty of [***] in the third Calendar Quarter, and a royalty of [***] in the fourth Calendar Quarter.

For the purpose of further clarification, if the [***] of a [***] is [***] or does not [***] in a [***], the [***] of such [***] in such [***] shall not be [***] under this Agreement and, thereby, in no way will such sales be counted in determining whether a [***] has been [***] under Section 5.2.2 or determining the applicable [***] pursuant to this Section 5.3.”

2.14. Section 5.5.3 of the Agreement is hereby amended and restated in its entirety as follows:

“5.5.3 Currency. Other than the amounts specifically indicated for payment in US Dollars in this Agreement, all amounts payable hereunder shall be in Euros.

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
Currency translation into Euros shall be made by using the simple arithmetic average of the telegraphic transfer selling (TTS) rates on the last business day of each calendar month of the relevant Calendar Quarter quoted by Bank of Tokyo-Mitsubishi UFJ. If, due to restrictions or prohibitions imposed by a national or international authority, payments cannot be made as provided in this Section 5, the Parties shall consult with a view to finding a prompt and acceptable solution, and the paying Party shall deal with such payments as the other Party may lawfully direct at no additional out-of-pocket expense to the paying Party. ”

2.15. The Agreement shall be amended by adding a new subsection (c) to Section 6.3.1 to read as follows:

“(c) Solely for purposes of this Section 6.3.1, neither [***] nor any of its [***] shall be considered to be [***].”

2.16. The Agreement is hereby amended by adding the following new Section 6.5 to read as follows:

“6.5 Albireo Third Party Licenses. Albireo agrees that, prior to granting any new License to a Licensee after the Second Amendment Date, Albireo shall use commercially reasonable efforts to secure the right to grant to Ajinomoto, its Affiliates and Sublicensees access, a license or a sublicense, in each case on a non-exclusive basis, to Know-How that (i) [***] and (ii) [***]; provided that (A) [***], and (B) [***] agrees that, if (1) [***] will (1) [***] and (2) [***].”

3. Current Payment. As the result of the insertion of the row covering the “EVENT” of “The Second Amendment Date” into the table in Section 5.2.1 of the Agreement via this Second Amendment, and notwithstanding the period for payment provided in Section 5.2.1, it is hereby confirmed that the amount of Eight Million U.S. Dollars ($8,000,000) will be paid to Elobix by EA on or before April 15, 2016 by wire transfer to the bank account which has been previously designated by Elobix pursuant to Section 5.5.4 of the Agreement.

4. Elobix. EA and Elobix hereby agree that each reference in the Agreement to Albireo (to the extent referring to Albireo AB and not speaking expressly as of the Effective Date (for clarity, of the Original License Agreement)) is deemed to be a reference to Elobix.

5. Effect. The amendments to the Agreement set forth in Section 2 of this Second Amendment shall take effect on and as of the date of this Second Amendment.

6. No Other Amendments. This Second Amendment shall be deemed to be part of and incorporated into the Agreement. Except as expressly set forth in this Second Amendment, all of the terms and conditions of the Agreement shall remain unchanged, are ratified and confirmed in all respects, and remain in full force and effect.

7. Counterparts. This Second Amendment may be executed in counterparts, each of which shall constitute an original and all of which, when taken together, shall constitute one and the

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
same agreement. An executed signature page to this Second Amendment delivered by facsimile transmission shall be as effective as an original executed signature page.

[THE REMAINDER OF THE PAGE INTENTIONALLY LEFT BLANK]

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
IN WITNESS WHEREOF, each of the parties has caused this Second Amendment to be executed on its behalf by their respective officers thereunto duly authorized all as of the date first written above.

ELOBIX AB

By: /s/ Jan Mattsson
Name: Jan Mattsson, Ph.D.
Title: Chief Operating Officer

EA PHARMA CO., LTD.

By: /s/ H. Shimizu
Name: Hajime Shimizu
Title: Representative Director, President & CEO

Portions of this Exhibit, indicated by the mark “[***],” were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant’s application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.
Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-144407) pertaining to the 2005 Employee Stock Purchase Plan, 2004 Stock Incentive Plan and 2005 Non-Employee Directors’ Stock Option Plan;

2. Registration Statement (Form S-8 No. 333-168903) pertaining to the Amended and Restated 2010 Stock Incentive Plan;

3. Registration Statement (Form S-8 No. 333-180409) pertaining to the Amended and Restated 2010 Stock Incentive Plan;

4. Registration Statement (Form S-3 No. 333-182877);

5. Registration Statement (Form S-3 No. 333-215263); and

6. Registration Statement (Form S-8 No. 333-215264) pertaining to the 2016 Equity Incentive Plan and the Amended and Restated 2010 Stock Incentive Plan;

of our report dated 13 July 2016, with respect to the consolidated financial statements of Albireo Pharma, Inc. for the year ended 31 December 2015 included in this Annual Report (Form 10-K) of Albireo Pharma, Inc. for the year ended 31 December 2016.

/s/ Ernst & Young LLP

Reading, England

27 March 2017
We consent to the incorporation by reference in the following Registration Statements of Albireo Pharma, Inc.:  

(1) Registration Statement (Form S-8 No. 333-144407) pertaining to the 2005 Employee Stock Purchase Plan, 2004 Stock Incentive Plan and 2005 Non-Employee Directors’ Stock Option Plan;  

(2) Registration Statement (Form S-8 No. 333-168903) pertaining to the Amended and Restated 2010 Stock Incentive Plan;  

(3) Registration Statement (Form S-8 No. 333-180409) pertaining to the Amended and Restated 2010 Stock Incentive Plan;  

(4) Registration Statement (Form S-3 No. 333-182877);  

(5) Registration Statement (Form S-3 No. 333-215263); and  

(6) Registration Statement (Form S-8 No. 333-215264) pertaining to the 2016 Equity Incentive Plan and the Amended and Restated 2010 Stock Incentive Plan;  

of our report dated March 27, 2017, with respect to the consolidated financial statements of Albireo Pharma, Inc. included in this Annual Report (Form 10-K) of Albireo Pharma, Inc. for the year ended December 31, 2016.

/s/ Ernst & Young LLP  
Boston, Massachusetts  
March 27, 2017
I, Ronald H.W. Cooper, certify that:

1. I have reviewed this annual report on Form 10-K of Albireo Pharma, 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(s) 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; and

5. The registrant’s other certifying officer(s) 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: March 27, 2017

/s/ Ronald H.W. Cooper
Ronald H.W. Cooper
President and Chief Executive Officer
(principal executive officer)
I, Thomas A. Shea, certify that:

1. I have reviewed this annual report on Form 10-K of Albireo Pharma, 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(s) and I am 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; and

5. The registrant’s other certifying officer(s) 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: March 27, 2017

/s/ Thomas A. Shea
Thomas A. Shea
Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)
CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Albireo Pharma, Inc., a Delaware corporation (the “Company”), does hereby certify, to such officer’s knowledge, that:

The Annual Report for the year ended December 31, 2016 (the “Form 10-K”) of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 27, 2017

/s/ Ronald H.W. Cooper
Ronald H.W. Cooper
President and Chief Executive Officer
(principal executive officer)

Dated: March 27, 2017

/s/ Thomas A. Shea
Thomas A. Shea
Chief Financial Officer and Treasurer
(principal financial officer and principal accounting officer)