Heron Therapeutics, Inc.

Date of Report (Date of earliest event reported): January 8, 2018

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Item 2.02 Results of Operations and Financial Condition.

On January 8, 2018, Heron Therapeutics, Inc. (the “Company”) issued a press release announcing, among other things, certain of its financial results for the three and twelve months ended December 31, 2017 (the “Press Release”). A copy of the Press Release is furnished herewith as Exhibit 99.1.

This Item 2.02 and the Press Release attached hereto as Exhibit 99.1 are being furnished to the Securities and Exchange Commission.

Item 7.01 Regulation FD Disclosure.

Press Release.

On January 8, 2018, the Company issued the Press Release providing, among other things, a general update on corporate progress, as described in the Press Release.

Corporate Presentation.

A copy of presentation materials describing the business of the Company, all or a part of which may be used by the Company in investor or scientific presentations from time to time, is furnished herewith as Exhibit 99.2 (the “Corporate Presentation”). The Corporate Presentation has also been posted on the Company’s website at www.herontx.com. The Company does not undertake any obligation to update the Corporate Presentation.

This Item 7.01, the Press Release and the Corporate Presentation are being furnished to the Securities and Exchange Commission.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Press Release, dated January 8, 2018</td>
</tr>
<tr>
<td>99.2</td>
<td>Corporate Presentation, dated January 2018</td>
</tr>
</tbody>
</table>
Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Heron Therapeutics, Inc.

Date: January 8, 2018

/s/ David L. Szekeres
David L. Szekeres
Senior Vice President, General Counsel,
Business Development and Corporate Secretary
Heron Therapeutics Highlights Progress in CINV and Pain Management Franchises

- SUSTOL ® Fourth-Quarter 2017 Net Sales of Approximately $10 Million, Up 16% from Third-Quarter 2017 Net Sales of $8.6 Million; Full-Year 2017 Net Sales of Approximately $31 Million, versus Guidance of $25 Million to $30 Million -

- 2018 Net Sales Guidance for CINV Franchise of $60 Million to $70 Million –

- Enrollment Complete in Both Pivotal Phase 3 Studies for HTX-011; Top-line Results Expected in First Half of 2018 -

SAN DIEGO, Calif. – (BUSINESS WIRE) – January 8, 2018 – Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on developing novel, best-in-class treatments to address some of the most important unmet patient needs, today highlighted progress in the Company’s pain management and CINV franchises.

CINV Franchise

- SUSTOL ® Sales. SUSTOL (granisetron) extended-release injection fourth-quarter 2017 net product sales were approximately $10 million, up 16% from third-quarter 2017 net product sales of $8.6 million. SUSTOL full-year 2017 net product sales were approximately $31 million, versus guidance of $25 million to $30 million.

- 2018 CINV Sales Guidance. Net product sales guidance for full-year 2018 for the CINV franchise is $60 million to $70 million.

- Permanent J-Code Now Effective. On January 1, 2018, a product-specific billing code, or permanent J-code, for SUSTOL became available. The new J-code was assigned by the Centers for Medicare and Medicaid Services (CMS) and will help simplify the billing and reimbursement process for prescribers of SUSTOL.

- CINVANTI ™ Now Available. In November 2017, the U.S. Food and Drug Administration (FDA) approved the Company’s New Drug Application (NDA) for CINVANTI (aprepitant) injectable emulsion, the first and only polysorbate 80-free intravenous (IV) formulation of a neurokinin-1 (NK1) receptor antagonist indicated for the prevention of acute and delayed CINV. CINVANTI became commercially available in the United States on January 4, 2018.
Enrollment Complete in Phase 3 Pivotal Trials for HTX-011 in Postoperative Pain. Heron completed enrollment in its two pivotal Phase 3 efficacy studies in bunionectomy and hernia repair. Heron anticipates reporting top-line results in the first half of 2018 and expects to file an NDA with the FDA in the second half of 2018.

"Heron had a strong year in 2017, led by the advancement of the HTX-011 program toward an NDA filing, the success of our commercial team with SUSTOL and the expansion of our CINV franchise with the approval of CINVANTI,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron. "We expect to build on our momentum in 2018 by reporting top-line pivotal Phase 3 results for HTX-011, filing an NDA for HTX-011 and growing our CINV franchise, which now includes two innovative products.”

About HTX-011 for Postoperative Pain
HTX-011, which utilizes Heron’s proprietary Biochronomer® drug delivery technology, is an investigational, long-acting, extended-release formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the prevention of postoperative pain. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction. The Phase 2 development program for HTX-011 was designed to target the many patients undergoing a wide range of surgeries who experience significant postoperative pain. Heron completed enrollment in its two pivotal Phase 3 efficacy studies in bunionectomy and hernia repair and anticipates reporting top-line results in the first half of 2018 and expects to file an NDA with the FDA in the second half of 2018.

