Company Update

June 2015
Legal Disclaimer

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve risks and uncertainties, including uncertainties associated with the development, regulatory approval, manufacture, launch and acceptance of new products, completion of clinical studies and the results thereof, the ability to establish strategic alliances and/or acquire desirable assets, progress in research and development programs and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. The Company's lead product candidate, SUSTOL, which is discussed in this presentation, has not been approved by the FDA or any other regulatory authority. Actual results may differ materially from the results anticipated in our forward-looking statements. We caution investors that forward-looking statements reflect our analysis only on their stated date. We do not intend to update them except as required by law.
## Status of Development Programs

<table>
<thead>
<tr>
<th></th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
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<tbody>
<tr>
<td><strong>SUSTOL (APF530)</strong></td>
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<tr>
<td>CINV: Acute- and Delayed-Onset after MEC, and Acute-Onset after HEC</td>
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<tr>
<td><strong>HTX-011</strong></td>
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<tr>
<td>Bupivacaine + meloxicam for post-operative pain</td>
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<tr>
<td><strong>HTX-019</strong></td>
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<tr>
<td>Intravenous NK₁ for CINV</td>
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<td></td>
<td></td>
<td>505(b)(2) registration pathway should lead to NDA filing 2H2016</td>
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<tr>
<td><strong>HTX-003</strong></td>
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<tr>
<td>30-Day Buprenorphine for chronic pain and addiction</td>
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Heron owns worldwide rights to all these programs
CINV FRANCHISE
CINV Highlights

- **SUSTOL®** (granisetron injection, extended release), is a long-acting, injectable product for the prevention of chemotherapy-induced nausea and vomiting (CINV)
  - 1,341-patient, randomized, controlled, Phase 3 study demonstrated activity in acute-and delayed-onset CINV after moderately emetogenic chemotherapy (MEC), and acute-onset CINV after highly emetogenic chemotherapy (HEC)
  - **MAGIC**: Complete Response in delayed nausea and vomiting in patients receiving HEC was significantly greater with the SUSTOL-based, three-drug regimen compared to standard-of-care. Significantly more patients had no or infrequent nausea with SUSTOL and SUSTOL patients reported a significantly greater satisfaction with therapy

- **HTX-019** is a proprietary intravenous (IV) formulation of aprepitant, an NK₁ receptor antagonist and is distinguished from the only IV NK₁ receptor antagonist presently approved in the U.S. in that it does not contain polysorbate 80, which may cause infusion site reactions, hypersensitivity or other adverse reactions in some patients.

- **Rapid development utilizing the 505(b)(2) registration pathway is anticipated to achieve NDA submission in 2H2016**
Granisetron is released rapidly following injection of APF530 and continues to be released for 5-days, providing long-acting coverage for CINV.

*Data from patent application 20120258164 for transdermal granisetron*
SUSTOL Pivotal Phase 3 Study
Overview

• Randomized, controlled, multi-center study
• 1,341 patients in primary efficacy population stratified by chemotherapy using Hesketh criteria
• Primary end point compared complete response between groups in both the acute (day 1) and delayed (days 2-5) phase
  – Complete response defined as no emesis and no rescue medications
• Achieved primary endpoint of non-inferiority for acute and delayed CINV with MEC, and acute CINV with HEC
FDA-Requested ASCO 2011 Reanalysis Improves Difference Between SUSTOL and Aloxi in HEC Patients

Protocol Specified HEC Population

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloxi 0.25 mg</td>
<td>81</td>
<td>64</td>
</tr>
<tr>
<td>APF530 10 mg</td>
<td></td>
<td>67</td>
</tr>
</tbody>
</table>

ASCO 2011 Guideline HEC Population

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloxi 0.25 mg</td>
<td>67</td>
<td>51</td>
</tr>
<tr>
<td>APF530 10 mg</td>
<td>75</td>
<td>56</td>
</tr>
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</table>
A Delayed-HEC Indication Would Provide Clear Differentiation in an Important Segment of the CINV Market

Distribution of Aloxi Sales\(^1\)

- **HEC**: HEC regimens account for ~20% (500K) of palonosetron administrations
- **LEC**: This is the same segment of the CINV market where NK\(_1\) receptor antagonists are extensively used
- **Minimal**

\(^1\) IntrinsiQ data from July 2012 – June 2013
MAGIC Study Design

The First Three-Drug Regimen Versus Three-Drug Regimen

Efficacy Study

942 patients scheduled to receive HEC* randomized 1:1

**Standard-of-Care**
- Ondansetron 0.15 mg/kg IV (up to 16 mg IV) d1
- + fosaprepitant 150 mg IV d1
- + dexamethasone 12 mg IV d1 & 8 mg PO QD d2 + 8 mg PO BID d3-4 + placebo SC d1

