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 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>CINV*</th>
<th>SUSTOL® (granisetron) extended-release injection</th>
<th>US FDA Approved for CINV Prevention*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fast Track and Breakthrough Therapy designations granted</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NDA received Priority Review; CRL received 30 Apr 2019</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The CRL identified issues relating to CMC and non-clinical</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No issues related to clinical efficacy or safety were noted.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EU MAA filing by Centralised Procedure in 1H2019</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CINVANTI® (aprepitant) injectable emulsion</th>
<th>US FDA Approved for CINV Prevention*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2-minute IV Push Approved 26 Feb 2019</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PAIN MANAGEMENT</th>
<th>HTX-011</th>
<th>Under Investigation for Postoperative Pain via Local Application</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>PAIN MANAGEMENT</th>
<th>HTX-034</th>
<th>Under Investigation for Postoperative Pain via Local Application</th>
</tr>
</thead>
</table>

HTX-011 and HTX-034 are an investigational new drugs and are not approved by the FDA or other regulatory authority.
HTX-011 NDA for Postoperative Pain Management
Received Complete Response Letter 30 April 2019

• FDA granted Priority Review to HTX-011 NDA
• CRL was received 30 April 2019
  – The CRL identified issues relating to CMC and non-clinical
  – No issues related to clinical efficacy or safety were noted
• Heron plans to provide responses to the CRL as quickly as feasible with a request for a Type A meeting with the FDA
  – Once agreement is reached on our responses, we will refile the NDA
  – HTX-011 maintains its Fast Track and Breakthrough Therapy designations
Postoperative Pain and its Impact on the Opioid Crisis
As many as 6.5% of patients who take opioids to manage pain after surgery may become persistent opioid users.¹ That equals about 2.9 MILLION PEOPLE.¹

Of these 2.6 million persistent opioid users, approximately ~500,000 will become addicted to opioids.³

In addition, opioid discharge prescriptions filled by recovering surgical patients result in more than 1 billion unused pills.⁴,⁵

70% of all these opioid tablets go unused.²

90% of these pills remain inside the home in unsecured locations.⁶

32% of all opioid addicts report first opioid exposure through leftover pills.⁷

More than $13 billion of the annual healthcare costs associated with addiction can be attributed to postoperative pain management.¹,³,⁸

Heron’s Goals For Postoperative Pain Program

• Our philosophy is that:
  1. Opioids play an important role for reduction of severe pain, but should be used as a last resort, rather than the first step in pain management.
  2. Reduction in the use of opioids should not come at the cost of patients experiencing more pain.
  3. Using our technology as part of a multi-modal postoperative pain regimen, our goal is to:
     • Eliminate the need for opioids to control postoperative pain in as close to 100% of patients as possible, making discharge prescriptions for opioids unnecessary in the outpatient setting; and
     • Provide better pain control than conventional reliance on opioids.
HTX-011
Mechanism of Action
A Potential Hypothesis: Inflammation, pH, and Local Anesthetic Failure

- With a pKa of 8.1, bupivacaine is sensitive to reduced pH
- The acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects

Inflammation produces an acidic environment
With a one pH unit drop, 10-fold less bupivacaine is able to penetrate the nerve cell membrane

2. Local anesthetic nerve penetration model adapted from Becker and Reed. Anesth Prog 53:98–109 2006
In Pig Post-op Pain Model Both Biochronomer Bupivacaine and Liposomal Bupivacaine Showed Loss of Activity at 24 Hours

Pig Postoperative Pain Model

Increasing Analgesia

% of Maximal Force (60 gm) Tolerated

Saline Control
Liposomal Bupivacaine
Biochronomer Bupivacaine

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)
Meloxicam Normalizes the pH Which Enables More Bupivacaine to Enter Nerves

% Increase of Un-ionized Bupivacaine

Tissue pH (SEM)

24 30 48
Time Post Incision (hrs)

- 11% for HTX-011 (n=4)
- 289% for HTX-011 (n=4)
- 1218% for Sham Control (n=4)
Combining Bupivacaine and Meloxicam in Biochronomer Produced Complete Sustained Analgesia

Pig Postoperative Pain Model

Increasing Analgesia

% of Maximal Force (60 gm) Tolerated

Hours

0 1 3 5 24 48 72 96 120 144

Saline Control
Liposomal Bupivacaine
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)
Activity of HTX-011 Cannot Be Replicated By Systemic Administration of High-Dose Meloxicam Along With Extended Release Bupivacaine

Pig Postoperative Pain Model

- Saline Placebo
- Bupivacaine ER + Meloxicam (Human dose = 30 mg daily)
- HTX-011

Post-operative pain model in pigs from Castle et al, 2013 EPJ
(n=4 pigs in each arm)
HTX-011 Reduces Pain Better Than the Individual Components in Both Bunionectomy and Herniorrhaphy Phase 2 Studies

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 is Applied into the Surgical Site at the End of Surgery Without a Needle

HTX-011 is a single-dose application administered via a needle-free syringe to directly coat the affected tissue within the surgical site prior to suturing.

