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 full-year 2019 net product sales guidance for the CINV franchise; whether the FDA approves the NDA for HTX-011; the timing of the FDA’s review process for HTX-011; the timing of the commercial launch of HTX-011; the timing of the CHMP’s review process for HTX-011; whether the European Commission authorizes the MAA for HTX-011; the potential market opportunity for CINVANTI, SUSTOL and HTX-011; the timing and results of the studies in the HTX-011 and HTX-034 development programs; the expected future balances of Heron’s cash, cash equivalents and short-term investments; the expected duration over which Heron’s cash, cash equivalents and short-term investments balances will fund its operations; 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.
**Heron Pipeline**

We are currently developing and commercializing pharmaceutical products for patients suffering from cancer or postoperative pain:

<table>
<thead>
<tr>
<th>Product</th>
<th>Stage</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSTOL®</strong>&lt;br&gt;(granisetron) extended-release injection</td>
<td>CLINICAL</td>
<td>US FDA Approved for CINV Prevention&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>CINVANTI®</strong>&lt;br&gt;(aprepitant) injectable emulsion</td>
<td>CLINICAL</td>
<td>US FDA Approved for CINV Prevention&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>HTX-011</strong></td>
<td>PRECLINICAL</td>
<td>Under Investigation for Postoperative Pain via Local Application</td>
</tr>
<tr>
<td><strong>HTX-034</strong></td>
<td>PRECLINICAL</td>
<td>Under Investigation for Postoperative Pain via Local Application</td>
</tr>
</tbody>
</table>

* CINV: Chemotherapy-induced nausea and vomiting. **SUSTOL®** (granisetron) extended-release injection 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. **CINVANTI®** (aprepitant) injectable emulsion, in combination with other antiemetic agents, is indicated in adults 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** has not been studied for treatment of established nausea and vomiting.

- Fast Track and Breakthrough Therapy designations granted
- NDA received Priority Review; CRL received 30 Apr 2019
- The CRL identified issues relating to CMC and non-clinical
- No issues related to clinical efficacy or safety were noted.
- Revised NDA submitted 26 Sep 2019 addressing CRL
- EU MAA filing by Centralised Procedure in March 2019

**HTX-011 and HTX-034** are investigational new drugs and are not approved by the FDA or other regulatory authority.
As many as 6.5% of patients who take opioids to manage pain after surgery may become persistent opioid users. That equals about 2.9 MILLION PEOPLE.

90% of patients undergoing a surgical procedure are prescribed opioids for pain management.

2.6 million persistent opioid users, approximately ~500,000 will become addicted to opioids.

Of these 2.6 million persistent opioid users, approximately ~500,000 will become addicted to opioids.

90% of patients undergoing a surgical procedure are prescribed opioids for pain management.

In addition, opioid discharge prescriptions filled by recovering surgical patients result in more than 1 billion unused pills.

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.

More than $13 billion of the annual healthcare costs associated with addiction can be attributed to postoperative pain management.
Clinical Studies in High-Value Procedures Have Demonstrated Significantly Better Pain Reduction Than Bupivacaine

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Annual Volume ('000s, US, 2015)</th>
<th>Overall % Local Anesthetic Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Procedures</td>
<td>Inpatient</td>
</tr>
<tr>
<td>Knee arthroplasty</td>
<td>1,043</td>
<td>977</td>
</tr>
<tr>
<td>Hip arthroplasty</td>
<td>599</td>
<td>579</td>
</tr>
<tr>
<td>Shoulder arthroplasty</td>
<td>161</td>
<td>149</td>
</tr>
<tr>
<td>Rotator cuff repair</td>
<td>319</td>
<td>6</td>
</tr>
<tr>
<td>Spine procedures</td>
<td>1,459*</td>
<td>928</td>
</tr>
<tr>
<td>Bunionectomy &amp; Phalangectomy</td>
<td>597</td>
<td>42</td>
</tr>
<tr>
<td>Hernia repair</td>
<td>1,064</td>
<td>212</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>987</td>
<td>323</td>
</tr>
<tr>
<td>Colon and small bowel resection</td>
<td>476</td>
<td>457</td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>130</td>
<td>23</td>
</tr>
<tr>
<td>Mammoplasty</td>
<td>292</td>
<td>32</td>
</tr>
<tr>
<td>OB/GYN</td>
<td>1,168</td>
<td>1158</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Completed studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ortho Surgery</td>
<td>On-going studies</td>
</tr>
<tr>
<td>General Surgery</td>
<td></td>
</tr>
<tr>
<td>Plastic Surgery</td>
<td></td>
</tr>
</tbody>
</table>

