Heron Therapeutics
JPM Update
January 13, 2020
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 fourth-quarter 2019 and full-year 2019 net product sales 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 timing of Health Canada’s New Drug Submission (NDS) review process for HTX-011; whether Health Canada issues a Notice of Compliance for the NDS 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:

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

- US FDA Approved for CINV Prevention*

**CINVANTI® (aprepitant)**
injectable emulsion

- US FDA Approved for CINV Prevention*

**HTX-011**
Under Investigation for Postoperative Pain via Local Application

- 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
  - New PDUFA date: 26 March 2020
- EU MAA filing by Centralised Procedure in March 2019
  - Potential CHMP opinion 2Q2020
- Canadian NDS screening completed
  - Potential approval in early 3Q2020

**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 an 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.

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

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>Total Procedures</th>
<th>Inpatient</th>
<th>Outpatient (C-code)</th>
<th>ASC (C-Code)</th>
<th>Medicare</th>
<th>Non-Medicare**</th>
<th>% Local Anesthetic Use</th>
<th>Significantly Reduced Pain vs BPV†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee arthroplasty</td>
<td>1,043</td>
<td>977</td>
<td>41</td>
<td>25</td>
<td>41%</td>
<td>59%</td>
<td>86%</td>
<td>√</td>
</tr>
<tr>
<td>Hip arthroplasty</td>
<td>599</td>
<td>579</td>
<td>8</td>
<td>12</td>
<td>42%</td>
<td>58%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Shoulder arthroplasty</td>
<td>161</td>
<td>149</td>
<td>9</td>
<td>3</td>
<td>47%</td>
<td>53%</td>
<td>85%</td>
<td></td>
</tr>
<tr>
<td>Rotator cuff repair</td>
<td>319</td>
<td>6</td>
<td>193</td>
<td>120</td>
<td>27%</td>
<td>73%</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>Spine procedures</td>
<td>1,459*</td>
<td>928</td>
<td>456</td>
<td>75</td>
<td>34%</td>
<td>66%</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td>Bunionectomy</td>
<td>597</td>
<td>42</td>
<td>343</td>
<td>212</td>
<td>25%</td>
<td>75%</td>
<td>88%</td>
<td>√</td>
</tr>
<tr>
<td>Hernia repair</td>
<td>1,064</td>
<td>212</td>
<td>731</td>
<td>121</td>
<td>26%</td>
<td>74%</td>
<td>82%</td>
<td>√</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>987</td>
<td>323</td>
<td>600</td>
<td>64</td>
<td>10%</td>
<td>90%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>Colon and sm bowel resection</td>
<td>476</td>
<td>457</td>
<td>18</td>
<td>1</td>
<td>33%</td>
<td>67%</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Abdominoplasty</td>
<td>130</td>
<td>23</td>
<td>95</td>
<td>12</td>
<td>16%</td>
<td>84%</td>
<td>75%</td>
<td>√</td>
</tr>
<tr>
<td>Mammoplasty</td>
<td>292</td>
<td>32</td>
<td>208</td>
<td>52</td>
<td>16%</td>
<td>84%</td>
<td>79%</td>
<td>√</td>
</tr>
<tr>
<td>OB/GYN C-Section</td>
<td>1,168</td>
<td>1158</td>
<td>10</td>
<td>0</td>
<td>2%</td>
<td>98%</td>
<td>58%</td>
<td></td>
</tr>
</tbody>
</table>

* Includes Laminectomy, Foraminotomy, Discectomy, Fusion
** Non Medicare includes Commercial, Medicaid and Cash
† HTX-011 produced significantly greater pain reduction than bupivacaine in Phase 2 and/or Phase 3 trials

Sources: DRG Claims Data 2017/ update 2018
The Link Group ATU survey May 2019

Completed studies

On-going studies

*5*
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
- 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
Heron has Successfully Launched a Hospital Product and Achieved >40% Market Share From Entrenched Competitor