Seven Active-Controlled Studies Showing Significantly Better Pain Reduction With HTX-011 Than Bupivacaine Included in NDA

<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Surgical Model</th>
<th>Tissue Type</th>
<th>Significant for Pain Reduction vs. PBO</th>
<th>Significant for Pain Reduction vs. BPV</th>
<th>Significant Reduction in Opioid Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>202</td>
<td>2</td>
<td>Herniorrhaphy</td>
<td>Soft</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>203</td>
<td>2</td>
<td>Abdominoplasty</td>
<td>Soft</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>208</td>
<td>2</td>
<td>Bunionectomy</td>
<td>Bony</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>209</td>
<td>2b</td>
<td>TKA</td>
<td>Bony</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>211</td>
<td>2b</td>
<td>Breast Augmentation</td>
<td>Soft</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>301</td>
<td>3</td>
<td>Bunionectomy</td>
<td>Bony</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>302</td>
<td>3</td>
<td>Herniorrhaphy</td>
<td>Soft</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

PBO = placebo; BPV = bupivacaine solution; TKA = total knee arthroplasty

HTX-011 is an investigational new drug and not approved by the FDA
EPOCH 1: Bunionectomy Results (Study 301)

EPOCH 1 Follow-on: Opioid Elimination Study in Bunionectomy
EPOCH 1 (Study 301) Bunionectomy: Study Design

- N = 412 (3:2:3 to HTX-011 60 mg, saline placebo, or bupivacaine HCl 50 mg)
- 438 subjects were randomized and 412 were dosed (ITT Population)
- 13 sites in the United States

Screening Period | Inpatient Period | Outpatient Follow-up Period

Randomization and Surgery | Primary Endpoint | End of Study (Day 42)

72 Hours | 39 Days

HTX-011 60 mg (N=157)
Saline Placebo 2.1 mL (N=100)
Bupivacaine HCl 50 mg (N=155)

1 subject (006-1018) was randomized to Bupivacaine HCl but received saline placebo

HTX-011 is an investigational new drug and not approved by the FDA
**EPOCH 1 Bunionectomy: All Key Endpoints Favor HTX-011**

Hierarchical hypothesis testing \( (P \leq .05) \)

<table>
<thead>
<tr>
<th></th>
<th>Endpoints</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>NRS Pain Intensity (AUC(_{0-72})) vs placebo</td>
<td>( p &lt; 0.0001 )</td>
</tr>
<tr>
<td>1(^{st}) Key Secondary</td>
<td>NRS Pain Intensity (AUC(_{0-72})) vs bupivacaine HCl</td>
<td>( p = 0.0002 )</td>
</tr>
<tr>
<td>2(^{nd}) Key Secondary</td>
<td>Opioid Use (0-72 hours) vs placebo</td>
<td>( p &lt; 0.0001 )</td>
</tr>
<tr>
<td>3(^{rd}) Key Secondary</td>
<td>Opioid Free (0-72 hours) vs bupivacaine HCl</td>
<td>( p = 0.0001 )</td>
</tr>
<tr>
<td>4(^{th}) Key Secondary</td>
<td>Opioid Use (0-72 hours) vs bupivacaine HCl</td>
<td>( p = 0.0022 )</td>
</tr>
</tbody>
</table>

**HTX-011** is an investigational new drug and not approved by the FDA.
EPOCH 1 Bunionectomy: HTX-011 Provides Superior Pain Reduction Through 72-hours

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

HTX-011 is an investigational new drug and not approved by the FDA.
Epoch 1 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours

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

HTX-011 is an investigational new drug and not approved by the FDA
Significantly Fewer Patients Experience Severe Pain with HTX-011

EPOCH 1 (Bunionectomy)

- Saline Placebo: 83.0% (N=100)
- Bupivacaine HCl 50 mg: 75.5% (N=155)
- HTX-011 60 mg: 53.5% (N=157)

EPOCH 1 Follow-on

- HTX-011 ≤ 60 mg + OTC: 29.0% (N=31)

% of Patients with Severe Pain at Any Time (NRS ≥ 7)

p < 0.0001

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

**EPOCH 1 (Bunionectomy)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Opioid Consumption (Mean MME ± SE) 0-72 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline Placebo</td>
<td>30.1</td>
</tr>
<tr>
<td>Bupivacaine HCl</td>
<td>25.1</td>
</tr>
<tr>
<td>HTX-011 60 mg</td>
<td>18.8</td>
</tr>
</tbody>
</table>

HTX-011 ≤ 60 mg + OTC

N=31

---

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)

- Saline Placebo: 2.0% (N=100)
- Bupivacaine HCI 50 mg: 11.0% (N=155)
- HTX-011 60 mg: 28.7% (N=157)

HTX-011 ≤ 60 mg + OTC: 77.4% (N=31)

100% remained opioid free through Day 28

Opioid-free Through 72 Hours

p < 0.0001
p = 0.0001

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
HTX-011 Safety Profile Similar to Bupivacaine and Saline
Most Common AEs were Nausea, Constipation, Dizziness