About CINVANTI (aprepitant) injectable emulsion
CINVANTI is indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC), including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). CINVANTI is an intravenous formulation of aprepitant, a substance P/neurokinin-1 (NK₁) receptor antagonist. CINVANTI is the first intravenous (IV) formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK₁ receptor antagonist to significantly reduce CINV in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy). CINVANTI does not contain polysorbate 80 or any other synthetic surfactant. Pharmaceutical formulations containing polysorbate 80 have been linked to hypersensitivity reactions, including anaphylaxis and irritation of blood vessels resulting in infusion-site pain. FDA-approved dosing administration included in the United States prescribing information for CINVANTI is a 30-minute infusion.
About SUSTOL (granisetron) extended-release injection

SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-HT₃ receptor antagonist that utilizes Heron's Biochronomer® polymer-based drug delivery technology to maintain therapeutic levels of granisetron for ≥ 5 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL’s efficacy and safety in more than 2,000 patients with cancer. SUSTOL’s efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy).

About Chemotherapy-Induced Nausea and Vomiting (CINV)

While chemotherapy is one of the most effective and commonly used therapies to help patients fight cancer, it is accompanied by debilitating side effects, including varying degrees of nausea and vomiting, often attributed as a leading cause of premature discontinuation of cancer treatment. The goal of antiemetic therapy is to prevent CINV in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy). The National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) have categorized chemotherapy regimens based on the degree to which they cause nausea and vomiting: low emetogenic chemotherapy (LEC); moderately emetogenic chemotherapy (MEC); and highly emetogenic chemotherapy (HEC).

About Heron Therapeutics, Inc.

Heron is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments that address some of the most important unmet patient needs. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents for patients suffering from cancer or pain. For more information, visit www.herontx.com.
Forward-Looking Statements

This news release contains “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers that forward-looking statements are based on management’s expectations and assumptions as of the date of this news release and are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, those associated with: the potential market opportunities for SUSTOL and CINVANTI; the timing of completion and results of the Phase 3 studies for HTX-011; the timing of the NDA filing for HTX-011; and other risks and uncertainties identified in the Company’s filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and Heron takes no obligation to update or revise these statements except as may be required by law.

Investor Relations and Media Contact:

David L. Szekeres
Senior VP, General Counsel, Business Development and Corporate Secretary
dzekeres@herontx.com
858-251-4447

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Company Update

JP Morgan Conference
January 2018
Forward-Looking Statements

This presentation contains “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: the potential market opportunity for SUSTOL®, CINVANTI™ and HTX-011; the potential net sales for SUSTOL® and CINVANTI™; the timing of completion and results of the Phase 2 and Phase 3 trials for HTX-011; the timing of the NDA filing for HTX-011; the projected sufficiency of our capital position for future periods; the progress in the research and development of HTX-011 and our other programs, including the timing of clinical and manufacturing activities, and safety and efficacy results from our studies; and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and we take no obligation to update or revise these statements except as may be required by law.
# Status of Product Portfolio

<table>
<thead>
<tr>
<th></th>
<th>Preclinical</th>
<th>Clinical</th>
<th>NDA</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSTOL®</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(granisetron) extended-release injection</td>
<td>Approved by U.S. Food and Drug Administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CINVANTI™</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>Approved by U.S. Food and Drug Administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HTX-011</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bupivacaine + mecloxocam ER Local Administration</td>
<td>Postop Pain with Local Administration</td>
<td>Fast Track designation granted</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HTX-011</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bupivacaine + mecloxocam ER Nerve Block</td>
<td>Postop Pain with Nerve Block</td>
<td>Phase 2 program in nerve block underway</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CINV Commercial Products
The Management of CINV Remains a Significant Clinical Challenge

Despite treatment with previously available therapies, many patients experience breakthrough CINV particularly in the delayed phase (days 2-5). CINV has a high clinical burden - impacting patients' QOL and cancer treatment. Prior to SUSTOL®, there were no single-agent 5-HT₃ antagonists indicated to prevent delayed CINV from a HEC regimen (including palonosetron). Prior to CINVANTI®, there were no NK₁ receptor antagonists approved for both acute and delayed CINV that were free of synthetic surfactants. HCPs cite the need for new therapies that deliver long-acting CINV prevention in both MEC and HEC.

<table>
<thead>
<tr>
<th>Unmet Need</th>
</tr>
</thead>
<tbody>
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<td>- Despite treatment with previously available therapies, many patients experience breakthrough CINV particularly in the delayed phase (days 2-5).</td>
</tr>
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<td>- CINV has a high clinical burden - impacting patients’ QOL and cancer treatment.</td>
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<tr>
<td>- HCPs cite the need for new therapies that deliver long-acting CINV prevention in both MEC and HEC.</td>
</tr>
</tbody>
</table>

In the U.S., over 1 million people receive CINV therapy each year:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.4 M</td>
<td>Cancer treatment</td>
</tr>
<tr>
<td>1.3 M</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>1 M</td>
<td>CINV therapy</td>
</tr>
</tbody>
</table>

1.3 Million patients receive chemotherapy

1 Million patients receive CINV therapy

Source: IPSOS Q2 2015 Cancer Tracking
Despite Previously Available Therapies, a Large Percentage of Patients Experience Breakthrough CINV

% of MEC/HEC patients with breakthrough CINV despite prophylaxis

Community practice observational study

- HEC: 51% (n=132)
- MEC: 46% (n=610)

Data from a prospective observational study enrolling chemotherapy-naive patients who received single-day HEC or MEC at four oncology practice networks, all using electronic medical record (EMR) systems, in Georgia, Tennessee, and Texas. CINV = emesis or clinically significant nausea on days 1-5. Regimen for HEC was a 5-HT3 + NK1 + dexamethasone (CS) on Day 1; NK1 on Days 2-3; CS on Days 2-4; for MEC it was 5-HT3 + NK1 + CS on Day 1; CS, NK1, or CS on Days 2-3 (n=610) (n=132).


