Corporate Update

June 5, 2019
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:

**SUSTOL®**
(granisetron) extended-release injection

- US FDA Approved for CINV Prevention*
- 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.
- EU MAA filing by Centralised Procedure in 1H2019

**CINVANTI®**
(aprepitant) injectable emulsion

- US FDA Approved for CINV Prevention*
- 2-minute IV Push Approved 26 Feb 2019

---

**PAIN MANAGEMENT**

**HTX-011**

- Under Investigation for Postoperative Pain via Local Application
- Produce complete elimination of pain for 7 days in validated pig model of postoperative pain

**HTX-034**

- Under Investigation for Postoperative Pain via Local Application
- Produces complete elimination of pain for 7 days in validated pig model of postoperative pain

---

*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.

HTX-011 and HTX-034 are 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
## 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 Bunionectomy: All Key Endpoints Favor HTX-011

**Hierarchical hypothesis testing (P ≤ .05)**

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

NRS: numeric rating scale  AUC: area under the curve; placebo: saline placebo

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

**AUC**

<table>
<thead>
<tr>
<th>Time (hour)</th>
<th>AUC&lt;sub&gt;0-24&lt;/sub&gt;</th>
<th>AUC&lt;sub&gt;24-72&lt;/sub&gt;</th>
<th>AUC&lt;sub&gt;0-72&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-24</td>
<td>HTX-011 vs P: p &lt; 0.0001</td>
<td>HTX-011 vs P: p &lt; 0.0001</td>
<td>HTX-011 vs P: p &lt; 0.0001</td>
</tr>
<tr>
<td>24-72</td>
<td>HTX-011 vs B: p &lt; 0.0001</td>
<td>HTX-011 vs B: p = 0.0072</td>
<td>HTX-011 vs B: p = 0.0001</td>
</tr>
</tbody>
</table>

**Severe pain (≥ 7)**

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

* 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

EPOCH 1 (Bunionectomy)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean MME ± SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline Placebo</td>
<td>30.1 ± 5</td>
<td></td>
</tr>
<tr>
<td>Bupivacaine HCl 50</td>
<td>25.1 ± 5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HTX-011 60 mg</td>
<td>18.8 ± 5</td>
<td>0.0022</td>
</tr>
</tbody>
</table>

EPOCH 1 Follow-on

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean MME ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTX-011 ≤ 60 mg + OTC</td>
<td>1.6 ± 0.5</td>
</tr>
</tbody>
</table>

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

Through 72 Hours

Saline Placebo
N=100

Bupivacaine HCl 50 mg
N=155

HTX-011 60 mg
N=157

EPOCH 1 (Bunionectomy)

p < 0.0001

p = 0.0001

HTX-011 ≤ 60 mg + OTC
N=31

EPOCH 1 Follow-on

p = 0.0001

100% 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: All Key Endpoints Favor HTX-011

<table>
<thead>
<tr>
<th>Primary</th>
<th>NRS Pain Intensity (AUC$_{0-72}$) vs placebo</th>
<th>p = 0.0004</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Key Secondary</td>
<td>NRS Pain Intensity (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>

Hierarchical hypothesis testing (P ≤ .05)

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)

Time (hour)

AUC

AUC$_{0-24}$

AUC$_{24-72}$

AUC$_{0-72}$

HTX-011 vs P: $p < 0.0001$

HTX-011 vs B: $p < 0.0001$

HTX-011 vs P: $p = 0.0264$

HTX-011 vs B: $p = 0.0007$

HTX-011 vs P: $p = 0.0004$

HTX-011 vs B: $p < 0.0001$

HTX-011 300 mg (N=164)

Saline Placebo (N=82)

Bupivacaine HCl 75 mg (N=172)

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

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

Opioid Consumption (Mean MME$^1 \pm SE$) 0-72 Hours

- **Saline Placebo**: N=82, 17.5
- **Bupivacaine HCl 75 mg**: N=172, 14.5
- **HTX-011 300 mg**: N=164, 10.9
- **HTX-011 300 mg + OTC**: N=33, 0.6

EPOCH 2 (Herniorrhaphy)

- p < 0.0001
- p = 0.0240

EPOCH 2 Follow-on

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% (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)

\[ p < 0.0001 \]
\[ p = 0.0486 \]

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

93% remained opioid free through Day 28
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
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>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;
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)
CINV Commercial Products
CINV Portfolio Achieved $97.5M in Net Product Sales Over Last Four Quarters and Over $140M Since Inception
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
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

**Palo and Ondansetron ASP over time**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Branded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 17</td>
<td>$206</td>
</tr>
<tr>
<td>Q1 18</td>
<td>$200</td>
</tr>
<tr>
<td>Q2 18</td>
<td>$197</td>
</tr>
<tr>
<td>Q3 18</td>
<td>$222</td>
</tr>
<tr>
<td>Q4 18</td>
<td>$168</td>
</tr>
<tr>
<td>Q1 19</td>
<td>$147</td>
</tr>
<tr>
<td>Q2 19</td>
<td>$91</td>
</tr>
<tr>
<td>Q3 19</td>
<td>$77</td>
</tr>
<tr>
<td>Q4 19</td>
<td>$70</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Summary Statement of Operations and Net Cash Used in Operations</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(^1)</td>
<td>96,302</td>
</tr>
<tr>
<td>Other income, net</td>
<td>1,688</td>
</tr>
<tr>
<td>Net loss(^1)</td>
<td>$(63,012)</td>
</tr>
<tr>
<td>Net loss per share(^2)</td>
<td>$(0.80)</td>
</tr>
<tr>
<td>Net cash used in operations</td>
<td>$(49,024)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condensed Balance Sheet Data (In thousands)</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.

\(^1\) Includes $17.9 million of non-cash, stock-based compensation expense for the three months ended March 31, 2019.

\(^2\) 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><strong>• CRL was received 30 April 2019</strong></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><strong>• Heron plans to provide responses to the CRL as quickly as feasible with a request for a Type A meeting with the FDA</strong></td>
<td></td>
</tr>
<tr>
<td>➢ Once agreement is reached on our responses, we will refile the NDA</td>
<td></td>
</tr>
<tr>
<td><strong>• Launch the HOPE Project across the US</strong></td>
<td></td>
</tr>
<tr>
<td><strong>• Publication of Phase 3 and Phase 2b studies</strong></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><strong>• Phase 2 with HTX-034 in 2H2019</strong></td>
<td></td>
</tr>
</tbody>
</table>

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