Company Update

November 2017
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 and 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>Preclinical</th>
<th>Clinical</th>
<th>NDA</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSTOL®</strong> (granisetron) extended-release injection</td>
<td>Approved by U.S. Food and Drug Administration</td>
<td></td>
<td></td>
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<tr>
<td><strong>CINVANTI™</strong> (aprepitant) injectable emulsion</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>HTX-011</strong> bupivacaine + meloxicam ER Local Administration</td>
<td>Postop Pain with Local Administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HTX-011</strong> bupivacaine + meloxicam ER Nerve Block</td>
<td>Postop Pain with Nerve Block</td>
<td>Phase 2 program in nerve block underway</td>
<td></td>
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</table>
CINVANTI™ Now Approved

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

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
CINV Prophylaxis Requires Two Complimentary Mechanisms of Action

NK₁ receptor antagonists

- EMEND® IV (fosaprepitant) has 90% share of the US NK₁ market
- Infusion site reactions (predominately infusion site pain) observed with EMEND® IV are believed to be caused by the surfactant polysorbate 80 in the product
The Goal of Antiemetic Therapy is to Prevent CINV Across Both Acute and Delayed Phases

Patterns of CINV and Neurotransmitters Involved

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotransmitters Involved</td>
<td>✓ 5-HT&lt;sub&gt;3&lt;/sub&gt; ✓ NK&lt;sub&gt;1&lt;/sub&gt;</td>
<td>✓ NK&lt;sub&gt;1&lt;/sub&gt; ✓ 5-HT&lt;sub&gt;3&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

5-HT<sub>3</sub> and NK<sub>1</sub> pathways are important in both acute and delayed phases of CINV.

Martin 1996; Grundberg 2004
Heron Therapeutics Is the Only Company with Two Single-Agent Products Approved for Prevention of Acute and Delayed CINV
Despite an NCCN Category 1 Recommendation, NK\textsubscript{1}’s are Underutilized

NCCN Antiemetic Guidelines

<table>
<thead>
<tr>
<th>HEC</th>
<th>MEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 5-HT\textsubscript{3}</td>
<td>• 5-HT\textsubscript{3}</td>
</tr>
<tr>
<td>• dexamethasone</td>
<td>• dexamethasone</td>
</tr>
<tr>
<td>• NK\textsubscript{1}</td>
<td>• NK\textsubscript{1}</td>
</tr>
<tr>
<td>± olanzapine</td>
<td>± olanzapine</td>
</tr>
</tbody>
</table>

IPSOS “US Tandem Oncology Monitor Anti-Emetics Report” is based on chart audit data of 68,437 patient records between 2015 and 2016
Aprepitant Has Provided Unsurpassed Efficacy for CINV Prevention for Nearly 15 Years

<table>
<thead>
<tr>
<th>Overview of Aprepitant</th>
<th>Aprepitant is the only single-agent NK₁ that:</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA approved</td>
<td>• Is FDA-approved for prevention of CINV in <strong>both</strong> acute and delayed phases</td>
</tr>
<tr>
<td>2003</td>
<td>• Can be administered to patients receiving chemotherapy regardless of cycle length</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  

No other NK₁ has been proven more effective than aprepitant

*Both oral aprepitant and IV fosaprepitant combined  
^Source: IMS NPA 2016-2017
Polysorbate 80 Is a Synthetic Surfactant Associated with Adverse Events

- Polysorbate 80 (PS-80) is a synthetic surfactant used to solubilize injectable chemotherapy and supportive care drugs
- PS-80 is a pharmacologically active compound and has been linked to adverse events in oncology patients

Reactions related to PS-80

<table>
<thead>
<tr>
<th>SYSTEMIC ADVERSE EVENTS</th>
<th>INFUSION SITE ADVERSE EVENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>Pain</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Swelling</td>
</tr>
</tbody>
</table>

Injectable drugs containing PS-80

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Supportive Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabazitaxel</td>
<td>Darbepoetin alfa (Aranesp)</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Filgrastim (Neupogen)</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Fosaprepitant</td>
</tr>
</tbody>
</table>

Heron’s goal was to develop a new IV formulation of aprepitant that has the same efficacy as IV fosaprepitant without the potential risk of polysorbate 80-related AEs
CINVANTI™ Demonstrated Bioequivalence to Fosaprepitant and Fewer Treatment-Emergent Adverse Events Within 30 Minutes of Infusion