% of MEC/HEC patients with breakthrough CINV despite prophylaxis

Physician perception

- Experience breakthrough CINV: 50%
- Don't experience breakthrough CINV: 50%

Source: Instar Market Research, Dec 2015, N=75 oncologists.
CINV Has a High Clinical Burden – Impacting Patients’ QOL and Cancer Treatment

Patients identified CINV as the side effect of chemotherapy they most wanted to avoid.

CINV commonly disrupts patients’ cancer treatment.

32% of oncology HCPs delayed or discontinued chemotherapy due to CINV within the prior year.
CINV Prophylaxis Typically Requires Two Complimentary Mechanisms of Action

**NK₁ receptor antagonists**
- Substance P is primary driver of delayed CINV, but related to ~15% of acute failures
- EMEND® IV (fosaprepitant), which has 90% share of the US NK₁ market, contains the synthetic surfactant polysorbate 80 that has been associated with hypersensitivity and infusion site reactions

**5-HT₃ receptor antagonists**
- These are the backbone of CINV prophylaxis
- Excessive serotonin release is the primary driver for CINV in the acute phase and secondary driver in the delayed phase
Heron Therapeutics Is the Only Company with Two Single-Agent Products Approved for Prevention of Acute and Delayed CINV
SUSTOL® Outperformed ALL Recent CINV New Brand Launches

SUSTOL® Outperformed ALL Recent CINV New Brand Launches Since 2008

Sources: IMS DDD; Heron actuals (distributor 867 reports) are for 4Q2016 through 3Q2017; due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2.

Administrations in First 12 Months (launch aligned)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Administrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sancuso (2008)</td>
<td>32,338</td>
</tr>
<tr>
<td>Akynzeo (2014)</td>
<td>2,766</td>
</tr>
<tr>
<td>Varubi (2015)</td>
<td>11,739</td>
</tr>
<tr>
<td>SUSTOL (2016)</td>
<td>68,694</td>
</tr>
</tbody>
</table>

Sources: IMS DDD; Heron actuals (distributor 867 reports) are for 4Q2016 through 3Q2017; due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2.
SUSTOL® Net Revenue Up 16% to $10 Million in Q4
Over 100,000 Units of SUSTOL Sold to Practices in 2017
Full Year 2017 Net Revenue Was Approximately $31M

SUSTOL Quarterly Unit Performance
(Provider Demand)

<table>
<thead>
<tr>
<th>Units (000's)</th>
<th>Q4 2016</th>
<th>Q1 2017</th>
<th>Q2 2017</th>
<th>Q3 2017</th>
<th>Q4 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net Sales</td>
<td>$1.3M</td>
<td>$3.6M</td>
<td>$8.5M</td>
<td>$8.6M</td>
<td>$10M</td>
</tr>
</tbody>
</table>

Source: Heron 867 data

↑ 16% ↑
Market Insights Suggest SUSTOL® May Decline Modestly Through the Arbitrage and Grow Thereafter – Consistent with Aloxi® Analogue

Recent Market Insights

- Practitioners that are converting to SUSTOL are likely to maintain use.
- ~67% of current “dabblers” likely to stop or reduce use of SUSTOL during arbitrage.
- ~20% of SUSTOL non-users would consider initiating SUSTOL during arbitrage.
  - “If generic Aloxi is available, it’s going to allow me to start using SUSTOL without having to worry about maintaining my Aloxi contract.” – PM
- ~55% of HCPs said they would be interested in using SUSTOL post-arbitrage (equating to an addressable market of ~660k units).
  - “When ASP erodes, we would switch all patients from generic Aloxi to SUSTOL.” – PM
  - “SUSTOL usage would increase. There’s no reason to keep people on generic Aloxi.” – PM

1 Customer discussions
2 Putnam Associates Qual Research Findings, June 2017
Study Conducted to Evaluate Hydration Rates With SUSTOL® vs ALOXI® Based on Prior Observation of Fewer Unscheduled Visits Due to CINV by HEC Patients Receiving SUSTOL

STUDY DESIGN

Patients receiving HEC and a 3-drug antiemetic regimen of an NK-1 receptor antagonist, dexamethasone and either SUSTOL or ALOXI

ALOXI only

SUSTOL only

Initial ALOXI then switched to SUSTOL

Group 1 analysis: SUSTOL vs ALOXI

Group 2 analysis: initial ALOXI followed by SUSTOL

HEC Patients Treated With SUSTOL Experienced Significantly Lower Requirements For Hydration Compared to ALOXI