**CINVANTI Hospital Share/Units**

- **Hospital Share**
- **Hospital Units**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Hospital Share</th>
<th>Hospital Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018-Q1</td>
<td>0%</td>
<td>528</td>
</tr>
<tr>
<td>2018-Q2</td>
<td>3%</td>
<td>7,990</td>
</tr>
<tr>
<td>2018-Q3</td>
<td>12%</td>
<td>28,751</td>
</tr>
<tr>
<td>2018-Q4</td>
<td>21%</td>
<td>51,471</td>
</tr>
<tr>
<td>2019-Q1</td>
<td>25%</td>
<td>66,774</td>
</tr>
<tr>
<td>2019-Q2</td>
<td>32%</td>
<td>87,803</td>
</tr>
<tr>
<td>2019-Q3</td>
<td>39%</td>
<td>103,124</td>
</tr>
<tr>
<td>2019-Q4</td>
<td>43%</td>
<td>118,767</td>
</tr>
</tbody>
</table>

**SOURCE:** 867/1.8.20, IMS DDD 12.27.19
CINVANTI Achieved Significant Penetration in Both the 340B and Non-340B Hospital Market

SOURCE: 867 1.8.20, IMS DDD 12.27.19
## Hospital Launch Analysis

**HTX-011 and CINVANTI Have Very Similar Profiles**

<table>
<thead>
<tr>
<th></th>
<th>CINVANTI</th>
<th>HTX-011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Market Category</strong></td>
<td>NK1 - CINV</td>
<td>Local Anesthetics</td>
</tr>
<tr>
<td><strong>Annual Units</strong></td>
<td>800,000 NK1 units in hospital</td>
<td>14M*</td>
</tr>
<tr>
<td><strong>Brand Leader - Unit Share</strong></td>
<td>EMEND IV 100%</td>
<td>EXPAREL 7% 1.0M** units</td>
</tr>
<tr>
<td><strong>Generics at Launch - Unit Share</strong></td>
<td>No 0%</td>
<td>YES 93%</td>
</tr>
<tr>
<td><strong>New P&amp;T Review</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Clinical Differentiation</strong></td>
<td>Yes – PS-80 free</td>
<td>Yes – beat SOC</td>
</tr>
<tr>
<td><strong>Ease of Use</strong></td>
<td>High – IV push, infusion</td>
<td>High - installation</td>
</tr>
<tr>
<td><strong>Price Strategy vs. Brand</strong></td>
<td>20% discount</td>
<td>Discount to brand likely</td>
</tr>
<tr>
<td><strong>340b Pricing Offer</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Brand 340b Pricing</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>3-year pass-through</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Lexus Target Procedures Q3 17-Q3 18
** SHA Pac units Q3 17 –Q3 18

**HTX-011 is an investigational new drug and not approved by the FDA**
The Market is Large and Waiting for an Effective Non-opioid Solution

Potential Target Market

~30M Annual U.S. Surgical Procedures Requiring Postoperative Pain Management

**Potential Market Size**

~$2.8B

~$1.3B

~$1.7B

**Potential Target Market**

~14M Initial Target Procedures

~7M Procedures

~9M Procedures

**Target Procedures (Initial Targets)**

Higher-volume procedures across 4 major specialties
- ~6.0M Orthopedic procedures
- ~4.5M General surgery procedures
- ~2.6M OB/GYN procedures
- ~900K Plastic surgery procedures

**Secondary Targets**

Higher-volume procedures in non-core specialties (eg, ENT, urology, hand, others)

**Tertiary Targets**

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

Source: DRG Claims Analysis, 2016 and 2019
### Branded Product Utilization Has Grown and is Approaching ~$1B

**Shift Away From Opioids Continues**

<table>
<thead>
<tr>
<th>Product</th>
<th>Pack Units</th>
<th>% Change</th>
<th>WAC</th>
<th>% Change</th>
<th>Avg. Cost per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>20.8M</td>
<td>21%</td>
<td>$44M</td>
<td>31%</td>
<td>$5-7</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>1.6M</td>
<td>138%</td>
<td>$24M</td>
<td>159%</td>
<td>$39</td>
</tr>
<tr>
<td>Exparel</td>
<td>1.1M</td>
<td>20%</td>
<td>$323M</td>
<td>16%</td>
<td>$298</td>
</tr>
<tr>
<td>Ofirmev</td>
<td>10.8M</td>
<td>8%</td>
<td>$422M</td>
<td>14%</td>
<td>$86</td>
</tr>
<tr>
<td>On-Q*</td>
<td>-</td>
<td>-</td>
<td>~$150M</td>
<td>-</td>
<td>~$320</td>
</tr>
<tr>
<td>Opioids</td>
<td>178.6M</td>
<td>(18%)</td>
<td>$1.1B</td>
<td>(13%)</td>
<td>-</td>
</tr>
</tbody>
</table>