<table>
<thead>
<tr>
<th></th>
<th>EPOCH 1 (Bunionectomy)</th>
<th>EPOCH 1 Follow-on</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saline Placebo (N=101)</td>
<td>Bupivacaine HCl 50 mg (N=154)</td>
</tr>
<tr>
<td>Any AE</td>
<td>78%</td>
<td>85%</td>
</tr>
<tr>
<td>Severe AE</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Opioid-related AE</td>
<td>54%</td>
<td>51%</td>
</tr>
<tr>
<td>LAST</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>SAE</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>AE leading to study withdrawal</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

- Co-administration with NSAIDs was well tolerated

LAST: local anesthetic systemic toxicity
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
EPOCH 2: Herniorrhaphy Results (Study 302)

EPOCH 2 Follow-on: Opioid Elimination Study in Herniorrhaphy
EPOCH 2 (Study 302) Herniorrhaphy: Study Design

- N= 418 (2:1:2 to HTX-011 300 mg, saline placebo, or bupivacaine HCl 75 mg)
- 446 subjects were randomized and 418 were dosed (ITT Population)
- 17 sites in 2 countries (United States, Belgium)

```
Screening Period | Inpatient Period | Outpatient Follow-up Period

Randomization and Surgery | Primary Endpoint | End of Study (Day 28)

668 Screened
446 Randomized
418 Dosed

HTX-011 300 mg (N=164)
Saline Placebo 10.3 mL (N=82)
Bupivacaine HCl 75 mg (N=172)
```

1 subject (005-2018) was randomized to HTX-011 but received Bupivacaine HCl

HTX-011 is an investigational new drug and not approved by the FDA
**EPOCH 2 Herniorrhaphy: All Key Endpoints Favor HTX-011**

Hierarchical hypothesis testing ($P \leq .05$)

<table>
<thead>
<tr>
<th>Category</th>
<th>Endpoint Description</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>NRS Pain Intensity ($\text{AUC}_{0-72}$) vs placebo</td>
<td>$p = 0.0004$</td>
</tr>
<tr>
<td>1st Key Secondary</td>
<td>NRS Pain Intensity ($\text{AUC}_{0-72}$) vs bupivacaine HCl</td>
<td>$p &lt; 0.0001$</td>
</tr>
<tr>
<td>2nd Key Secondary</td>
<td>Opioid Use (0-72 hours) vs placebo</td>
<td>$p = 0.0001$</td>
</tr>
<tr>
<td>3rd Key Secondary</td>
<td>Opioid Free (0-72 hours) vs bupivacaine HCl</td>
<td>$p = 0.0486$</td>
</tr>
<tr>
<td>4th Key Secondary</td>
<td>Opioid Use (0-72 hours) vs bupivacaine HCl</td>
<td>$p = 0.0240$</td>
</tr>
</tbody>
</table>

AUC: area under the curve; placebo: saline placebo

HTX-011 is an investigational new drug and not approved by the FDA
EPOCH 2 Herniorrhaphy: HTX-011 Provides 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$_{0-24}$**
  - HTX-011 vs P: $p < 0.0001$
  - HTX-011 vs B: $p < 0.0001$

- **AUC$_{24-72}$**
  - HTX-011 vs P: $p = 0.0264$
  - HTX-011 vs B: $p = 0.0007$

- **AUC$_{0-72}$**
  - HTX-011 vs P: $p = 0.0004$
  - HTX-011 vs B: $p < 0.0001$

Severe pain ($\geq 7$)

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

Source: Figure 14.2
Epoch 2 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours

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

Source: Figure 14.2

HTX-011 is an investigational new drug and not approved by the FDA
Significantly Fewer Patients Experience Severe Pain with HTX-011

EPOCH 2 (Herniorrhaphy)

- Saline Placebo: N=82, 81.7% severe pain
- Bupivacaine HCl 75 mg: N=172, 60.5% severe pain, p = 0.0372
- HTX-011 300 mg: N=164, 48.8% severe pain

EPOCH 2 Follow-on

- HTX-011 300 mg + OTC: N=33, 15.2% severe pain

p < 0.0001

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

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>

EPOCH 2 Follow-on

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Opioid Consumption (Mean MME ± SE) 0-72 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTX-011 300 mg + OTC</td>
<td>33</td>
<td>0.6</td>
</tr>
</tbody>
</table>

p < 0.0001

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% (N=82)
- **Bupivacaine HCl 75 mg**: 40.1% (N=172)
- **HTX-011 300 mg**: 51.2% (N=164)

EPOCH 2 Follow-on

- **HTX-011 300 mg + OTC**: 90.9% (N=33)

Opioid-free Through 72 Hours

- **p < 0.0001**
- **p = 0.0486**

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
HTX-011 Safety Profile Similar to Bupivacaine and Saline
Most Common AEs were Nausea, Constipation, Dizziness