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of chemotherapy cycles</th>
<th>Hydration rate</th>
<th>P-value for difference in hydration vs Aloxi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>GROUP 1 HEC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALOXI (n = 78)</td>
<td>5.6 (2.9)</td>
<td>1.0 (1.2)</td>
<td></td>
</tr>
<tr>
<td>SUSTOL (n = 55)</td>
<td>4.0 (2.1)</td>
<td>0.3 (0.6)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>GROUP 2 HEC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALOXI (n = 32)</td>
<td>3.3 (3.1)</td>
<td>0.7 (1.2)</td>
<td></td>
</tr>
<tr>
<td>SUSTOL (n = 32)</td>
<td>2.9 (2.0)</td>
<td>0.5 (1.0)</td>
<td>p = 0.028</td>
</tr>
</tbody>
</table>

- In Group 1, 40% of patients treated with SUSTOL required hydration compared to 81% of patients treated with ALOXI.

HEC: Highly emetogenic chemotherapy; max: Maximum; min: Minimum; SD: Standard deviation.
CINVANTI™ Now Launched

- CINVANTI™ is the first and only polysorbate 80-free IV NK₁ receptor antagonist approved for the prevention of both acute and delayed CINV.

CINVANTI (aprepitant) injectable emulsion

CINVANTI™ is indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Please see Full Prescribing Information on www.CINVANTI.com.
Despite an NCCN Category 1 Recommendation, NK₁’s are Underutilized

NCCN Antiemetic Guidelines

HEC
- 5-HT₃
- dexamethasone
- NK₁
  ± olanzapine

MEC
- 5-HT₃
- dexamethasone
- ± NK₁
  ± olanzapine

NCCN 2017

Percent of Patients Receiving NK₁ Therapy

IP305 “US Tandem Oncology Monitor Anti-Erretica
Report” is based on chart audit data of 68,437 patient records between 2015 and 2016 NCCN 2017
### Aprepitant Has Provided Trusted Efficacy for CINV Prevention for Nearly 15 Years

#### Overview of Aprepitant

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA approved</td>
<td>2003</td>
</tr>
<tr>
<td>NCCN Category 1 recommendation</td>
<td>Yes</td>
</tr>
<tr>
<td>Phase 3/4 clinical trials*</td>
<td>22</td>
</tr>
<tr>
<td>Patients studied in clinical trials*</td>
<td>7100+</td>
</tr>
</tbody>
</table>

~1.4 million administrations per year**
~90% of which is IV fosaprepitant

#### Aprepitant is the only single-agent NK₁ that:

- Is FDA-approved for prevention of CINV in both acute and delayed phases
- Can be administered to patients receiving chemotherapy regardless of cycle length

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**No other NK₁ has been proven more effective than aprepitant**

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*Both oral aprepitant and IV fosaprepitant combined

**Source: IMS NPA 2016-2017 Overview of Aprepitant
CINVANTI™ Is the First and Only Polysorbate 80-Free IV NK₁ Approved for the Prevention of Both Acute and Delayed CINV

<table>
<thead>
<tr>
<th>Feature</th>
<th>CINVANTI™ IV</th>
<th>EMEND® IV</th>
<th>Varubi® IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicated for prevention of both acute and delayed CINV</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Can be administered regardless of chemo cycle length</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Preliminary data supports administration by IV push</td>
<td>Yes¹</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Polysorbate 80-free formulation</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Emulsion formulation requires no reconstitution</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Aloxi® and dexamethasone are stable when added to the product²</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be stored at room temperature for 60 days</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1. FDA-approved dosing administration included in the US prescribing information (PI) for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.
2. Aloxi® PI states that it should not be mixed with other drugs.
CINVANTI® Was Well Tolerated Given as an Infusion or as an IV Push

CINVANTI Was Well Tolerated When Given by Both 30-minute Infusion and 2-minute IV Push

2. FDA-approved dosing administration included in the US prescribing information for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.
With CINVANTI™, Heron Adds a Second Best-In-Class Therapy to Compete in a Branded CINV Market with ~3.6M Annual Units

Leading Branded CINV Products (Annual Units)

- Alox®: 1.31M
- Emend IV®: 2.33M

Source: IMS TTM Q3'17 Leading Branded CINV Products (Annual Units)
2018 CINV Franchise Outlook

**SUSTOL®**: We continue to expect core SUSTOL business to hold firm and with possibility of modest decline during arbitrage and growth thereafter
- Even with the potential for generic palonosetron, 4th quarter unit sales grew 22%
- Approximately $31M in net product sales in 2017
- Permanent J-code 1627 granted by CMS; effective January 1, 2018

**CINVANTI®**
- Commercially available in the US
- We believe it has the best overall profile compared to the other available NK1 antagonists
- Offers strong strategic and operational fit with existing commercial organization to win in a branded CINV market with ~3.6M annual units

**CINV Franchise**
- **CINV franchise 2018 guidance of $60M–$70M in net product sales**
Postoperative Pain Program
HTX-011: Proprietary Extended-Release Combination of Bupivacaine + Meloxicam
Postoperative Opioids: A Doorway to Addiction

MORE THAN 50 MILLION surgical procedures happen in the United States.