* Includes Laminectomy, Foraminotomy, Discectomy, Fusion
** Non Medicare includes Commercial, Medicaid and Cash

Sources: DRG Claims Data 2017/ update 2018
The Link Group ATU survey May 2019
EPOCH 1: Bunionectomy Results (Study 301)

EPOCH 1 Follow-on: Opioid Elimination Study in Bunionectomy
EPOCH 1 Bunionectomy: HTX-011 Provided Superior Pain Reduction Through 72-hours

- Using Numeric Rating Scale (NRS) with window worst observation carried forward (wWOCF)

<table>
<thead>
<tr>
<th>Pain Intensity Score* (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUC$_{0-24}$</strong></td>
</tr>
<tr>
<td>HTX-011 vs P: $p &lt; 0.0001$</td>
</tr>
<tr>
<td>HTX-011 vs B: $p &lt; 0.0001$</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>AUC$_{24-72}$</strong></td>
</tr>
<tr>
<td>HTX-011 vs P: $p &lt; 0.0001$</td>
</tr>
<tr>
<td>HTX-011 vs B: $p = 0.0072$</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>AUC$_{0-72}$</strong></td>
</tr>
<tr>
<td>HTX-011 vs P: $p &lt; 0.0001$</td>
</tr>
<tr>
<td>HTX-011 vs B: $p = 0.0002$</td>
</tr>
</tbody>
</table>

HTX-011 60 mg (N=157)
Saline Placebo (N=100)
Bupivacaine HCl 50 mg (N=155)

HTX-011 is an investigational new drug and not approved by the FDA

* Using Numeric Rating Scale (NRS) with window worst observation carried forward (wWOCF)
Epoch 1 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTX-011 60 mg</td>
<td>157</td>
</tr>
<tr>
<td>Saline Placebo</td>
<td>100</td>
</tr>
<tr>
<td>Bupivacaine HCl 50 mg</td>
<td>155</td>
</tr>
</tbody>
</table>

* Using Numeric Rating Scale (NRS) with window worst observation carried forward (wWOCF)

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 Significantly Reduced Total Opioid Consumption

1. Based on morphine milligram equivalents

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 Significantly Increased Proportion of Opioid-Free Patients

EPOCH 1 (Bunionectomy) vs. EPOCH 1 Follow-on:

- **Saline Placebo**:
  - N=100
  - 2.0% opioid-free through 72 hours

- **Bupivacaine HCl 50 mg**:
  - N=155
  - 11.0% opioid-free through 72 hours

- **HTX-011 60 mg**:
  - N=157
  - 28.7% opioid-free through 72 hours

**HTX-011** significantly increased the proportion of opioid-free patients compared to controls with p < 0.0001 and compared to follow-up with p = 0.0001.

**EPOCH 1 Follow-on**:

- **HTX-011 ≤ 60 mg + OTC**
  - N=31
  - 77.4% remained opioid-free through Day 28

**HTX-011** is an investigational new drug and not approved by the FDA.

**OTC**: Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h
EPOCH 2: Herniorrhaphy Results (Study 302)

EPOCH 2 Follow-on: Opioid Elimination Study in Herniorrhaphy
EPOCH 2 Herniorrhaphy: HTX-011 Provided Superior Pain Reduction Through 72-hours

Mean Pain Intensity Score (SE)

Saline Placebo (N=82)

Bupivacaine HCl 75 mg (N=172)

HTX-011 300 mg (N=164)

AUC<sub>0-24</sub>
- HTX-011 vs P: p < 0.0001
- HTX-011 vs B: p < 0.0001

AUC<sub>24-72</sub>
- HTX-011 vs P: p = 0.0264
- HTX-011 vs B: p = 0.0007

AUC<sub>0-72</sub>
- HTX-011 vs P: p = 0.0004
- HTX-011 vs B: p < 0.0001

Severe pain (≥ 7)

HTX-011 is an investigational new drug and not approved by the FDA
Epoch 2 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours

Mean Pain Intensity Score (SE)

Saline Placebo (N=82)

Bupivacaine HCl 75 mg (N=172)

HTX-011 300 mg (N=164)

EPOCH 2 Follow-on: HTX-011 300 mg + OTC (N=33)

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 is an investigational new drug and not approved by the FDA