- Local Anesthetics grew +22% in value and +26% in pack units in 2018, while opioids declined
- Large increase in ropivacaine driven by increased use of nerve block to decrease need for opioids
- Exparel volume growth was primarily driven by the 10ml vial and limited nerve block indication

* Avanos Earnings Call 11/05/19; Amazon.com: Halyard Health P400X5 ON-Q Pump Fixed Flow, 400 mL, 5 mL/hour Flow Rate (Pack of Price: $1,592.58 (5 pump pack)

Symphony PHAST – 2017-2019 Market Data
Clear Shift from Inpatient (no reimbursement) to Outpatient and ASC
With Opportunity for Pass-Through
HTX-011 has Strategic Advantages Across All Settings of Care

Hospitals account for 90% (down from 91%), with 5% decline in inpatient procedures

- 52% » 47%
  Hospital
  Inpatient
  (6.6M procedures)
  • Part of DRG payment
  • Multiple SKUs - lower average cost
  • ~50% connected 340B hospitals

39% » 43%
Hospital
Outpatient
(6M procedures)

- 3-year pass through (C-Code)
- 340B opportunity
- Multiple SKUs - lower average cost

8% » 9%
Ambulatory Surgical Centers (ASCs)
(1.3M procedures)

- ASP +6%
- Lower access barriers
- Targeted facilities
- Connected to top IDNs
- Multiple SKUs - lower average cost

52% of the opportunity lends itself to favorable pricing, access and reimbursement

The remaining 1% of procedures are performed at private physician practices

Source: 2015/2018 DRG Claims Data. Procedures validated with thorough medical review for applicable procedures, DRG Claims and Lexis Nexis for annual volume – SHA for Drug Sales
Improved Pain Management and Reduced Opioid Use with HTX-011 Can Potentially Move More Procedures to the Outpatient Setting

**Table 14.2.13.2**

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>HTX-011 400 mg</th>
<th>HTX-011 400 mg + Ropivacaine</th>
<th>Bupivacaine HCl</th>
<th>Saline Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 8</td>
<td>0.007</td>
<td>0.003</td>
<td>0.347</td>
<td>0.185</td>
</tr>
<tr>
<td>0 - 12</td>
<td>0.022</td>
<td>0.001</td>
<td>0.348</td>
<td>0.055</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>

*MPADSS, 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

**Significantly Faster Time to “Discharge Ready” with HTX-011 in TKA**

HTX-011 is an investigational new drug and not approved by the FDA
**Initial Launch Focus – Fast Moving 340b Hospitals Currently Using Branded Postop Pain Medication**

### 340B + Branded Postop Pain Medication Use

<table>
<thead>
<tr>
<th># of Hospitals</th>
<th>Formulary Timing</th>
<th># Target Procedures</th>
<th>Branded Pain Meds</th>
<th># Procedures</th>
<th>Branded Pain Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>0-3</td>
<td>200K</td>
<td>$23M</td>
<td>184K</td>
<td>$15M</td>
</tr>
<tr>
<td>201</td>
<td>4-8</td>
<td>676K</td>
<td>$65M</td>
<td>624K</td>
<td>$43M</td>
</tr>
</tbody>
</table>

### Non-340B + Branded Postop Pain Medication Use

<table>
<thead>
<tr>
<th># of Hospitals</th>
<th>Formulary Timing</th>
<th># Target Procedures</th>
<th>Branded Pain Meds</th>
<th># Procedures</th>
<th>Branded Pain Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>0-3</td>
<td>380K</td>
<td>$30M</td>
<td>182K</td>
<td>$20M</td>
</tr>
<tr>
<td>188</td>
<td>4-8</td>
<td>530K</td>
<td>$59M</td>
<td>489K</td>
<td>$39M</td>
</tr>
</tbody>
</table>

($38M) ($108M) ($50M) ($98M)
HTX-011 is Focused on the Largest Market Opportunity – Local Application