80% of patients undergoing a surgical procedure are prescribed opioids for pain management.

As many as 6.5% of patients that take opioids to manage pain after surgery may become persistent opioid users.

That equals about 2.6 MILLION PEOPLE.

Of these 2.6 million persistent opioid users, 26% or 676,000 will become addicted to opioids.

In addition, hundreds of millions of LEFTOVER PILLS are then brought home from the hospital after surgery.

70% of all these opioid tablets go unused.

90% of these pills remain inside the home in unsecured locations.

32% of all opioid addicts report first opioid exposure through leftover pills.

43% ($14.2 billion) of the healthcare costs associated with addiction can be attributed to postoperative pain management.
Market Is Large and Local Anesthetic Use Is Common, but Current Extended Release Anesthetics Have Not Fulfilled the Promise of Long-Acting Pain Relief

Procedures Requiring Postoperative Pain Relief, 2015-2020

Local Anesthetic Usage Across Key Surgeries, 2015

Key Limiters of Liposomal Bupivacaine Market Penetration

- Perceived inability to achieve marketed duration of efficacy
- No large scale studies have reproducibly shown superiority versus bupivacaine solution
- HCPs not persuaded that incremental efficacy is worth the cost
- Because of the above, there are significant formulary access restrictions
  - Restricted by Specialty
  - Restricted by Procedure
  - Not on Formulary
  - Very low penetration in ASC and outpatient settings

Local anesthetics (LAs) are used to manage postoperative pain in ~21M procedures in 2015; bupivacaine is the most commonly used LA for local administration with 11M procedures/year for postop pain.

Sources:
1. DRG claims analysis (2015), (942) Postoperative Pain Pharmacor
2. DRG physician and P&T member interviews (2016; n=156)
3. Based on analysis of current postoperative pain management across 40 target procedures (~28M procedures)
Surgeons Expect to Use Less Opioids and More Long-Acting Local Anesthetics as Better Options Become Available

Source: DRG Physician Survey (2016)

72% of surgeons expect to use fewer opioids
62% of surgeons expect to use more local anesthetics
73% of surgeons expect to use more long-acting local anesthetics

Future Pain Market Outlook

- 72% of surgeons expect to use fewer opioids
- 62% of surgeons expect to use more local anesthetics
- 73% of surgeons expect to use more long-acting local anesthetics

Source: DRG Physician Survey (2016)
Large US Market Opportunity

Theoretical and Target Market

~28M Annual US Surgical Procedures Requiring Postoperative Pain Management ($7.0 – 8.4B)

Initial Targets
Higher volume procedures across 4 major specialties
- ~6.5M Orthopedic procedures
- ~4.3M General Surgery procedures
- ~3.3M OB/GYN procedures
- ~1.1M Plastic Surgery procedures

Secondary Targets
Higher volume procedures in non-core specialties (e.g., ENT, urology, hand, others)

Tertiary Targets
Lower volume procedures and procedures where local anesthetics are not widely used today

Theoretical Market Size

~15M procedures

~6M procedures

~7M procedures

Initial Targets $3.8 – 4.5B

Secondary Targets $1.6 – 1.9B

Tertiary Targets $1.7 – 2.1B

~15M procedures

~6M procedures

~7M procedures

Theoretical Market Size
### High Procedure Volume in Target Markets Provides a Robust ROW Market Opportunity

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Surgical Procedures</th>
<th>Total Procedures Requiring Postop Pain Management</th>
<th>Initial Target Procedures</th>
<th>Remaining Secondary, Lower Volume &amp; Procedures Currently Not Using Local Anesthetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>22,545,000</td>
<td>6,838,000</td>
<td>3,649,000</td>
<td>3,189,000</td>
</tr>
<tr>
<td>France</td>
<td>14,545,000</td>
<td>4,357,000</td>
<td>2,232,000</td>
<td>2,065,000</td>
</tr>
<tr>
<td>UK</td>
<td>13,882,000</td>
<td>3,835,000</td>
<td>1,790,000</td>
<td>2,045,000</td>
</tr>
<tr>
<td>Italy</td>
<td>5,637,000</td>
<td>2,530,000</td>
<td>1,919,000</td>
<td>611,000</td>
</tr>
<tr>
<td>Canada</td>
<td>3,416,000</td>
<td>1,638,000</td>
<td>1,282,000</td>
<td>356,000</td>
</tr>
<tr>
<td>Japan</td>
<td>25,959,000</td>
<td>6,600,000</td>
<td>2,658,000</td>
<td>3,332,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>85,984,000</strong></td>
<td><strong>25,788,000</strong></td>
<td><strong>13,600,000</strong></td>
<td><strong>12,198,000</strong></td>
</tr>
</tbody>
</table>
Why Haven’t Extended Release Local Anesthetics Penetrated This Large Market