Source: Figure 14.2.7
HTX-011 Significantly Reduced Total Opioid Consumption

EPOCH 2 (Herniorrhaphy)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Opioid Consumption (Mean MME ± SE) 0-72 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline Placebo</td>
<td>82</td>
<td>17.5</td>
</tr>
<tr>
<td>Bupivacaine HCl 75 mg</td>
<td>172</td>
<td>14.5</td>
</tr>
<tr>
<td>HTX-011 300 mg</td>
<td>164</td>
<td>10.9</td>
</tr>
</tbody>
</table>

Opioid Consumption (Mean MME ± SE) 0-72 Hours

- Saline Placebo N=82
- Bupivacaine HCl 75 mg N=172
- HTX-011 300 mg N=164

p = 0.0240
p < 0.0001

EPOCH 2 Follow-on

HTX-011 300 mg + OTC N=33

0.6

1. Based on morphine milligram equivalents

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 Significantly Increased Proportion of Opioid-Free Patients

EPOCH 2 (Herniorrhaphy)

- Saline Placebo: 22.0% Opioid-free
- Bupivacaine HCl 75 mg: 40.1% Opioid-free
- HTX-011 300 mg: 51.2% Opioid-free

EPOCH 2 Follow-on

- HTX-011 300 mg + OTC: 90.9% Opioid-free

p = 0.0486
p < 0.0001

93% remained opioid-free through Day 28

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 is an investigational new drug and not approved by the FDA
HOPE-1: Real World Evidence of Opioid-Free Recovery Post Inguinal Herniorrhaphy with HTX-011 + OTC Analgesics
HOPE-1: Near Total Opioid-Free Recovery with HTX-011 + OTC

- Complete Opioid-Free Recovery: 95%
- Received an Opioid Predischarge: 5%
- Received an Opioid Prescription: 9% (10 pills)
- Took an Opioid Post Discharge: 3% (all patients had received predischarge opioid)
- Call Backs if Discharged Without an Opioid Prescription: 0%
- Satisfied, Very Satisfied, Extremely Satisfied With Medication: 93%

N=93 in initial pilot program

HTX-011 is an investigational new drug and not approved by the FDA
# Potential Reduction of Discharge Opioids Based on HOPE-1

Currently, following inguinal hernia repair an average of 30 opioid pills are prescribed per patient of which an average of 9 pills are consumed.\(^1\)

## Potential Impact if HOPE-1 Extrapolated to the ~800,000 Inguinal Hernia Surgeries Annually

<table>
<thead>
<tr>
<th>Pills Prescribed</th>
<th>Pills Consumed</th>
<th>Pills Leftover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Practice Estimates</td>
<td>24,000,000</td>
<td>7,200,000</td>
</tr>
<tr>
<td>HOPE-1 Estimates</td>
<td>774,194</td>
<td>283,871</td>
</tr>
<tr>
<td>Potential Reduction with HTX-011 + OTC</td>
<td>23,225,806↓</td>
<td>6,916,129↓</td>
</tr>
</tbody>
</table>

1. Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) November 15, 2018
2. Decisions Resources Group claims data 2017

HTX-011 is an investigational new drug and not approved by the FDA.
Phase 2b Total Knee Arthroplasty (TKA) (Study 209)

Study 209 Follow-on: HTX-011 + MMA in TKA* (Study 306)

*The multimodal analgesic (MMA) regimen used in this study was identical to the PILLAR Study of liposomal bupivacaine
Study 209 TKA: Results Hierarchy

HTX-011 via instillation achieved primary and key secondary endpoints for reduction in pain intensity scores:

- **AUC\(_{0-48}\) HTX-011 400 mg + Ropivacaine vs. Placebo**: p < 0.0001
- **AUC\(_{0-48}\) HTX-011 400 mg vs. Placebo**: p = 0.0002
- **AUC\(_{0-72}\) HTX-011 400 mg+ Ropivacaine vs. Placebo**: p < 0.0001
- **AUC\(_{0-72}\) HTX-011 400 mg vs. Placebo**: p = 0.0004

HTX-011 is an investigational new drug and not approved by the FDA
Study 209 TKA: HTX-011 Significantly Superior to Both Placebo and Bupivacaine Through 72 Hours Without Adjusting for Opioid Use

Notes:
Pain intensity collected using Numeric Rating Scale (NRS)
LOCF for missing data and no adjustment for use of opioid rescue medication

HTX-011 is an investigational new drug and not approved by the FDA
Study 209 Follow-on: HTX-011 + Generic Analgesics* Kept Pain in the Mild Range Through 72 Hours With 68% Less Opioid Than Bupivacaine