<table>
<thead>
<tr>
<th></th>
<th>EPOCH 2 (Herniorrhaphy)</th>
<th>EPOCH 2 Follow-on</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saline Placebo (N=82)</td>
<td>HTX-011 300 mg + OTC (N=33)</td>
</tr>
<tr>
<td>Any AE</td>
<td>74%</td>
<td>36%</td>
</tr>
<tr>
<td>Severe AE</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Opioid-related AE</td>
<td>44%</td>
<td>6%</td>
</tr>
<tr>
<td>LAST</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>SAE</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>AE leading to study withdrawal</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

- Co-administration with NSAIDs was well tolerated

LAST = local anesthetic systemic toxicity
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 Study Design
HTX-011 + OTC in Adult Open Inguinal Herniorrhaphy With Mesh

- Initial 93 patients treated in pilot program
- HOPE-1 will now be expanded across the US

IBP: Ibuprofen; APAP: acetaminophen; NRS-R: numeric rating scale of pain intensity at rest.
**HOPE-1: Near Total Opioid-Free Recovery with HTX-011 + OTC**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Opioid-Free Recovery</td>
<td>95%</td>
</tr>
<tr>
<td>Received an Opiod Predischarge</td>
<td>5%</td>
</tr>
<tr>
<td>Received an Opioid Prescription</td>
<td>9% (10 pills)</td>
</tr>
<tr>
<td>Took an Opioid Post Discharge</td>
<td>3% (all patients had received predischarge opioid)</td>
</tr>
<tr>
<td>Call Backs if Discharged Without an Opiod Prescription</td>
<td>0%</td>
</tr>
<tr>
<td>Satisfied, Very Satisfied, Extremely Satisfied With Medication</td>
<td>93%</td>
</tr>
</tbody>
</table>

N=93 in initial pilot program
Potential Impact of 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\(^2\) Inguinal Hernia Surgeries Annually

<table>
<thead>
<tr>
<th></th>
<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>
<td>16,800,000</td>
</tr>
<tr>
<td>HOPE-1 estimates</td>
<td>774,194</td>
<td>283,871</td>
<td>490,323</td>
</tr>
<tr>
<td>Potential Reduction with HTX-011 + OTC</td>
<td>23,225,806↓</td>
<td>6,916,129↓</td>
<td>16,309,677↓</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;
Phase 2b Total Knee Arthroplasty (TKA) Study (Study 209)
Study 209 Phase 2b: Total Knee Arthroplasty

- Pre-op Medication: acetaminophen (IV) 1 g, pregabalin (oral) 150 mg

- HTX-011 Administration Technique: needle-free instillation of 100 mg for posterior capsule & 300 mg for remaining tissue

- Ropivacaine Administration Technique: 50 mg injected into posterior capsule

- Post-op Medication: only opioid rescue medication available

HTX-011 is an investigational new drug and not approved by the FDA
Study 209 TKA: Results Hierarchy

HTX-011 via instillation achieved primary and key secondary endpoints for reduction in pain intensity scores at rest (NRS-R)

- 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: Significant Separation between HTX-011 Arms and Placebo through 72 Hours (Primary Endpoint)

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 at rest
LOCF for missing data and no adjustment for use of opioid rescue medication
Study 209 TKA: HTX-011 Reduces Opioid Use through 72 Hours

Opioid consumption is measured in milligram morphine equivalents (MME).

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

Use of Geometric Mean Based on Log Transformed Data for Opioid Use Misrepresents the Difference Between Arms Due to Handling of Zero

<table>
<thead>
<tr>
<th>Total Postsurgical Opioid Consumption (MME) 0-24 Hours Postsurgery¹</th>
<th>With Liposomal Bupivacaine (N = 70)</th>
<th>Without Liposomal (N = 69)</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arithmetic Mean (SD)</td>
<td>45.5 (35.01)</td>
<td>56.8 (38.26)</td>
<td>20%</td>
</tr>
<tr>
<td>Geometric Mean</td>
<td>3.5</td>
<td>38.5</td>
<td>91%</td>
</tr>
</tbody>
</table>

The Value Imputed for Zero Has a Big Impact on Geometric Mean and Predominately Impacts Active Arm

<table>
<thead>
<tr>
<th>Imputation for Zero</th>
<th>Exparel Geometric Mean Opioid Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 – 24 hrs¹</td>
</tr>
<tr>
<td>0.00001</td>
<td>3.5</td>
</tr>
<tr>
<td>0.00010</td>
<td>5.2</td>
</tr>
<tr>
<td>0.00100</td>
<td>7.7</td>
</tr>
<tr>
<td>0.01000</td>
<td>11.4</td>
</tr>
<tr>
<td>0.10000</td>
<td>17.0</td>
</tr>
<tr>
<td>1.00000</td>
<td>25.2</td>
</tr>
</tbody>
</table>

## Study 209 TKA: Significant Increase Compared to Placebo in Patients Achieving “Discharge Ready” MPADDS Criteria* with HTX-011

*MPADDS, modified postanaesthetic discharge scoring system. The proportion of subjects who first achieve an MPADSS score ≥9 at each timepoint was analyzed cumulatively. P-values from Fisher's exact test.