- Regardless of delivery technology, extended release bupivacaine products do not reduce pain sufficiently beyond 24 hours to beat bupivacaine HCl:
  - Exparel® (liposomal ER bupivacaine)
  - Xaracoll™ (bupivacaine collagen matrix)
  - Posimur™ (SABER-bupivacaine)
  - HTX-002 (Biochronomer ER bupivacaine)
  - ON-Q® bupivacaine pump (continuous infusion)

60-Hour Continuous Infusion of Bupivacaine With On-Q Pump in Hernia Repair Was Significantly Different From Placebo for Only 24 hr (Schurr et. al. Surgery 2004;136:761-9)
Inflammation Plays a Key Role in Pain Management
(Current local anesthetics do not address this)

- Surgical insult produces an immediate drop in pH
- As inflammatory cytokines are released and inflammation sets in, the acidic environment is maintained for many days
- The acidic environment shifts the balance to the ionized form, which is unable to enter the nerve

Acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects.1,2
Bupivacaine is very sensitive to reduced pH
Addition of meloxicam is designed to help reduce local inflammation and allow bupivacaine to work better in the first several days after surgery

2. Local anesthetic nerve penetration model adapted from Becker and Rand, Anesth Prog 53:98–109 2006
HTX-011 Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery

1 Postoperative pain model in pigs from Castle et al, 2013 EPJ
2 Human dose of liposomal bupivacaine with 40% smaller incision
(n=4 pigs in each arm)
Activity of HTX-011 Cannot Be Replicated By Systemic Administration of Meloxicam Along With ER Bupivacaine

Pig Post-Operative Pain Model

Saline Placebo  HTX-011 (Bupivacaine + Meloxicam)  Biochronomer ER Bupivacaine With Simultaneous Injectable Meloxicam

*Supratherapeutic dose of meloxicam administered SQ
Post-operative pain model in pigs from Castle et al, 2013 EPJ Pig Post-Operative Pain Model (n=4 pigs in each arm)

Increasing Analgesia
Percent of Maximum Force
Hours
0 1 3 5 24 48 72 96 120
0 10 20 30 40 50 60 70 80 90 100

(n=4 pigs in each arm)
The Unique Mechanism of Action of HTX-011 Has Been Demonstrated in the Pig Post-Op Pain Model

The normalization of pH starting at 8 hours with HTX-011 allows almost 10x more bupivacaine (BPV) to enter the nerve to block the pain signal.

<table>
<thead>
<tr>
<th>Time Post-Incision (hrs)</th>
<th>Incision pH ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HTX-011-56 (N=3)</td>
</tr>
<tr>
<td>0</td>
<td>6.94%</td>
</tr>
<tr>
<td>8</td>
<td>7.00%</td>
</tr>
<tr>
<td>16</td>
<td>7.00%</td>
</tr>
<tr>
<td>24</td>
<td>7.00%</td>
</tr>
<tr>
<td>32</td>
<td>7.00%</td>
</tr>
<tr>
<td>40</td>
<td>7.00%</td>
</tr>
<tr>
<td>48</td>
<td>7.00%</td>
</tr>
</tbody>
</table>

7.94% vs. 0.76%
Unique MOA of HTX-011 Produces Significantly Greater Pain Reduction Than ER Versions of Bupivacaine or Meloxicam

*P-value from ANOVA, LSMD of area under the curve for HTX-011 vs. HTX-002 or HTX-009
Unique MOA of HTX-011 Results in an Excellent PK-PD Relationship Not Seen With Other ER Bupivacaine Formulations

Source: Data on File, Heron Therapeutics, Inc.

*LOCF method used to account for missing data, with WWOCF adjustment for use of rescue medications.
Exparel® Does Not Demonstrate a PK-PD Relationship

Exparel® (liposomal bupivacaine)

No PK-PD Relationship

Mean Pain Intensity vs Time


Mean Pain Intensity vs Time

HTX-011 PHASE 2 RESULTS
Study 202: HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Herniorrhaphy 

Increasing Pain

Mean ± (SE) Pain Intensity (W/WOCF)

Severe Pain

AUC

300 mg vs. P: p<0.0001
300 mg vs. B: p=0.0682
300 mg vs. B: p=0.0129
300 mg vs. B: p=0.0427

WOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data.
Study 208: HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Bunionectomy

Increasing Pain

Mean ± SE Pain Intensity (wWOCF)

Saline Placebo (N=103)  Bupivacaine 50 mg (N=28)  HTX-011 60 mg (N=52)

Severe Pain

AUC2.5h  AUC6h  AUC24h

60 mg vs. P: p<0.0001  60 mg vs. P: p<0.0001  60 mg vs. P: p=0.0003

60 mg vs. B: p=0.0029  60 mg vs. B: p=0.0020  60 mg vs. B: p=0.0165

wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data.
In a Cross-Study Comparison of a Standardized Bunionectomy Model Two Forms of Extended-Release Bupivacaine Produced Remarkably Similar Results

Greater Pain Reduction vs Placebo

[Graph showing pain reduction over time with different forms of bupivacaine]

Liposomal ER Bupivacaine 120 mg*  HTX-002 ER Bupivacaine 60 mg  HTX-011 (60 mg)