* Patients received oral acetaminophen 975 to 1000 mg every 8 hours (maximum 3000 mg/d) and oral celecoxib 200 mg every 12 hours until discharge. Mont doi: 10.1016/j.arth.2017.07.024

HTX-011 is an investigational new drug and not approved by the FDA.
# Cross-Study Comparison of Day 1 in Study 306 and Exparel PILLAR Study (Dysart 2019)

<table>
<thead>
<tr>
<th>Cross-Study Comparison of 0 – 24 Hour Results in TKA Using Pillar-Based MMA and the Same Analysis¹</th>
<th>Study 306 HTX-011 (N=51)</th>
<th>PILLAR Study</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC0-24 VAS Pain²</td>
<td>59.5</td>
<td>Exparel + Bupivacaine¹ (N = 70)</td>
<td>98.5</td>
</tr>
<tr>
<td>Opioid-Free</td>
<td>21.6%</td>
<td>17.1%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Mean Opioid Consumption MME (SD)</td>
<td>10.6 (9.2)</td>
<td>45.5 (35.01)</td>
<td>56.8 (38.26)</td>
</tr>
<tr>
<td>Log-transformed Geometric Mean Opioid Consumption MME</td>
<td>0.54</td>
<td>3.5</td>
<td>38.5</td>
</tr>
<tr>
<td>Discharge Ready in 12 hours Based MPADSS &gt; 9</td>
<td>60.8%</td>
<td>42.9%</td>
<td>27.5%</td>
</tr>
</tbody>
</table>

2. Assumes LOCF as publication does not describe any correction for opioid use

## Disclaimer
- This is a cross-study comparison of Study 306 to the PILLAR Study of Exparel plus bupivacaine; these comparisons do not imply a clinical benefit of HTX-011 over Exparel

HTX-011 is an investigational new drug and not approved by the FDA
# Cross-Study Comparison of 48 Hour Results From Study 306 (Preliminary Results) and Exparel Pillar Study (Mont 2017)

<table>
<thead>
<tr>
<th>Comparison of 48 Hr Results in TKA Using Pillar-Based MMA and the Same Analysis&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Study 306 HTX-011 (N=51)</th>
<th>PILLAR Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean AUC&lt;sub&gt;12-48&lt;/sub&gt; VAS Pain</td>
<td>143.2</td>
<td>Exparel + Bupivacaine&lt;sup&gt;1&lt;/sup&gt; (N = 70)</td>
</tr>
<tr>
<td>Opioid-Free</td>
<td>11.8%</td>
<td>10%</td>
</tr>
<tr>
<td>Mean Opioid Consumption (MME)</td>
<td>19.6 (Median=16.7)</td>
<td>Not Shown</td>
</tr>
<tr>
<td>Log-transformed Geometric Mean Opioid Consumption MME</td>
<td>3.0</td>
<td>18.7</td>
</tr>
<tr>
<td>≤ 20 MME @ 48 hr</td>
<td>56.9%</td>
<td>18.6%</td>
</tr>
<tr>
<td>&gt; 20 and ≤ 220 MME @ 48 hr</td>
<td>43.1%</td>
<td>78.6%</td>
</tr>
<tr>
<td>&gt; 220 MME @ 48 hr</td>
<td>0</td>
<td>2.9%</td>
</tr>
<tr>
<td>DID NOT Receive a Discharge Prescription for Opioids</td>
<td>74.5%</td>
<td>Not Shown</td>
</tr>
</tbody>
</table>

---

**Disclaimer**

- This is a cross-study comparison of Study 306 to the PILLAR Study of Exparel plus bupivacaine; these comparisons do not imply a clinical benefit of HTX-011 over Exparel

---

HTX-011 is an investigational new drug and not approved by the FDA

---

Potential Reduction of Discharge Opioids Based on Study 306

- Currently, following TKA an average of 90 opioid pills are prescribed per patient at the time of discharge, with an additional 4 refills over the next year\(^1\)

<table>
<thead>
<tr>
<th>Potential Impact on Discharge Opioids of Study 306 Extrapolated to the 1,043,000 TKA Surgeries Annually(^2)</th>
<th>Pills Prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Practice Estimates With Initial Rx</td>
<td>93,870.000</td>
</tr>
<tr>
<td>Study 306 Results (25.5% only)</td>
<td>23,936,850</td>
</tr>
<tr>
<td>Potential Reduction with HTX-011 + MMA</td>
<td><strong>69,933,150(\downarrow)</strong></td>
</tr>
</tbody>
</table>

1. Truven Database – Commercial patients
2. Decisions Resources Group claims data 2018;

HTX-011 is an investigational new drug and not approved by the FDA
Safety Summary