Local Anesthetic Route of Delivery

- All Local, 85%
- NB, 15%

THE LARGEST OPPORTUNITY TO DRIVE VALUE AND CREATE CHANGE

Local Anesthetic Volume Share

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

HTX-011 is Focused on the Largest Market Opportunity – Local Application

HTX-011 Demonstrated Significant Pain Reduction in Nerve Block
HTX-011 Instillation has Also Demonstrated Superiority to Bupivacaine NB
and Similar Pain Reduction to HTX-011 Nerve Block

Study 211: Compared to Placebo, Pain Reduction with HTX-011 Instillation Approximately
Triple that of Bupivacaine Nerve Block

Study 211: Compared to Placebo, Pain Reduction with HTX-011 Instillation Approximately
Triple that of Bupivacaine Nerve Block

<table>
<thead>
<tr>
<th>Mean Percent Reduction in Pain Intensity Scores vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value vs. PBO</td>
</tr>
<tr>
<td>0.0055</td>
</tr>
<tr>
<td>0.0620</td>
</tr>
<tr>
<td>p-value vs. BPV</td>
</tr>
<tr>
<td>0.0623</td>
</tr>
<tr>
<td>0.0383</td>
</tr>
</tbody>
</table>

2.8x Greater Pain Reduction Than BPV Nerve Block vs PBO
2.9x Greater Pain Reduction Than BPV Nerve Block vs PBO

Reference: Table 14.2.4.1
Program: J:\htx011\211\csr\prog\posthoc_f_14.2.10_auc_r_24h_htx400_wwoof_pctchg.sas.sas

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 Demonstrated Significant Reduction in Opioid Use with both Nerve Block and Instillation

Study 211: Compared to Placebo, HTX-011 Instillation has Demonstrated Significantly Greater Opioid Reduction Compared to Bupivacaine NB

Study 211: Phase 2b Breast Augmentation Mammoplasty

Opioid consumption is presented in mean milligrams of morphine equivalents

HTX-011 is an investigational new drug and not approved by the FDA
Cross-Study Comparison of TKA Study 306 to Published Adductor Canal Nerve Block Study

HTX-011 + MMA Produced Comparable or Better Pain Scores Than Nerve Block

HTX-011 + MMA with APAP and Celecoxib in Study 306

Single-Shot Adductor Canal Block (SACB) & Continuous Adductor Canal Block (CACB) with MMA

Nerve Block Conclusions

- HTX-011 nerve block significantly reduced pain
- Instillation of HTX-011 reduced pain just as well and appears to be as good or better than bupivacaine nerve block, even with continuous infusion

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


Patients received either a single administration or continuous infusion of bupivacaine plus IV diclofenac or APAP as MAA
Physicians indicated a raw preference share of 56% for HTX-011 across the covered procedures

- 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 (Actual): 25% (11%), Future Therapy (Applying HTX-011 preference share): 14% (44%)
- **Bupivacaine HCl**:
  - Current Therapy (Actual): 64%, Future Therapy (Applying HTX-011 preference share): 6%
- **Exparel**:
  - Current Therapy (Actual): 64%, Future Therapy (Applying HTX-011 preference share): 6%
- **HTX-011**:
  - Current Therapy (Actual): 11%, Future Therapy (Applying HTX-011 preference share): 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 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% would stay the same
- 33% would be made more restrictive
- 20% 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)
  - Not on Formulary: 43%
  - On Formulary, No Restrictions: 56%
  - On Formulary, With Restrictions: 22%

- Exparel (Stated)
  - Not on Formulary: 44%
  - On Formulary, No Restrictions: 18%
  - On Formulary, With Restrictions: 43%

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?
## 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>18.6M</td>
<td>6.8M</td>
<td>4.0M</td>
<td>2.8M</td>
</tr>
<tr>
<td>France</td>
<td>13.5M</td>
<td>4.4M</td>
<td>2.5M</td>
<td>1.9M</td>
</tr>
<tr>
<td>UK</td>
<td>11.8M</td>
<td>3.8M</td>
<td>2.4M</td>
<td>1.4M</td>
</tr>
<tr>
<td>Italy</td>
<td>10.1M</td>
<td>2.6M</td>
<td>1.9M</td>
<td>0.7M</td>
</tr>
<tr>
<td>Spain</td>
<td>6.5M</td>
<td>2.1M</td>
<td>1.6M</td>
<td>0.5M</td>
</tr>
<tr>
<td>Top 5 EU Total</td>
<td>60.5M</td>
<td>19.7M</td>
<td>12.4M</td>
<td>7.3M</td>
</tr>
<tr>
<td>Canada</td>
<td>6.0M</td>
<td>1.6M</td>
<td>1.2M</td>
<td>0.4M</td>
</tr>
<tr>
<td>Japan</td>
<td>26.0M</td>
<td>6.6M</td>
<td>2.7M</td>
<td>3.9M</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.
HTX-011 Development Program
Advancing Pain Management