Sources: Data on File, Heron Therapeutics, Inc., and
HTX-011 Reduces Total Opioid Use vs Bupivacaine and Placebo in Phase 2

Study 202 - Herniorrhaphy Study

Study 208 - Bunionectomy Study

Source: Data on File, Heron Therapeutics, Inc.
HTX-011 Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo in Phase 2

Study 202 - Herniorrhaphy Study

- ITX-011 300 mg (N=16)
- Bupivacaine HCl 75 mg (N=32)
- Saline Placebo (N=83)

Study 208 - Bunionectomy Study

- ITX-011 60 mg (N=45)
- Bupivacaine HCl 50 mg (N=25)
- Saline Placebo (N=103)

Source: Data on File, Heron Therapeutics, Inc.
ENROLLMENT COMPLETED IN BOTH PHASE 3 PIVOTAL TRIALS
Study 301: Phase 3 Bunionectomy

Study Design

Randomization (3:3:2)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTX-011 60 mg Instillation</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Bupivacaine 50 mg Injection</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Saline Placebo Instillation</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Endpoints

- **Primary**: Pain Intensity AUC$_{0-72}$ vs. placebo
- **1st Key Secondary**: Pain Intensity AUC$_{0-72}$ vs. bupivacaine
- **2nd Key Secondary**: Opioid use vs. placebo
- **3rd Key Secondary**: Opioid-free vs. bupivacaine
- **4th Key Secondary**: Opioid use vs. bupivacaine

The trial design provides at least 90% power to detect a statistically significant difference between HTX-011 and each of the control groups for primary and all key secondary endpoints.
Study 302: Phase 3 Herniorrhaphy
Study Design

Randomization (2:2:1)

- HTX-011 300 mg Instillation N = 160
- Bupivacaine 75 mg Injection N = 160
- Saline Placebo Instillation N = 80

**Study 302 Endpoints**

- Primary: Pain Intensity AUC\textsubscript{0-72} vs. placebo
- 1\textsuperscript{st} Key Secondary: Pain Intensity AUC\textsubscript{0-72} vs. bupivacaine
- 2\textsuperscript{nd} Key Secondary: Opioid use vs. placebo
- 3\textsuperscript{rd} Key Secondary: Opioid-free vs. bupivacaine
- 4\textsuperscript{th} Key Secondary: Opioid use vs. bupivacaine

The trial design provides at least 90% power to detect a statistically significant difference between HTX-011 and each of the control groups for primary and all key secondary endpoints.
On-Going Phase 2b Studies
Phase 2b Study 211: Nerve Block in Breast Augmentation
Study Design

Protocol includes additional optional cohorts to evaluate other doses and administration techniques.
Phase 2b Total Knee Arthroplasty
Study Design

Cohort 1
- HTX-011 200 mg Instillation
  N = 20
- HTX-011 200 mg Instillation + Injection
  N = 20
- Saline Placebo Injection
  N = 10
- Bupivacaine 125 mg Injection
  N = 10

Cohort 2
- HTX-011 400 mg Instillation
  N = 50
- HTX-011 400 mg Instillation + Ropi Injection
  N = 50
- Saline Placebo Injection
  N = 50
- Bupivacaine 125 mg Injection
  N = 50

IRG

Stand-alone, adequate and well-controlled study cohort
## Summary: HTX-011 Is Poised to Fulfill the Promise of a Long-Acting Extended-Release Local Anesthetic

<table>
<thead>
<tr>
<th>Benefit</th>
<th>✔</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large, growing market opportunity</td>
<td></td>
</tr>
<tr>
<td>Differentiated, synergistic mechanism addresses inflammation – a key inhibitor of both generic and long-acting local anesthetics</td>
<td></td>
</tr>
<tr>
<td>Demonstrated superiority vs. generic bupivacaine solution in 3 diverse surgical models in Phase 2; both pivotal Phase 3 trials include a comparison to bupivacaine</td>
<td></td>
</tr>
<tr>
<td>Consistent 72-hour efficacy</td>
<td></td>
</tr>
<tr>
<td>- Pain reduction</td>
<td></td>
</tr>
<tr>
<td>- Opioid reduction</td>
<td></td>
</tr>
<tr>
<td>Applicable in large and small procedures without admixture with bupivacaine solution – reducing chance of dosing errors and systemic toxicity</td>
<td></td>
</tr>
<tr>
<td>Simple administration with potential safety advantages</td>
<td></td>
</tr>
<tr>
<td>Potential to address most pressing unmet needs cited by key stakeholders – patients, surgeons, anesthesiologists &amp; formulary decision makers</td>
<td></td>
</tr>
<tr>
<td>Extensive patent protection through 2035</td>
<td></td>
</tr>
</tbody>
</table>
Overwhelmingly Positive Response by Physicians and Pharmacists to HTX-011’s Target Product Profile