Source: Table 14.2.13.2

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Saline Placebo</th>
<th>Bupivacaine HCl</th>
<th>HTX-011 400 mg</th>
<th>HTX-011 400 mg + Ropivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 8</td>
<td>0.077</td>
<td>0.037</td>
<td>0.007</td>
<td>0.003</td>
</tr>
<tr>
<td>0 - 12</td>
<td>0.347</td>
<td>0.185</td>
<td>0.022</td>
<td>0.001</td>
</tr>
<tr>
<td>0 - 24</td>
<td>0.077</td>
<td>0.010</td>
<td>0.243</td>
<td>0.068</td>
</tr>
</tbody>
</table>

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 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)
HTX-034 Development
Next Generation Product for Postoperative Pain
HTX-034 Produces Complete Elimination of Pain Through 7 Days in Pig Postoperative Pain Model

Saline Placebo  | Liposomal Bupivacaine  | HTX-011  | HTX-034 (Cohort 1)  | HTX-034 (Cohort 2)

0.0  | 10.0  | 20.0  | 30.0  | 40.0  | 50.0  | 60.0  | 70.0

1h  | 3h   | 5h   | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7

Withdrawal Force (g)

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

This validated pig model of postoperative pain has been predictive of clinical observations with HTX-011, HTX-002 and HTX-009.
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.

**EXISTING PLATFORM ADVANTAGES**

- Strong KOL relationships
- Successful hospital and pain management launch experience
- IND/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
CINVANTI Accounts and Market Share Continue to Grow

CINVANTI Ordering Accounts Since Launch

CINVANTI Ordering Accounts Since Launch

Total Market Share

Source: Heron 867 data March 31, 2019
CINVANTI Market Share is Climbing Steadily Across All Segments

**EMEND IV**

<table>
<thead>
<tr>
<th></th>
<th>Clinic (000s)</th>
<th>Hospital (000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NK1 Units</td>
<td>Q1'18</td>
<td>Q2'18</td>
</tr>
<tr>
<td>Clinic</td>
<td>139</td>
<td>158</td>
</tr>
<tr>
<td>Hospital</td>
<td>194</td>
<td>211</td>
</tr>
</tbody>
</table>

**CINVANTI**

<table>
<thead>
<tr>
<th></th>
<th>Clinic (000s)</th>
<th>Hospital (000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NK1 Units</td>
<td>Q1'18</td>
<td>Q2'18</td>
</tr>
<tr>
<td>Clinic</td>
<td>139</td>
<td>158</td>
</tr>
<tr>
<td>Hospital</td>
<td>194</td>
<td>211</td>
</tr>
</tbody>
</table>

Source(s): Heron 867 data. Heron DDD 5HT3, NK1 Data

* Share calculation Q1’18 – Q1’19 = CINVANTI Q Units/CINVANTI+ Emend IV Q Units.
** Total includes units classified as “Other” Class of Trade in data.
Key CINVANTI Learnings to Support HTX-011 Launch

**HTX-011**
- MOA, Superior efficacy vs. SOC
- Broad Access Pricing
- 3-year pass through (C-Code)
- Top 200 IDNs
- 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

Any Local, 85%

NB Only, 15%

NB: Nerve Block

* Local Anesthetics are used in ~70% of procedures

THE LARGEST OPPORTUNITY TO DRIVE VALUE AND CREATE CHANGE
HTX-011 is focused on the largest market opportunity

Local Anesthetic Route of Delivery

- All Local, 85%
- NB, 15%

NB: Nerve Block

Local Anesthetic Volume Share

- Bupivacaine: 15%
- Lidocaine: 4%
- Exparel: 4%
- Ropivacaine NB: 14%
- Others: 10%
- Bupivacaine NB: 53%

N = 22M Procedures

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

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Raw 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>56%</td>
</tr>
<tr>
<td>Laminectomy, Foraminotomy, Discotomy</td>
<td>57%</td>
</tr>
<tr>
<td>Spinal Fusion</td>
<td>56%</td>
</tr>
<tr>
<td>Hip Arthroplasty</td>
<td>56%</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; Phalangectony</td>
<td>51%</td>
</tr>
<tr>
<td>Mammaplasty</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>

• 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

Reference: DRG Postoperative Pain Quantitative Research (Nov 2018) - n = 290 physicians; "Less than 100K procedures at peak
HTX-011 Enjoyed a Physician Preference Share of 44%

Adjusted Physician Preference Share Distribution

- **HTX-011** enjoyed a Physician Preference Share of 44%.
- **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 (Actual)**
- Other "caines" (e.g. lidocaine, ropivacaine, generic combo, etc.)
- Bupivacaine HCl
- Exparel
- HTX-011

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

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
Customers Value HTX-011’s Superior Product Profile

- **Highly favorable feedback** from both physicians and pharmacy directors, driven by key differentiators versus bupivacaine, including a novel MOA supported by superior pain reduction, opioid reduction, and opioid-free endpoints.