HTX-011 is an investigational new drug and not approved by the FDA
A Potential Hypothesis: Inflammation, pH, and Local Anesthetic Failure

Local Anesthetics Exist in a Balance Between Water- and Lipid-Soluble Forms

Inflammation produces an acidic environment

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

- 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\(^1,2\)

HTX-011 is an investigational new drug and not approved by the FDA
HTX-011 is Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery as Demonstrated in this Preclinical Model¹

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

¹ Postoperative pain model in pigs from Castle et al, 2013 EPJ
² Human dose of liposomal bupivacaine with 40% smaller incision
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 a single-dose application administered via a needle-free syringe to directly coat the affected tissue within the surgical site prior to suturing.


HTX-011 is an investigational new drug and not approved by the FDA.
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: HTX-011 Provided Superior Pain Reduction Through 72-hours

Pain Intensity Score* (Mean ± SE)

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

* 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

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

Pain Intensity Score*
(Mean ± SE)

Severe pain ≥ 7
Mild pain (0-4)

EPOCH 1 Follow-on: HTX-011 ≤ 60 mg + OTC (N=31)

* 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)

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

EPOCH 1 Follow-on

- HTX-011 ≤ 60 mg + OTC (N=31): 77.4%

100% remained opioid free through Day 28

% Opioid-free 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
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)

<table>
<thead>
<tr>
<th>Time (hour)</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC0-24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTX-011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine HCl 75 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC24-72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTX-011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine HCl 75 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC0-72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTX-011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Source: Figure 14.2.7

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

Source: Figure 14.2.7

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>Group</th>
<th>Opioid Consumption Mean MME1 ± SE</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline Placebo</td>
<td>17.5</td>
<td>82</td>
</tr>
<tr>
<td>Bupivacaine HCl 75 mg</td>
<td>14.5</td>
<td>172</td>
</tr>
<tr>
<td>HTX-011 300 mg</td>
<td>10.9</td>
<td>164</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

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

EPOCH 2 Follow-on: 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\(^2\) 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(\downarrow)</td>
<td>6,916,129(\downarrow)</td>
<td>16,309,677(\downarrow)</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
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 Produced Significantly Superior Pain Reduction to Both Placebo and Bupivacaine Through 72 Hours

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

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

* 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 Analysis(^1)</th>
<th>Study 306 HTX-011 (N=51)</th>
<th>PILLAR Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Exparel + Bupivacaine(^1) (N = 70)</td>
</tr>
<tr>
<td>AUC0-24 VAS Pain (^2)</td>
<td>59.5</td>
<td>98.5</td>
</tr>
<tr>
<td>Opioid-Free</td>
<td>21.6%</td>
<td>17.1%</td>
</tr>
<tr>
<td>Mean Opioid Consumption MME (SD)</td>
<td>10.6 (9.2)</td>
<td>45.5 (35.01)</td>
</tr>
<tr>
<td>Log-transformed Geometric Mean Opioid Consumption MME</td>
<td>0.54</td>
<td>3.5</td>
</tr>
<tr>
<td>Discharge Ready in 12 hours Based MPADSS &gt; 9</td>
<td>60.8%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

\(^1\) https://doi.org/10.1016/j.arth.2018.12.026.  
\(^2\) 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†</th>
<th>Study 306 HTX-011 (N=51)</th>
<th>PILLAR Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Exparel + Bupivacaine† (N = 70)</td>
</tr>
<tr>
<td>Mean AUC12-48 VAS Pain</td>
<td>143.2</td>
<td>180.8</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 @ 48hr</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>69,933,150(\downarrow)</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)

HTX-011 is an investigational new drug and not approved by the FDA.
HTX-034 Development