**Demonstrated Bioequivalence to Fosaprepitant**

**Fewer TEAEs Within 30 Minutes of Infusion**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>CINVANTI 130 mg (n=196)</th>
<th>Fosaprepitant 150 mg (n=200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion site pain</td>
<td>0%</td>
<td>7%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>0.5%</td>
<td>3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Sources: CINVANTI US PI; data on file
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></th>
<th>CINVANTI™ IV</th>
<th>EMEND® IV</th>
<th>Varubi® IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant emulsion</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>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>Can be stored at room temperature for 60 days</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
With CINVANTI™, Heron Adds a Second Best-In-Class Therapy to Compete in a Branded CINV Market with ~3.6M Annual Units

Source: IMS TTM Q3’17
SUSTOL® Delivered 28.7K Units in Q3 (8% Growth Vs. Q2)

SUSTOL Quarterly Unit Performance
(Provider Demand)

Q4 2016: 3.2K
Q1 2017: 10.3
Q2 2017: 26.4
Q3 2017: 28.7

Net Sales:
- Q4 2016: $1.3M
- Q1 2017: $3.6M
- Q2 2017: $8.5M
- Q3 2017: $8.6M

Source: Heron 867 data
As Expected, SUSTOL® Core Business was Steady, but Growth Slowed in Anticipation of Generic Aloxi®

Source: Heron 867 data
Market Insights Suggest SUSTOL® May Decline Modestly Through the Arbitrage and Grow Thereafter – Consistent with Aloxi® Analogue

Recent Market Insights

- Practices that are converting to SUSTOL are likely to maintain use¹
- ~67% of current “dabblers” likely to stop or reduce use of SUSTOL during arbitrage²
- ~20% of SUSTOL non-users would consider initiating SUSTOL during arbitrage²
  - “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 ~650K units)²
  - “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
Despite Expectations of Generic Aloxi®, SUSTOL® Continues to Outperform Recent CINV New Brand Launches

CINV New Brand Launches Since 2008

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>33,530</td>
</tr>
<tr>
<td>Akynzeo (2014)</td>
<td>2,756</td>
</tr>
<tr>
<td>Varubi (2015)</td>
<td>11,759</td>
</tr>
<tr>
<td>SUSTOL (2016)</td>
<td>68,694</td>
</tr>
</tbody>
</table>

Sources: IMS DDD; Heron actuals (distributor 867 reports); due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2
SUSTOL®: We continue to expect core SUSTOL business to hold firm and with possibility of modest decline during arbitrage and growth thereafter

- Maintain guidance of $25M–$30M in SUSTOL net sales in 2017
- Permanent J-code granted by CMS; effective January 1, 2018

CINVANTI™ Now Approved

- First and only polysorbate 80-free IV NK₁ approved for the prevention of both acute and delayed CINV
- Product, pricing, and contracting available Jan 3, 2018
- Offers strong strategic and operational fit with existing commercial organization
- Heron will build on the success of SUSTOL to win in a branded CINV market with ~3.6M annual units
Postoperative Pain Program
HTX-011: Proprietary Extended-Release Combination of Bupivacaine + Meloxicam
Market Is Large and Local Anesthetic Use Is Common, but Long-Acting Anesthetics Have Not Fulfilled the Promise

~100M surgeries are performed each year in the US with an estimated ~28M (in 2015) required postoperative pain management with non-OTC pain medications.

Local anaesthetics (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.

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

Sources:
1 DRG claims analysis (2015), DRG Postoperative Pain Pharmacor
2 DRG physician and P&T member interviews (2016; n=106)
*Based on analysis of current postoperative pain management across 40 target procedures (~28M procedures)
Surgeons Expect to Use More Long-Acting Local Anesthetics as Better Options Become Available

**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)
Risk of Chronic Opioid Use After Selected Surgeries

Adjusted Odds Ratio for Chronic Opioid Use

- Total Knee Arthroplasty: 5.1
- Open Cholecystectomy: 3.6
- Simple Mastectomy: 2.6
- Total Hip Arthroplasty: 2.5
- Open Appendectomy: 1.7
- Laparoscopic Cholecystectomy: 1.6
- Cesarean Delivery: 1.3

Based on data from 641,941 opioid-naïve surgical patients compared to 18 million opioid-naïve non-surgical patients (Sun, et al. JAMA Internal Med 2016; 176(9):1286-1293)
In Addition to Potential Addiction, Opioids Increase Healthcare Costs Due to a High Rate of Side Effects