HTX-011 was generally well tolerated across all Phase 2 and Phase 3 studies with no clinically meaningful differences from placebo and bupivacaine in:

• Overall adverse events
• The incidence of serious adverse events
• Premature discontinuations due to adverse events
• Potential local anesthetic systemic toxicity (LAST) adverse events
• Potential wound healing related adverse events
• No deaths on HTX-011 (one on bupivacaine)
The Commercialization of HTX-011

Advancing Pain Management

HTX-011 is an investigational new drug and not approved by the FDA
Established Platform With Experienced Teams in Place

We are prepared for the launch of HTX-011. Our critical teams are already in place, with extensive experience in successful hospital launches.

- Strong KOL relationships
- Successful hospital and pain management launch experience
- IDN/hospital/ASC expertise and relationships
- Reimbursement infrastructure in place
- GPO contracts in place*
- Full Line Wholesaler agreements and 3PL in place*
- Safety monitoring structure in place
- Proven compliant execution
- Robust systems in place and pressure tested for blockbuster launch
Until Generic Emend, CINVANTI Market Share Rose Steadily Across All Segments

Data Source(s): 867 through 7/6/19, DDD through 6/21/19, Chargeback Report 7/3/19
Key CINVANTI Learnings to Support HTX-011 Launch

**HTX-011**
- MOA, First and Only DALA
- Broad Access Pricing
- 3-year pass through (C-Code)
- Top 200 IDNs, 965 Hospitals and 340B
- Selected GPOs / IDNs
- Ambulatory Surgical Centers
- Exparel, On-Q
- Leverage ASCs and Outpatient for access and confidence
- Reduce / Eliminate Risk with ASCs
- Hospital driven / Multiple Surgical lines

**KEY DRIVERS**
- DIFFERENTIATED PRODUCT
  - WAC
  - 340B
- FOCUS
- CONTRACTING
- ACCELERATE SALES
- COMPETITION
- REIMBURSEMENT
- VALUE ADDED SERVICES
- IMPLEMENTATION

**CINVANTI**
- First and only polysorbate 80-free NK1 RA
- Lower Acquisition Cost (-$40)
- 3-year pass through (C-Code)
- Top 200 IDNs, 340B
- Selected GPOs / IDNs
- Community Oncology
- Merck
- Leverage Community to create confidence
- Reduce / Eliminate Risk community setting
- IDN driven pull through at affiliated hospitals
The Market is Large and Waiting for an Effective Non-opioid Solution

Theoretical and Target Market

~29M Annual US Surgical Procedures Requiring Postoperative Pain Management

* Initial Targets
  Higher volume procedures across 4 major specialties
  - ~5.9M Orthopedic
  - ~4.2M General Surgery
  - ~2.6M OB/GYN
  - ~0.8M Plastic Surgery

* Secondary Targets
  Other procedures requiring postoperative pain management but not amongst initial targets for one or more of these reasons:
  - Non-core specialties
  - Relatively lower pain scores
  - Lower volume per procedure