Next Generation Product for Postoperative Pain
In Addition to Changes in pH, Inflammation From Surgery Modifies Pain Pathways and Can Produce Hyperalgesia

Local tissue damage activates a variety of cells, which release inflammatory mediators\(^1,2\)

### Peripheral mediators of inflammation

- Macrophage
- Mast cell
- Tissue damage
- Platelets
- Immune cells
- Substance P
- CGRP

**References:**


HTX-034 is an investigational new drug and not approved by the FDA
**HTX-034 Produces Complete Elimination of Pain Through 7 Days in Pig Postoperative Pain Model**

<table>
<thead>
<tr>
<th>Withdrawal Force (g)</th>
<th>Saline Placebo</th>
<th>Liposomal Bupivacaine</th>
<th>HTX-011</th>
<th>HTX-034 (Cohort 1)</th>
<th>HTX-034 (Cohort 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -1</td>
<td>50</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>1h</td>
<td>40</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>3h</td>
<td>30</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>5h</td>
<td>20</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 2</td>
<td>10</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 3</td>
<td>5</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 4</td>
<td>0</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 5</td>
<td>0</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 6</td>
<td>0</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Day 7</td>
<td>0</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
</tbody>
</table>

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

---

HTX-011 & HTX-034 are investigational new drugs and not approved by the FDA.
CINV Commercial Products
With CINVANTI Leading the Way, Heron’s CINV Portfolio Achieved 2019 Net Sales of $145.7M, an 88% Increase from 2018

- Launch of generic Emend IV in September resulted in a small decline in CINVANTI sales in 4Q
  - Clinic-based practices are much faster to take advantage of the arbitrage
- SUSTOL sales declined in 4Q due to the Refresh Program; sales should return in 1Q2021

CINV portfolio net sales by quarter

<table>
<thead>
<tr>
<th>Quarter</th>
<th>CINVANTI (Millions)</th>
<th>SUSTOL (Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2016</td>
<td>$-1.3</td>
<td>$3.6</td>
</tr>
<tr>
<td>Q1 2017</td>
<td>$3.6</td>
<td>$8.5</td>
</tr>
<tr>
<td>Q2 2017</td>
<td>$8.6</td>
<td>$8.6</td>
</tr>
<tr>
<td>Q3 2017</td>
<td>$10.1</td>
<td>$10.1</td>
</tr>
<tr>
<td>Q4 2017</td>
<td>$11.6</td>
<td>$11.2</td>
</tr>
<tr>
<td>Q1 2018</td>
<td>$11.2</td>
<td>$16.4</td>
</tr>
<tr>
<td>Q2 2018</td>
<td>$16.4</td>
<td>$16.4</td>
</tr>
<tr>
<td>Q3 2018</td>
<td>$17.3</td>
<td>$19.8</td>
</tr>
<tr>
<td>Q4 2018</td>
<td>$19.8</td>
<td>$23.4</td>
</tr>
<tr>
<td>Q1 2019</td>
<td>$23.4</td>
<td>$28.0</td>
</tr>
<tr>
<td>Q2 2019</td>
<td>$28.0</td>
<td>$31.6</td>
</tr>
<tr>
<td>Q3 2019</td>
<td>$31.6</td>
<td>$36.7</td>
</tr>
<tr>
<td>Q4 2019</td>
<td>$36.7</td>
<td>$42.6</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>$36.4</td>
<td>$36.4</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>$34.8</td>
<td>$34.4</td>
</tr>
</tbody>
</table>
CINVANTI – Hospital Share/Units Continued to Grow in 4Q2019

SOURCE: 867 1.8.20, IMS DDD 12.27.19
CINVANTI – Clinic Share/Units Declined in 4Q2019 Due to the Emend IV Arbitrage

SOURCE: 867 1.8.20, IMS DDD 12.27.19
CINVANTI Maintains Market Leadership 15 Weeks After the Launch of Multiple EMEND IV Generics

Source: IMS DDD 12.20.19
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
- Practices are staying with CINVANTI due to the improved safety profile they have observed
- CINVANTI has become an established brand across both clinics and hospital capturing 45% of the market in Q3 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.