Cost of Opioid-Related Adverse Drug Events\(^1,2\)

<table>
<thead>
<tr>
<th>Moderate to Severe Opioid-Induced ADE</th>
<th>Cost per ADE Events in 2013 $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ileus</td>
<td>$6,141</td>
</tr>
<tr>
<td>Pruritus</td>
<td>$502</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>$1,867</td>
</tr>
<tr>
<td>Respiratory Depression</td>
<td>$1,504</td>
</tr>
<tr>
<td>PONV</td>
<td>$1,225</td>
</tr>
<tr>
<td>Mental Status Change</td>
<td>$2,263</td>
</tr>
</tbody>
</table>

*All ADE costs derived from Oderda 2003 with exception of ileus which is from Simons et al.  
†Calculated from the half-year (January-June) data of the "Inpatient Hospital Services" component of the medical consumer price index in 1999-2013.  

Reducing Pain at the Source Can Eliminate the Need for Opioids and May Decrease the Development of Chronic Pain.

HTX-011 directly blocks transmission of the pain signal, potentially reducing the chance of chronic pain.

Acting on opiate receptors in the brain, opioids can reduce the sensation of pain, but do not block transmission of the pain signals. Occasionally, the affected nerves become hyper-stimulated resulting in chronic pain.
Inflammation Plays a Key Role in Pain Management
(Current local anesthetics do not address this)

- Inflammation produces an acidic environment
- Shifts the balance to ionized form, which is unable to penetrate nerve cell membrane

- 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 Reed, Anesth Prog 53:98–109 2006
Unique Fixed-Dose Combination of Bupivacaine & Meloxicam Delivered Into the Incision Produced Complete Analgesia\(^1\)

Pig Post-Operative Pain Model\(^1\)

- Saline Control
- Liposomal Bupivacaine\(^2\)
- Biochronomer Bupivacaine
- Biochronomer Bupivacaine + Meloxicam 6-Day Release

1. Post-operative pain model in pigs from Castle et al, 2013 EPJ
2. Human dose of bupivacaine liposome with 40% smaller incision

(n=4 pigs in each arm)
>72 Hour Duration of Action Seen as “Ideal”

**Ideal Duration of Efficacy for Long-Acting Local Anesthetic**

- 48 hours: 27%
- 72 hours: 46%
- 4 days: 9%
- 5 days: 4%
- >5 days: 2%
- ≤ 24 hours: 12%

**Minimally Acceptable Duration of Efficacy for Long-Acting Local Anesthetic**

- ≤ 24 hours: 11%
- 48 hours: 44%
- 72 hours: 11%
- >5 days: 2%
- 4 days: 9%

Source: Decision Resources Post-Operative Pain Physician Research Initiative 2014 (N=30 qualitative interviews; N=184 quantitative survey)
HTX-011 Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery

Percentage of Maximal Force (60 gm) Tolerated

- Saline Control
- Liposomal Bupivacaine
- Biochronomer Bupivacaine
- Biochronomer Meloxicam
- HTX-011 (Biochronomer Bupivacaine + Meloxicam with 3-day release)

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

*Supratherapeutic dose of meloxicam administered SQ
Post-operative pain model in pigs from Castle et al, 2013 EPJ

(n=4 pigs in each arm)
HTX-011 Clinical Experience Shows It Has the Potential to Transform Postoperative Pain Control

Phase 2 data has demonstrated:

- Statistically significant reductions in both pain and opioid use lasting up to 72 hours after surgery

- Utility in a broad selection of surgical procedures, including small procedures (bunion), medium size procedures (hernia), and one of the largest incisions (abdominoplasty)

- Synergy between meloxicam and bupivacaine in HTX-011 results in significantly greater analgesia compared to bupivacaine alone

Product attributes of HTX-011 optimized in Phase 2 for Phase 3 efficacy studies:

- Formulation, where the product has shown the versatility to be used in a wide variety of surgical procedures

- Dose, where the lowest highly effective dose has been chosen for Phase 3

- Route of administration, where instillation, a faster, easier and potentially safer route of administration was demonstrated to be equally effective to standard injections
End-of-Phase 2 Meeting Agreements with FDA