~13.5M procedures

~15.5M procedures

Local Anesthetic Route of Delivery

Any Local, 85%

NB Only, 15%

The Largest Opportunity to Drive Value and Create Change

* Local Anesthetics are used in ~70% of procedures

NB: Nerve Block
HTX-011 is focused on the largest market opportunity

Local Anesthetic Route of Delivery

- All Local, 85%
- NB, 15%

THE LARGEST OPPORTUNITY TO DRIVE VALUE AND CREATE CHANGE

Local Anesthetic Volume Share

- Bupivacaine
- Lidocaine
- Exparel
- Others
- Ropivacaine NB
- Bupivacaine NB

HTX-011 is focused on the largest market opportunity

All Local, 85%

NB, 15%

53%

15%

14%

10%

4%

4%

Physicians indicated a raw preference share of 56% for HTX-011 across the covered procedures.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preference Share (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Arthroplasty</td>
<td>67%</td>
</tr>
<tr>
<td>Hernia Repair - Open</td>
<td>67%</td>
</tr>
<tr>
<td>Hernia Repair - Laparoscopic</td>
<td>67%</td>
</tr>
<tr>
<td>Roux-en-Y Gastric Bypass</td>
<td>63%</td>
</tr>
<tr>
<td>Hysterectomy - Laparoscopic</td>
<td>62%</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>61%</td>
</tr>
<tr>
<td>C-Section</td>
<td>61%</td>
</tr>
<tr>
<td>Hysterectomy - Open</td>
<td>58%</td>
</tr>
<tr>
<td>Laminectomy, Foraminotomy, Discetomy</td>
<td>57%</td>
</tr>
<tr>
<td>Spinal Fusion</td>
<td>56%</td>
</tr>
<tr>
<td>Hip Arthroplasty</td>
<td>55%</td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>55%</td>
</tr>
<tr>
<td>Cholecystectomy - Laparoscopic</td>
<td>55%</td>
</tr>
<tr>
<td>Rotator Cuff Repair</td>
<td>54%</td>
</tr>
<tr>
<td>Fracture - Hip</td>
<td>53%</td>
</tr>
<tr>
<td>Fracture - Leg</td>
<td>53%</td>
</tr>
<tr>
<td>Fracture - Pelvis*</td>
<td>53%</td>
</tr>
<tr>
<td>Appendectomy - Laparoscopic</td>
<td>53%</td>
</tr>
<tr>
<td>Colon &amp; Small Bowel Resection - Laparoscopic</td>
<td>52%</td>
</tr>
<tr>
<td>Bunionectomy &amp; Phalangectomy</td>
<td>51%</td>
</tr>
<tr>
<td>Mammooplasty</td>
<td>50%</td>
</tr>
<tr>
<td>Colon &amp; Small Bowel Resection - Open</td>
<td>47%</td>
</tr>
<tr>
<td>Fracture - Arm</td>
<td>37%</td>
</tr>
<tr>
<td>Fracture - Ankle</td>
<td>37%</td>
</tr>
<tr>
<td>Fracture - Hand</td>
<td>37%</td>
</tr>
<tr>
<td>Fracture - Foot*</td>
<td>37%</td>
</tr>
<tr>
<td>Rhinoplasty</td>
<td>36%</td>
</tr>
<tr>
<td>Carpal Tunnel Release</td>
<td>20%</td>
</tr>
</tbody>
</table>

Reference: DRG Postoperative Pain Quantitative Research (Nov 2018) - n = 290 physicians; *Less than 100K procedures at peak

- Raw preference share for HTX-011 from physicians: 56%
- The top procedures where physicians expected to use HTX-011 were knee arthroplasty and hernia repair
- Several procedures saw higher raw preference shares than prior market research, notably knee & hip arthroplasty, C-section, laparoscopic hysterectomy and spine procedures.
HTX-011 Enjoyed a Physician Preference Share of 44%

Adjusted Physician Preference Share Distribution

- **Other "caines"**
  (e.g. lidocaine, ropivacaine, generic combo, etc.)
  - Current Therapy: 25%
  - Future Therapy: 14%
  - Decrease: 44%

- **Bupivacaine HCl**
  - Current Therapy: 64%
  - Future Therapy: 6%
  - Decrease: 44%

- **Exparel**
  - Current Therapy: 44%
  - Future Therapy: 6%
  - Decrease: 45%

- **HTX-011**
  - Current Therapy: 11%
  - Future Therapy: 44%
  - Increase: 33%

- **Future Therapy (Applying HTX-011 preference share)**

- HTX-011 is likely to initially convert share from Exparel, as well as the rest of the local anesthetics (bupivacaine & other “caines”)
- There is an additional opportunity to convert physicians not using local anesthetics; physicians indicated a willingness to use HTX-011 in ~30% of procedures where they are currently not using local anesthetics

Current therapy based on Claims data from 2017 for Exparel, other agents are based on 2018 Physician Survey
Data from analysis of physician static survey & conjoint - Sample includes n = 330 physicians
Pharmacy Directors Surveyed Prefer HTX-011 to Exparel®

**Impact of HTX-011 Launch on Exparel Formulary Status**
- 43% of pharmacy directors indicate that Exparel status would stay the same.
- 33% of pharmacy directors indicate that Exparel formulary status/purchasing would be made more restrictive.
- 22% of pharmacy directors indicate that Exparel would be removed.

**Formulary Status of Exparel vs. Expected HTX-011 Status**
- HTX-011 (Predicted): 22% Not on Formulary, 56% On Formulary, With Restrictions, 12% On Formulary, No Restrictions.
- EXPAREL (Stated): 44% Not on Formulary, 44% On Formulary, With Restrictions, 12% On Formulary, No Restrictions.

**Most pharmacy directors indicate HTX-011 would displace Exparel on formulary**
- Over 50% of pharmacy directors report that if HTX-011 became available on their institution’s formulary, Exparel would be subject to greater restrictions or would be entirely removed from formulary.
- For institution’s with less formulary consolidation, Exparel may continue to be stocked to accommodate a small segment of patients not using HTX-011.