---

**Sustol and Palo Reimbursement (ASP + 4.3%) Over Time**

- **Branded**
  - Q4 '17: $480
  - Q1 '18: $453
  - Q2 '18: $427
  - Q3 '18: $382
  - Q4 '18: $352
  - Q1 '19: $314
  - Q2 '19: $276
  - Q3 '19: $300
  - Q4 '19: $270
  - Q1 '20: $162

- **Palo Reimbursement (ASP + 4.3%)**
  - Q4 '17: $206
  - Q1 '18: $200
  - Q2 '18: $197
  - Q3 '18: $222
  - Q4 '18: $169
  - Q1 '19: $147
  - Q2 '19: $115
  - Q3 '19: $88
  - Q4 '19: $78
  - Q1 '20: $61

---

**Quarter**

- Q4 '17
- Q1 '18
- Q2 '18
- Q3 '18
- Q4 '18
- Q1 '19
- Q2 '19
- Q3 '19
- Q4 '19
- Q1 '20
2020 CINV Franchise Outlook

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 expect to maintain XX% of our market during the 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 and essentially be over by the end of 2020

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.

CINV Franchise
- 2019 net product sales: ~$145.7M
  - 2019 guidance: $115M - 120M raised to $135M
- 2020 net sales guidance for CINV franchise will be provided after 1Q2020 when the impact of the arbitrage is known
### Financial Summary

**Heron ended 2019 with cash, cash equivalents and short-term investments of ~$391 million.**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Net product sales</td>
<td>$ 42,624</td>
<td>$ 110,885</td>
</tr>
<tr>
<td>Operating expenses(^1)</td>
<td>77,477</td>
<td>262,217</td>
</tr>
<tr>
<td>Other income, net</td>
<td>1,258</td>
<td>4,503</td>
</tr>
<tr>
<td>Net loss(^1)</td>
<td>$(33,595)</td>
<td>$(146,829)</td>
</tr>
<tr>
<td>Net loss per share(^2)</td>
<td>$(0.42)</td>
<td>$(1.85)</td>
</tr>
<tr>
<td>Net cash used in operations</td>
<td>$(25,471)</td>
<td>$(97,603)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condensed Balance Sheet Data (In thousands)</th>
<th>September 30, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents and short-term investments (see note above)</td>
<td>$ 256,278</td>
</tr>
<tr>
<td>Accounts receivable, net</td>
<td>$ 66,955</td>
</tr>
<tr>
<td>Total assets</td>
<td>$ 392,962</td>
</tr>
<tr>
<td>Total stockholders’ equity</td>
<td>$ 285,442</td>
</tr>
</tbody>
</table>

Common shares outstanding at September 30, 2019 totaled 80.0 million. Adjusting for our October 2019 public offering of common stock, as of September 30, 2019, pro forma common shares outstanding totaled 89.9 million.

\(^1\) Includes $9.7 million and $40.3 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2019, respectively.

\(^2\) Based on 79.9 million and 79.3 million weighted-average common shares outstanding for the three and nine months ended September 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>
<tbody>
<tr>
<td>▪ Revised NDA submitted 26 Sep 2019 addressing CRL</td>
<td>▪ 2020 net sales guidance for CINV franchise will be provided after 1Q2020 when the impact of the arbitrage is known</td>
</tr>
<tr>
<td>➢ New PDUFA date: 26 March 2020</td>
<td></td>
</tr>
<tr>
<td>▪ EU MAA filing by Centralised Procedure in March 2019</td>
<td></td>
</tr>
<tr>
<td>➢ Potential CHMP opinion 2Q2020</td>
<td></td>
</tr>
<tr>
<td>▪ Canadian NDS screening completed</td>
<td></td>
</tr>
<tr>
<td>▪ Potential approval in early 3Q2020</td>
<td></td>
</tr>
<tr>
<td>• HOPE Project launched across the US</td>
<td></td>
</tr>
<tr>
<td>• Publication of Phase 3 and Phase 2b studies</td>
<td></td>
</tr>
<tr>
<td>✓ Phase 3 studies published in peer-reviewed journals</td>
<td></td>
</tr>
<tr>
<td>doi:10.1136/rapm-2019-100531</td>
<td></td>
</tr>
<tr>
<td>➢ EPOCH 2: Hernia. doi: 10.1007/s10029-019-02023-6</td>
<td></td>
</tr>
<tr>
<td>• Phase 2 with HTX-034 planned for 1Q2020</td>
<td></td>
</tr>
</tbody>
</table>

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