• Two Phase 3 adequate and well-controlled efficacy studies and a Phase 3 safety study of approximately 200 subjects in multiple surgical models are adequate to support an NDA for a broad indication for reduction in postoperative pain for 72 hours
  – Primary and key secondary endpoints for Phase 3 studies are acceptable
  – Adjustment of pain intensity data for opioid use by the wWOCF methodology is acceptable
• Phase 3 efficacy studies with bupivacaine as an active control meets FDA Combination Rule
  – One ingredient is intended to enhance effectiveness of principal active component
  – Factorial design study not required
• Size of proposed safety database adequate
• No renal or hepatic impairment studies or drug-drug interaction studies required for NDA
PHASE 3 PROGRAM HAS BEEN INITIATED
Study 301: Phase 3 Bunionectomy
Study Design

Randomization (3:3:2)

HTX-011 60 mg Instillation
N = 150

Bupivacaine 50 mg Injection
N = 150

Saline Placebo Instillation
N = 100

Study 301 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.
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**

<table>
<thead>
<tr>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary: Pain Intensity AUC&lt;sub&gt;0-72&lt;/sub&gt; vs. placebo</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Key Secondary: Pain Intensity AUC&lt;sub&gt;0-72&lt;/sub&gt; vs. bupivacaine</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Key Secondary: Opioid use vs. placebo</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Key Secondary: Opioid-free vs. bupivacaine</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; Key Secondary: Opioid use vs. bupivacaine</td>
</tr>
</tbody>
</table>

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.
HTX-011 STUDY 208:
Phase 2 Bunionectomy

Updated Results With the Phase 3 Dose Analyzed by the FDA Requested Methodology (wWOCF)
(5 Clinical Sites Enrolled Subjects)
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=25)  HTX-011 60 mg (N=52)

Severe Pain

wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data
HTX-011 60 mg Produces 24-Fold Greater Reduction in Pain Compared to Bupivacaine 50 mg Through 72 Hours in Bunionectomy

p-values are from ANOVA using AUC of Pain Intensity with wWOCF for HTX-011 vs. bupivacaine
AUC, area under the curve; LSMD, least squares mean difference
Bunionectomy Study: HTX-011 Significantly Reduces Total Opioid Use vs Bupivacaine and Placebo

Source: Data on File, Heron Therapeutics, Inc.
Bunionectomy Study: HTX-011 Significantly Increases the Proportion of Opioid-Free Subjects vs Placebo

Source: Data on File, Heron Therapeutics, Inc.
# Bunionectomy Study: Drug-Related Treatment-Emergent Adverse Events*

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Pooled HTX-011 (N = 174)</th>
<th>Bupivacaine 50mg (N = 25)</th>
<th>Saline Placebo (N = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Drug-related TEAEs</td>
<td>28.2%</td>
<td>28.0%</td>
<td>24.0%</td>
</tr>
<tr>
<td>Nausea</td>
<td>12.1%</td>
<td>8.0%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Erythema</td>
<td>8.0%</td>
<td>8.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3.4%</td>
<td>4.0%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Hypertransaminasaemia</td>
<td>1.1%</td>
<td>8.0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Source: Data on File, Heron Therapeutics, Inc.
*Adverse events considered at least possibly related with an incidence of >5%
HTX-011 Has Demonstrated Significantly Greater Pain Reduction Than Extended-Release Versions of Bupivacaine or Meloxicam Using the Same Formulation

Study 208

AUC, area under the curve; LSMD, least squares mean difference

p-value from ANOVA, LSMD of area under the curve for HTX-011 vs. HTX-002 or HTX-009
HTX-011 STUDY 202:
Phase 2 Hernia Repair

Updated Results With the Phase 3 Dose Analyzed by the FDA Requested Methodology (wWO CF)
(3 Clinical Sites Enrolled Subjects)
HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Herniorrhaphy

Increasing Pain

Mean ± (SE) Pain Intensity (wWOCF)

Saline Placebo (N=83)  Bupivacaine 75 mg (N=32)  HTX-011 300 mg Instilled (N=16)

AUC0-24
300 mg vs. P: p<0.0001
300 mg vs. B: p=0.0052

AUC0-48
300 mg vs. P: p=0.0005
300 mg vs. B: p=0.0128

AUC0-72
300 mg vs. P: p=0.0045
300 mg vs. B: p=0.0427

wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data
HTX-011 300 mg Produces 4-Fold Greater Reduction in Pain Compared to Bupivacaine 75 mg Through 72 Hours in Hernia Repair

p-values are from ANOVA using AUC of Pain Intensity with wWOCF for HTX-011 vs. bupivacaine AUC, area under the curve; LSMD, least squares mean difference
Herniorrhaphy Study: HTX-011 Significantly Reduces Total Opioid Use vs Placebo