“We can encourage use of [HTX-011] by making use of standing order sets and our EMR system, so if we continued to carry Exparel, we would make it restricted to only patients contraindicated to Product X.”
- Pharmacy Director

**Reference:** DRG Pharmacy Director Survey (2018): Q27. What would happen to EXPAREL if Product X was approved on formulary at your institution?
HTX-011 has Potential Strategic Advantages Across Each Setting of Care

Clearly differentiated strategy supported by building advocacy with pharmacy, surgeons, and anesthesiologists

13.5 MILLION INITIAL TARGET PROCEDURES

Hospitals account for 91%, including top 200 IDNs (12.3M procedures)

- 52% Hospital Inpatient (7M procedures)
  - Part of DRG payment
  - Multiple SKUs - lower average cost
  - ~50% connected 340B hospitals

- 39% Hospital Outpatient (5.3M procedures)
  - 3-year pass through (C-Code)
  - 340B opportunity
  - High value IDN and procedure focus

Ambulatory surgical centers account for 8% (1.1M procedures)

- 8% Ambulatory Surgical Centers (ASCs) (1.1M procedures)
  - ASP +6%
  - Lower access barriers
  - Targeted facilities
  - Connected to top IDNs
  - Targeted high value procedures

47% of the opportunity lends itself to favorable reimbursement and access

The remaining 1% of procedures are performed at private physician practices
340B Hospital Summary

• ~2258 hospitals (excluding children’s & psych)
  • Perform 8.4M outpatient surgeries
  • 4.4M inpatient surgeries/year

• Manufacturers required to provide 23.1% discount off ASP/WAC
• Discount does not impact ASP or best price calculations
• Products used in the OR that are considered part of the surgical package are not reimbursed, unless they have pass-through status
• Approximately 3 months after approval, HTX-011 will receive a C-Code providing pass-through status

340B Drug Reimbursement for Postoperative Pain

<table>
<thead>
<tr>
<th>With C-Code</th>
<th>Without C-Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP + 6%</td>
<td>Bundled Payment – No Direct Reimbursement</td>
</tr>
</tbody>
</table>
# 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>2,292,000</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>Top 4 EU Total</td>
<td>56,609,000</td>
<td>17,560,000</td>
<td>9,650,000</td>
<td>7,910,000</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>2,668,000</td>
<td>3,932,000</td>
</tr>
</tbody>
</table>
Heron is Well Positioned to Execute a Blockbuster Launch for HTX-011

- Proven track record with hospital launch success
- Existing robust platform and structure to support launch
- Significant unmet need and market opportunity
- Highly focused launch strategy to accelerate sales
- Unprecedented value proposition

HTX-011 is an investigational new drug and not approved by the FDA.
CINV Commercial Products
CINV Portfolio Continues to Grow With Over $177M Since Inception

CINV portfolio net sales by quarter

<table>
<thead>
<tr>
<th>Quarter</th>
<th>CINVANTI</th>
<th>SUSTOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2016</td>
<td>$1.3</td>
<td>-</td>
</tr>
<tr>
<td>Q1 2017</td>
<td>$3.6</td>
<td>$3.6</td>
</tr>
<tr>
<td>Q2 2017</td>
<td>$8.5</td>
<td>$8.6</td>
</tr>
<tr>
<td>Q3 2017</td>
<td>$8.6</td>
<td>$10.1</td>
</tr>
<tr>
<td>Q4 2017</td>
<td>$11.6</td>
<td>$5.2</td>
</tr>
<tr>
<td>Q1 2018</td>
<td>$11.2</td>
<td>$6.1</td>
</tr>
<tr>
<td>Q2 2018</td>
<td>$17.3</td>
<td>$16.4</td>
</tr>
<tr>
<td>Q3 2018</td>
<td>$19.8</td>
<td>$3.4</td>
</tr>
<tr>
<td>Q4 2018</td>
<td>$28.8</td>
<td>$5.4</td>
</tr>
<tr>
<td>Q1 2019</td>
<td>$31.6</td>
<td>$3.6</td>
</tr>
<tr>
<td>Q2 2019</td>
<td>$33.2</td>
<td>$3.5</td>
</tr>
</tbody>
</table>
After 6 weeks - CINVANTI Continues To Hold Share
Generic Fosaprepitant Cannibalizing IV EMEND

CINVANTI is the Market Leader

Source: IMS DDD 10.18.19
Strategy to Preserve CINVANTI Through Generic Arbitrage

• Leverage favorable 340B pass through status, ASP+ 6% through 2020

• IV push sNDA approved further differentiating CINVANTI from Emend and generics

• Long-term contracting

• CINVANTI has become an established brand across both clinics and hospital capturing 40% of the market in Q2 2019
ALOXI/Palonosetron Arbitrage Lasted Much Longer Than Projected, Resulting in an Accelerated Decline in Sustol ASP

- Even with multiple generics on the market, the price of palonosetron did not drop as quickly as in past arbitrage periods.