<table>
<thead>
<tr>
<th></th>
<th>Strength</th>
<th>Neither a Strength Nor Weakness</th>
<th>Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>More opioid-free patients</td>
<td>87%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Reduction in severe pain</td>
<td>85%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>72-hour Analgesia Duration</td>
<td>80%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Novel MOA</td>
<td>81%</td>
<td>17%</td>
<td></td>
</tr>
</tbody>
</table>

- **High preference shares across initial target procedures**
- Based on phase 3 and 2b procedures (bunion, hernia, TKA), **64% would use in all procedures they deemed appropriate**
- 95% preferred bupivacaine (versus placebo) as the Phase 3 comparator

Reference: DRG Postoperative Pain Quantitative Research (Nov 2018) - n = 290 physicians;

71% of physicians would advocate for HTX-011 to be on formulary

Aggregated preference share across specialties and key surgeries was 60%

68% of Pharmacy Directors found HTX-011’s profile more valuable than Exparel and 88% would grant access at an equivalent price.
Being Second to Market is NOT a Significant Obstacle to Commercial Success

Exparel® is a small obstacle to HTX-011 uptake as its penetration is less than 6%

- Across product attributes, surgeons and pharmacy directors surveyed consistently prefer HTX-011 over Exparel for the following reasons:
  - Significant reduction in severe pain resulting in significant increase in opioid-free patients
  - Superior efficacy profile of HTX-011 through 72 hours, with significant benefit over bupivacaine HCl
  - Unique mechanism of action
  - Simple route of administration eliminating the need for up to 120 injections, with no need for extensive training
- Surveyed pharmacy directors state that they would provide better access to HTX-011 than to Exparel

Reference: DRG Pharmacy Director Surveys
Pharmacy Directors Prefer HTX-011 to Exparel®

Impact of HTX-011 Launch on Exparel Formulary Status

- 43%: Exparel status would stay the same
- 33%: Exparel formulary status/purchasing would be made more restrictive
- 25%: Exparel would be removed

% of Pharmacy Directors (DRG Survey, 2018)
N = 40 Pharmacy Directors

Formulary Status of Exparel vs. Expected HTX-011 Status

- HTX-011 (Predicted)
  - 22%: Exparel status would stay the same
  - 56%: Exparel formulary status/purchasing would be made more restrictive
  - 22%: Exparel would be removed

- 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 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**

- **52%** Hospital Inpatient (7M procedures)
  - Part of DRG payment
  - 3 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

- **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
- Effective January 1, 2018, CMS reimbursement to hospitals for 340B drugs changed significantly from ASP+6% to ASP–22.5%
- Change enables CMS to capture most of the discounts manufacturers provide eligible hospitals
- **Products with pass-through status are exempt from this reimbursement change**

### 340B Drug Reimbursement

<table>
<thead>
<tr>
<th>With C-Code</th>
<th>Without C-Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP + 6%</td>
<td>ASP – 22.5%</td>
</tr>
</tbody>
</table>
## Comparative Reimbursement
(Derived From 2/20/2019 Leerink Report)

<table>
<thead>
<tr>
<th></th>
<th>Hospital Inpatient</th>
<th>Hospital Outpatient</th>
<th>Hospital Inpatient 340B</th>
<th>Hospital Outpatient 340B</th>
<th>Ambulatory Surgical Centers (ASCs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures (millions)</td>
<td>3.5</td>
<td>2.65</td>
<td>3.5</td>
<td>2.65</td>
<td>1.1</td>
</tr>
<tr>
<td>Procedures Mix</td>
<td>26.1%</td>
<td>19.8%</td>
<td>26.1%</td>
<td>19.8%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Financial advantage?</td>
<td>Heron Advantage</td>
<td>Heron Advantage</td>
<td>Heron Advantaged Due to Outpatient NCR</td>
<td>Large Heron Advantage</td>
<td>Same</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(assumes 10% discount &amp; 23.1% to 340B Outpatient)</td>
<td>90%</td>
<td>90%</td>
<td>90%</td>
<td>76.9%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Reimbursement</strong></td>
<td>0</td>
<td>106%</td>
<td>0</td>
<td>106%</td>
<td>106%</td>
</tr>
<tr>
<td><strong>Profit Margin</strong></td>
<td>-100.0%</td>
<td>17.8%</td>
<td>-100%</td>
<td>37.8%</td>
<td>17.8%</td>
</tr>
</tbody>
</table>

**HTX-011**

- Part of DRG payment
- C-Code for first 3 years allows for ASP+6%

**Exparel**

- Part of DRG payment
- C-Code for first 3 years allows for ASP+6% reimbursement
- ASP+6% reimbursement indefinitely

-90.0%  90%  90%  --  90%

-100.0%  100.0%  100%  100%  17.8%

-100.0%  100.0%  100%  100%  17.8%

Heron does not guarantee reimbursement for any of its products
## High-Value Procedures in Initial Target Market