Source: Data on File, Heron Therapeutics, Inc.
Herniorrhaphy Study: HTX-011 Significantly Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo

**Herniorrhaphy Study: Drug-Related Treatment-Emergent Adverse Events**

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>HTX-011 300/400 mg (n = 99)</th>
<th>Bupivacaine 75 mg (n = 32)</th>
<th>Saline Placebo (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Drug-Related TEAEs</td>
<td>30.3%</td>
<td>28.1%</td>
<td>29.4%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>8.1%</td>
<td>3.1%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.1%</td>
<td>0%</td>
<td>9.4%</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>5.1%</td>
<td>6.3%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5.1%</td>
<td>3.1%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3.0%</td>
<td>6.3%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

*Adverse events considered at least possibly related with an incidence of >5%*  
Source: Data on File, Heron Therapeutics, Inc.
HTX-011 STUDY 203:
Phase 2 Abdominoplasty

Updated Results Using wWOCF
(8 Clinical Sites Enrolled Subjects)
HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Abdominoplasty

Increasing Pain

Mean ± (SE) Pain Intensity (wWOCF)

Saline Placebo (N=32)  Bupivacaine 100 mg (N=17)  HTX-011 400 mg (N=25)

Severe Pain

AUC₀-₂₄
400 mg vs. P: p=0.0164
400 mg vs. B: p=0.0985

AUC₀-₄₈
400 mg vs. P: p=0.0087
400 mg vs. B: p=0.0460

AUC₀-₇₂
400 mg vs. P: p=0.0041
400 mg vs. B: p=0.0399

wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data
HTX-011 400 mg Produces 5-Fold Greater Reduction in Pain Compared to Bupivacaine 100 mg Through 72 Hours in Abdominoplasty

p-values are from ANOVA using AUC of Pain Intensity with wWOCF for HTX-011 vs. bupivacaine

AUC, area under the curve; LSMD, least squares mean difference
Abdominoplasty Study: HTX-011 Significantly Reduces Total Opioid Use vs Bupivacaine and Placebo

Source: Data on File, Heron Therapeutics, Inc.
Although Almost All Patients Took Opioids on Day 1, More HTX-011 Patients Were Opioid-Free by Day 3
## Abdominoplasty Study: Drug-Related Treatment-Emergent Adverse Events*

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>HTX-011 400 mg (n = 25)</th>
<th>Bupivacaine 100 mg (n = 17)</th>
<th>Saline Placebo (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Drug-Related TEAEs</td>
<td>44.0%</td>
<td>41.2%</td>
<td>31.3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>20.0%</td>
<td>29.4%</td>
<td>15.6%</td>
</tr>
<tr>
<td>Headache</td>
<td>12.0%</td>
<td>5.9%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8.0%</td>
<td>5.9%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Constipation</td>
<td>4.0%</td>
<td>11.8%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0%</td>
<td>5.9%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

*Adverse events considered at least possibly related with an incidence of >1 subject in any group.

Source: Data on File, Heron Therapeutics, Inc.
HTX-011 SIGNIFICANTLY BETTER THAN EXTENDED-RELEASE BUPIVACAINE (002) AND SHOWS A UNIQUE PK-PD RELATIONSHIP
Pharmacokinetic-Pharmacodynamic (PK-PD) Assessment Bunionectomy Study: 002 ER Bupivacaine 60 mg Was Significantly Better Than Placebo Through 24 hr, but Does Not Demonstrate a PK-PD Relationship

Source: Data on File, Heron Therapeutics, Inc.
PK-PD: Exparel® Bunionectomy Study
Exparel Significantly Better Than Placebo Through 24 hr, but Does Not Demonstrate a PK-PD Relationship

Exparel® (liposomal bupivacaine)

PK-PD: Bunionectomy Study
HTX-011 Significantly Better Than Placebo Through 72 hr
With an Excellent PK-PD Relationship

HTX-011 (bupivacaine + meloxicam)

Source: Data on File, Heron Therapeutics, Inc.
*LOCF method used to account for missing data, with wWOCF adjustment for use of rescue medications
In a Cross-Study Comparison of a Standardized Bunionectomy Model, HTX-011 Demonstrated Superior Pain Reduction vs Two Forms of Extended-Release Bupivacaine

In separate studies, two different formulations of ER bupivacaine produced remarkably similar results.