- Slow decline in prices resulted in a very long arbitrage, which also resulted in an accelerated decline in the Sustol ASP.

- The only way to rebuild value in the brand is to implement an innovative strategy:
  - Starting October 1, all discounting of Sustol was discontinued, which will result in lower sales.
  - In approximately 5 quarters the ASP of Sustol will reset to approximately the WAC.
  - Sustol will be re-launched with enhanced value for practices and Heron.
2019 CINV Franchise Outlook

**SUSTOL®**: To recover from the protracted palonosetron arbitrage, Heron has implemented an innovative strategy to refresh the ASP
- This will result in greatly reduced sales for approximately 5 quarters, followed by a significant rebound in units and revenue

**CINVANTI®**
- Cinvanti continues to have the best overall profile compared to the other available NK₁ antagonists and is completely differentiated from generic fosaprepitant with the 2-min IV Push administration
- CINVANTI (aprepitant) injectable emulsion received unique J-Code J0185 effective January 1, 2019, so generic pricing does not effect Cinvanti reimbursement
- Generic fosaprepitant IV entered the market in September 2019
  - Due to significant sales in 340b hospitals, IV push label and other factors, we do not expect this arbitrage to have the same magnitude as the Aloxi arbitrage
  - Based on early price reductions within weeks of the first generic entry, the duration of the arbitrage should also be shorter than with Aloxi

**CINV Franchise**
- **2019 guidance: $115M - $120M**
**Financial Summary**

Heron expects to end 2019 with more than $190 million in cash, cash equivalents and short-term investments.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Net product sales</td>
<td>$ 36,659</td>
<td>$ 68,261</td>
</tr>
<tr>
<td>Operating expenses¹</td>
<td>88,438</td>
<td>184,740</td>
</tr>
<tr>
<td>Other income, net</td>
<td>1,557</td>
<td>3,245</td>
</tr>
<tr>
<td>Net loss¹</td>
<td>$(50,222)</td>
<td>$(113,234)</td>
</tr>
<tr>
<td>Net loss per share²</td>
<td>$(0.63)</td>
<td>$(1.43)</td>
</tr>
<tr>
<td>Net cash used in operations</td>
<td>$(23,108)</td>
<td>$(72,132)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condensed Balance Sheet Data (In thousands)</th>
<th>June 30, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents and short-term investments</td>
<td>$ 276,005</td>
</tr>
<tr>
<td>Accounts receivable, net</td>
<td>$ 66,821</td>
</tr>
<tr>
<td>Total assets</td>
<td>$ 411,666</td>
</tr>
<tr>
<td>Total stockholders’ equity</td>
<td>$ 305,359</td>
</tr>
</tbody>
</table>

Common shares outstanding at June 30, 2019 totaled 79.8 million.

¹ Includes $12.7 million and $30.6 million of non-cash, stock-based compensation expense for the three and six months ended June 30, 2019, respectively.

² Based on 79.5 million and 79.0 million weighted-average common shares outstanding for the three and six months ended June 30, 2019, respectively.
## Key Catalysts in Pain Management & CINV Franchises

<table>
<thead>
<tr>
<th>HTX-011 &amp; HTX-034 for Postoperative Pain</th>
<th>CINVANTI® and SUSTOL® for CINV</th>
</tr>
</thead>
</table>
| • CRL received 30 April 2019 identified issues relating to CMC and non-clinical  
  ➢ No issues related to clinical efficacy or safety were noted  
  ➢ Revised NDA submitted 26 September 2019 addressing all the issues raised in the CRL – expect 6 month review | • 2019 net sales guidance for CINV franchise: $115M - $120M |
| • HOPE Project launched across the US |  |
| • Publication of Phase 3 and Phase 2b studies  
  ✓ Phase 3 studies published in peer-reviewed journals  
  ➢ EPOCH 2: Hernia. doi: 10.1007/s10029-019-02023-6 |  |
| • Phase 2 with HTX-034 initiated in late 2019 |  |

HTX-011 & HTX-034 are investigational new drugs and not approved by the FDA