**HTX-011 Target Product Profile: Strengths**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Strength (%)</th>
<th>Neither a Strength Nor Weakness (%)</th>
<th>Weakness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in Opioid Consumption</td>
<td>88%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Reduction in Pain Score</td>
<td>87%</td>
<td>13%</td>
<td>10%</td>
</tr>
<tr>
<td>Reduction in Opioid AEs*</td>
<td>80%</td>
<td>19%</td>
<td>9%</td>
</tr>
<tr>
<td>Analgesia Duration</td>
<td>79%</td>
<td>29%</td>
<td>12%</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>73%</td>
<td>23%</td>
<td>4%</td>
</tr>
<tr>
<td>No Impact on Wound Healing</td>
<td>69%</td>
<td>30%</td>
<td>11%</td>
</tr>
<tr>
<td>Indication</td>
<td>67%</td>
<td>31%</td>
<td>4%</td>
</tr>
<tr>
<td>Compatibility with NSAIDs</td>
<td>68%</td>
<td>31%</td>
<td>11%</td>
</tr>
<tr>
<td>No Impact on Implantables</td>
<td>60%</td>
<td>38%</td>
<td>12%</td>
</tr>
<tr>
<td>Overall Safety</td>
<td>60%</td>
<td>37%</td>
<td>13%</td>
</tr>
<tr>
<td>Dosing Regimen</td>
<td>59%</td>
<td>42%</td>
<td>9%</td>
</tr>
<tr>
<td>Phase 3 Procedures</td>
<td>46%</td>
<td>50%</td>
<td>4%</td>
</tr>
</tbody>
</table>

\[n = 376\ total (101 anesthesiologists, 51 general surgeons, 122 orthopedic surgeons, 50 plastic surgeons, 50 pharmacy directors)\]

*Opioid AEs are assumed to be reduced with significant reduction in use*
Pharmacy Directors Strongly Preferred HTX-011 over Exparel® Based on MOA, Reduction in Pain, and Reduction in Opioids

<table>
<thead>
<tr>
<th>Preference for HTX-011 vs. Exparel Based on Product Attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physician Responses</strong></td>
</tr>
<tr>
<td>Mechanism of Action</td>
</tr>
<tr>
<td>Duration of Analgesia</td>
</tr>
<tr>
<td>Reduction in Pain Score</td>
</tr>
<tr>
<td>Reduction in Opioids Consumed</td>
</tr>
<tr>
<td>Reduction in Opioid-Related AEs*</td>
</tr>
<tr>
<td>Local Admin Dosing</td>
</tr>
<tr>
<td>Procedures in Phase 3 Studies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>Strongly favors HTX-011</th>
<th>Somewhat favors HTX-011</th>
<th>Product X and Exparel generally equivalent</th>
<th>Strongly favors Exparel</th>
<th>Somewhat favors Exparel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of Action</td>
<td>37%</td>
<td>26%</td>
<td>27%</td>
<td>16%</td>
<td>46%</td>
</tr>
<tr>
<td>Duration of Analgesia</td>
<td>12%</td>
<td>48%</td>
<td>33%</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>Reduction in Pain Score</td>
<td>25%</td>
<td>35%</td>
<td>35%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Reduction in Opioids Consumed</td>
<td>24%</td>
<td>43%</td>
<td>33%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Reduction in Opioid-Related AEs*</td>
<td>14%</td>
<td>30%</td>
<td>41%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Local Admin Dosing</td>
<td>10%</td>
<td>37%</td>
<td>51%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Procedures in Phase 3 Studies</td>
<td>5%</td>
<td>28%</td>
<td>57%</td>
<td>7%</td>
<td>7%</td>
</tr>
</tbody>
</table>

n = 52 pharmacy directors

*Opioid AE’s are assumed to be reduced with significant reduction in use.
Financial Summary

<table>
<thead>
<tr>
<th>Condensed Balance Sheet Data (In thousands)</th>
<th>September 30, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents and short-term investments</td>
<td>$ 74,016</td>
</tr>
<tr>
<td>Accounts receivable, net</td>
<td>$ 28,851</td>
</tr>
<tr>
<td>Total assets</td>
<td>$ 118,196</td>
</tr>
<tr>
<td>Promissory note payable</td>
<td>$ 25,000</td>
</tr>
<tr>
<td>Total stockholders’ equity</td>
<td>$ 40,053</td>
</tr>
</tbody>
</table>

In December 2017, we issued 9.7 million shares of common stock for net proceeds of $142.7 million. Including the net proceeds, pro forma cash, cash equivalents and short-term investments totaled $216.7 million at September 30, 2017.

Common shares outstanding at December 31, 2017 totaled 64.6 million.
### Key Catalysts in Pain Management & CINV Franchises

<table>
<thead>
<tr>
<th>HTX-011 for Postoperative Pain</th>
<th>CINVANTI™ and SUSTOL® for CINV</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Fast Track designation granted</td>
<td>2018 net sales guidance for CINV franchise: $60M - $70M</td>
</tr>
<tr>
<td>✓ Completed enrollment in Phase 3 pivotal trials</td>
<td></td>
</tr>
<tr>
<td>Top-line Pivotal Phase 3 results 1H 2018</td>
<td></td>
</tr>
<tr>
<td>NDA filing 2H 2018</td>
<td></td>
</tr>
</tbody>
</table>