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Total Procedures</th>
<th>Inpatient</th>
<th>Outpatient (C-code)</th>
<th>ASC (C-Code)</th>
<th>Medicare</th>
<th>Non-Medicare</th>
<th>Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ortho Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee arthroplasty</td>
<td>815</td>
<td>721</td>
<td>65</td>
<td>28</td>
<td>41%</td>
<td>59%*</td>
<td>87%</td>
</tr>
<tr>
<td>Hip arthroplasty</td>
<td>337</td>
<td>325</td>
<td>7</td>
<td>5</td>
<td>43%</td>
<td>57%*</td>
<td>81%</td>
</tr>
<tr>
<td>Shoulder arthroplasty</td>
<td>107</td>
<td>96</td>
<td>8</td>
<td>2</td>
<td>47%</td>
<td>52%*</td>
<td>89%</td>
</tr>
<tr>
<td>Rotator cuff repair</td>
<td>550</td>
<td>11</td>
<td>343</td>
<td>192</td>
<td>27%</td>
<td>73%*</td>
<td>86%</td>
</tr>
<tr>
<td>Spine procedures</td>
<td>750</td>
<td>463</td>
<td>249</td>
<td>36</td>
<td>35%</td>
<td>65%*</td>
<td>95%</td>
</tr>
<tr>
<td><strong>General Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hernia repair</td>
<td>1,096</td>
<td>200</td>
<td>777</td>
<td>106</td>
<td>25%</td>
<td>74%</td>
<td>77%</td>
</tr>
<tr>
<td>Hemorrhoidectomy</td>
<td>504</td>
<td>10</td>
<td>147</td>
<td>73</td>
<td>9%</td>
<td>37%*</td>
<td>88%</td>
</tr>
<tr>
<td>Colon and small bowel resection</td>
<td>483</td>
<td>461</td>
<td>18</td>
<td>0.7</td>
<td>33%</td>
<td>66%*</td>
<td>82%</td>
</tr>
<tr>
<td><strong>Plastic Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>160</td>
<td>29</td>
<td>118</td>
<td>11</td>
<td>16%</td>
<td>83%</td>
<td>72%</td>
</tr>
<tr>
<td>Mammoplasty</td>
<td>&gt;300</td>
<td>10</td>
<td>92</td>
<td>19</td>
<td>6%</td>
<td>34%</td>
<td>85%</td>
</tr>
<tr>
<td><strong>OB/GYN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-Section</td>
<td>1,285</td>
<td>1273</td>
<td>6.1</td>
<td>0</td>
<td>2%</td>
<td>98%*</td>
<td>32%</td>
</tr>
</tbody>
</table>

*Note: For settings in which procedure-specific breakdown of Medicare vs. non-Medicare was not available, the overall Medicare vs. non-Medicare breakdown was applied to the total volume of procedures occurring in the given setting.*
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 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 serious 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’s CINV Portfolio Continues to Outperform All CINV Branded Launches in Past 10 Years

First 12 Months of Sales for All CINV Brand Launches in Last 10 Years

<table>
<thead>
<tr>
<th>Brand</th>
<th>Sales (Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sancuso (2008)</td>
<td>33,530</td>
</tr>
<tr>
<td>Akynzeo...</td>
<td>2,756</td>
</tr>
<tr>
<td>Varubi...</td>
<td>11,759</td>
</tr>
<tr>
<td>SUSTOL...</td>
<td>68,694</td>
</tr>
<tr>
<td>CINVANTI (2018)</td>
<td>277,000</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; Varubi includes actuals for months 1-12
CINV Portfolio Achieved $97.5M in Net Product Sales Over Last Four Quarters and Over $140M Since Inception
CINVANTI Accounts and Market Share Continue to Grow

CINVANTI Ordering Accounts Since Launch

Total Market Share

Source: Heron 867 data March 31, 2019
CINVANTI Market Share is Climbing Steadily Across All Segments

**Source(s):** Heron 867 data. Heron DDD 5HT3, NK1 Data
*Share calculation Q1'18 – Q1'19= CINVANTI Q Units/CINVANTI+ Emend IV Q Units.
**Total includes units classified as “Other” Class of Trade in data.
CINVANTI is Both Taking Share From Emend and Growing the NK1 Market

NK1 Receptor Antagonists U.S. CINV Market

NK1 Receptor Antagonists Monthly U.S. CINV Vials or Rx*

*1 Emend (oral CINV) Rx = 3.7 capsules or 125mg of oral solution, excludes PONV Rx; 1 Aprepitant (oral CINV) Rx = 3.6 capsules; 1 Varubi Rx =2.4 tablets; 1 Akynzeo Rx = 1.3 capsules
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 contracts extending beyond September of 2019
- CINVANTI has become an established brand across both clinics and hospital capturing 38% of the market in Q1 2019
Implications of USP 797 and 800 Regulations on Hospital Pharmacies