Sources: Data on File, Heron Therapeutics, Inc., and
On-Going Phase 2b Studies
Phase 2b Total Knee Arthroplasty Study Design

**Cohort 1**
- HTX-011 200 mg Instillation
  - N = 25
- HTX-011 200 mg Instillation + Injection
  - N = 20
- Saline Placebo Injection
  - N = 10
- Bupivacaine 125 mg Injection
  - N = 20

**Cohort 2**
- HTX-011 400 mg Instillation
  - N = 25
- HTX-011 400 mg Instillation + Injection
  - N = 20
- Saline Placebo Injection
  - N = 10
- Bupivacaine 125 mg Injection
  - N = 25

IRC
Phase 2b Nerve Block: Breast Augmentation Study Design

Cohort 1
- HTX-011 60 mg Nerve Block
  - N = 12
- Saline Placebo Nerve Block
  - N = 6
- Bupivacaine 50 mg Nerve Block
  - N = 6

IRC dose decision for Cohort 2

Cohort 2
- HTX-011 120 mg Nerve Block
  - N = 24
- Saline Placebo Nerve Block
  - N = 12
- Bupivacaine 50 mg Nerve Block
  - N = 12

IRC dose decision for Cohort 3

Cohort 3
- HTX-011 240 mg Nerve Block
  - N = 24
- Saline Placebo Nerve Block
  - N = 12
- Bupivacaine 50 mg Nerve Block
  - N = 12

Protocol includes additional optional cohorts to evaluate other doses and administration techniques.
Summary: HTX-011 Is Poised to Fulfill the Promise of a Long-Acting Extended-Release Local Anesthetic

- Large, growing market opportunity
- Differentiated, synergistic mechanism addresses inflammation – a key inhibitor of both generic and long-acting local anesthetics
- Demonstrated superiority vs. generic bupivacaine solution in 3 diverse surgical models
- Consistent 72-hour efficacy
  - Pain reduction
  - Opioid reduction
- Applicable in large and small procedures without admixture with bupivacaine solution – reducing chance of dosing errors and systemic toxicity
- Flexible administration with potential safety advantages
- Potential to address most pressing unmet needs cited by key stakeholders – patients, surgeons, anesthesiologists & formulary decision makers
- Phase 2 data reduced risk for Phase 3 development program and extensive patent protection anticipated through 2035
Financial Summary

Cash, cash equivalents and short-term investments were $74.0 million as of September 30, 2017. Heron also had accounts receivable of $28.9 million, the majority of which it expects to collect in the fourth quarter of 2017 and the first quarter of 2018.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share data)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Net product sales</td>
<td>$ 8,572</td>
<td>$ 20,714</td>
</tr>
<tr>
<td>Operating expenses¹</td>
<td>49,886</td>
<td>153,382</td>
</tr>
<tr>
<td>Other expenses, net</td>
<td>(552)</td>
<td>(2,326)</td>
</tr>
<tr>
<td>Net loss¹</td>
<td>$(41,866)</td>
<td>$(134,994)</td>
</tr>
<tr>
<td>Net loss per share²</td>
<td>$(0.77)</td>
<td>$(2.55)</td>
</tr>
<tr>
<td>Net cash used in operations</td>
<td>$(40,540)</td>
<td>$(123,151)</td>
</tr>
</tbody>
</table>

Condensed Balance Sheet Data (In thousands)

<table>
<thead>
<tr>
<th></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>

¹ Includes $7.5 million and $23.6 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2017, respectively.
² Based on 54.2 million and 52.8 million weighted-average common shares outstanding for the three and nine months ended September 30, 2017, respectively.
## Key Catalysts in Pain & CINV Franchises

<table>
<thead>
<tr>
<th>HTX-011 for Postoperative Pain</th>
<th>CINVANTI™ for CINV</th>
<th>SUSTOL® for CINV</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Top-line results abdominoplasty</td>
<td>✓ NDA submission</td>
<td>2017 net sales guidance: $25M - $30M</td>
</tr>
<tr>
<td>✓ Phase 2 program in nerve block initiated</td>
<td>✓ FDA approval</td>
<td></td>
</tr>
<tr>
<td>✓ Initiated TKA study (local administration)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ End-of-Phase 2 meeting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ Phase 3 program initiated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Top-line Pivotal Phase 3 results 1H 2018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NDA filing 2018</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>