Pharmacy Implications

- New regulations dictate need for separate preparation rooms, +ve pressure room for sterile preparations and -ve pressure room for hazardous drugs (e.g. chemo)
- Anti-emetics requiring dilution need to be prepared in the +ve pressure room
- Pharmacy staff need to work in both rooms. Transferring between the rooms requires changes of protective clothing which increases complexity of the process and time requirements
- Substantial capital expenditure for building infrastructure, hiring and training staff, documentation maintenance etc.
- ~20%* of institutions are currently compliant with new regulations. Deadline for to be compliant is Dec 1st 2019. Institutions may be excluded from Medicare reimbursement if they miss the deadline

CINVANTI IV Push Advantages

- New regulations increase the process complexity significantly. The drugs that can be prepared and administered safely outside of the clean rooms are highly desired
- IV push medications, such as CINVANTI, do not need to be prepared in +ve pressure rooms. This simplifies the pharmacy process.

Sources: 1. PharmD at Cone Health Cancer Center, Greensboro, NC 2. A former VP of Pharmacy at City of Hope
* Estimate from one of the sources
ALOXI/Palonosetron Arbitrage Lasted Much Longer Than Projected, but It’s Finally Coming to an End!

- Generic manufacturers have evolved and become more disciplined on pricing to maximize revenue.

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

- Slower decline in prices leads to a slower drop in ASP and a longer arbitrage.
  - Substantial drop in ASP in 2Q19 with rapid erosion expect to continue through 2019.

- The NCR benefit of the arbitrage will essentially be gone by the end of 2019.

Source: Heron Management.
2019 CINV Franchise Outlook

SUSTOL®: While we expect to see sales of SUSTOL slowly improve, the core business will continue to be weak during the protracted palonosetron arbitrage.

CINVANTI®
- We expect to see steady growth in the marketplace through mid-year due to what we believe is the best overall profile compared to the other available NK₁ antagonists.
- With recently approved 2-min IV Push sNDA, CINVANTI is now further differentiated from EMEND IV (fosaprepitant).
- CINVANTI (aprepitant) injectable emulsion received unique J-Code J0185 effective January 1, 2019.
- Generic fosaprepitant IV is expected 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.

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.

### Summary Statement of Operations and Net Cash Used in Operations

<table>
<thead>
<tr>
<th></th>
<th>Three Months Ended March 31, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net product sales</td>
<td>$ 31,602</td>
</tr>
<tr>
<td>Operating expenses&lt;sup&gt;1&lt;/sup&gt;</td>
<td>96,302</td>
</tr>
<tr>
<td>Other income, net</td>
<td>1,688</td>
</tr>
<tr>
<td>Net loss&lt;sup&gt;1&lt;/sup&gt;</td>
<td>$(63,012)</td>
</tr>
<tr>
<td>Net loss per share&lt;sup&gt;2&lt;/sup&gt;</td>
<td>$(0.80)</td>
</tr>
<tr>
<td>Net cash used in operations</td>
<td>$(49,024)</td>
</tr>
</tbody>
</table>

### Condensed Balance Sheet Data

<table>
<thead>
<tr>
<th></th>
<th>March 31, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents and short-term investments</td>
<td>$ 289,238</td>
</tr>
<tr>
<td>Accounts receivable, net</td>
<td>$ 74,007</td>
</tr>
<tr>
<td>Total assets</td>
<td>$ 435,794</td>
</tr>
<tr>
<td>Total stockholders’ equity</td>
<td>$ 331,814</td>
</tr>
</tbody>
</table>

Common shares outstanding at March 31, 2019 totaled 78.9 million.

<sup>1</sup> Includes $17.9 million of non-cash, stock-based compensation expense for the three months ended March 31, 2019.

<sup>2</sup> Based on 78.4 million weighted-average common shares outstanding for the three months ended March 31, 2019.
### 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>
<tbody>
<tr>
<td>• CRL was received 30 April 2019</td>
<td>• 2019 net sales guidance for CINV franchise: $115M - $120M</td>
</tr>
<tr>
<td>➢ The CRL identified issues relating to CMC and non-clinical</td>
<td></td>
</tr>
<tr>
<td>➢ No issues related to clinical efficacy or safety were noted</td>
<td></td>
</tr>
<tr>
<td>• Heron plans to provide responses to the CRL as quickly as feasible with a request for a Type A meeting with the FDA</td>
<td></td>
</tr>
<tr>
<td>➢ Once agreement is reached on our responses, we will refile the NDA</td>
<td></td>
</tr>
<tr>
<td>• Launch the HOPE Project across the US</td>
<td></td>
</tr>
<tr>
<td>• Publication of Phase 3 and Phase 2b studies</td>
<td></td>
</tr>
<tr>
<td>➢ 10 publications in process</td>
<td></td>
</tr>
<tr>
<td>✓ Phase 3 Bunion study published</td>
<td></td>
</tr>
<tr>
<td>• Phase 2 with HTX-034 in 2H2019</td>
<td></td>
</tr>
</tbody>
</table>

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