**SUSTOL** (granisetron injection, extended release) SC d1
- + fosaprepitant 150 mg IV d1
- + dexamethasone 12 mg IV d1 & 8 mg PO QD d2 + 8 mg PO BID d3-4 + placebo IV d1

Prospectively Defined Primary Endpoint:
Complete Response in the Delayed-Onset Phase

*HEC agents as defined in the 2011 ASCO CINV guidelines
## MAGIC Patient Disposition: Arms Well Balanced

<table>
<thead>
<tr>
<th></th>
<th>SUSTOL Regimen</th>
<th>Ondansetron Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized (ITT Population)</td>
<td>471</td>
<td>471</td>
</tr>
<tr>
<td>Treated (Safety Population)</td>
<td>456 (96.8%)</td>
<td>459 (97.5%)</td>
</tr>
<tr>
<td>Modified ITT Population</td>
<td>450 (95.5%)</td>
<td>452 (96.0%)</td>
</tr>
<tr>
<td>Cisplatin Regimen ≥50 mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>124 (27.6%)</td>
<td>128 (28.3%)</td>
</tr>
<tr>
<td>No</td>
<td>326 (72.4%)</td>
<td>324 (71.7%)</td>
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</table>
MAGIC Primary Analysis: SUSTOL Regimen Statistically Superior to Standard-of-Care

Delayed (24 to 120 Hours) Nausea and Vomiting after HEC

Complete Response Rate

<table>
<thead>
<tr>
<th></th>
<th>SUSTOL Regimen</th>
<th>Standard-of-Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>64.7%</td>
<td>p = 0.014</td>
<td></td>
</tr>
<tr>
<td>Delta = 8%</td>
<td></td>
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</tbody>
</table>

Complete Response defined as no emesis episodes and no rescue medications
SUSTOL Provides an Important Benefit in Nausea Reduction and Patient QoL

<table>
<thead>
<tr>
<th>Results for Delayed Phase (24 to 120 Hours)</th>
<th>p-value$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>0.014</td>
</tr>
<tr>
<td>Complete Control (CR plus no more than mild nausea)</td>
<td>0.022</td>
</tr>
<tr>
<td>No or Infrequent Nausea$^2$</td>
<td>0.032</td>
</tr>
<tr>
<td>Global Satisfaction with Therapy$^3$</td>
<td>0.040</td>
</tr>
</tbody>
</table>

1. P-values are based on the Cochran-Mantel-Haenszel chi-square test controlled by use of cisplatin, not adjusted for multiplicity
2. Patients with zero, one or two episodes of nausea
3. Patient quality of life (QoL) question: How satisfied are you with the study medication’s ability to control your nausea and vomiting?
MAGIC Safety Summary

- No clinically significant differences between arms on safety
  - No significant differences in SAEs
  - No significant differences in discontinuations, or discontinuations due to adverse events
- Consistent with previous trials, injection site reactions were relatively common, but generally mild and usually resolved prior to the next cycle of chemotherapy
  - Not an impediment to treatment as evidenced by the significant improvement in patient satisfaction with SUSTOL therapy, with over 80% of patients either very satisfied or satisfied with SUSTOL treatment
Conclusion

SUSTOL, as part of a three-drug regimen, is the first 5-HT₃ antagonist to demonstrate superiority to a standard-of-care, three-drug regimen in delayed nausea and vomiting in patients receiving HEC

- Detailed results to be presented at future medical meeting
- NDA resubmission on schedule for mid-2015
SUSTOL Has the Potential to be the Next Generation 5-HT₃ Receptor Antagonist

<table>
<thead>
<tr>
<th>5-HT₃ RAs</th>
<th>1st generation</th>
<th>2nd generation</th>
<th>3rd generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Products</td>
<td>ondansetron</td>
<td>palonosetron</td>
<td>SUSTOL</td>
</tr>
<tr>
<td>Duration of action</td>
<td>Short acting 8 hr half-life</td>
<td>Longer acting 40 hr half-life</td>
<td>Long acting PK profile 5-7 days</td>
</tr>
<tr>
<td>Indications</td>
<td>Prevention of CINV in emetogenic chemo including high-dose cisplatin</td>
<td>MEC – acute &amp; delayed CINV HEC – acute CINV</td>
<td>MEC – acute &amp; delayed CINV HEC – acute &amp; delayed CINV*</td>
</tr>
</tbody>
</table>

*Obtaining delayed nausea and vomiting after HEC will be based on FDA’s assessment of MAGIC trial results
SUSTOL REGULATORY STATUS
How We Are Addressing the CRL

• Chemistry, Manufacturing, and Controls  ✔
  – Sites with PAI issues have been eliminated from the supply chain, with work transferred to a well-established site with no PAI issues
    • Transition is complete, with secondary benefit of improvement in the COGS
      – New in-vitro release method has been developed and validated
      – Multiple validation batches of finished product have now been completed
• Human Factors Validation Study  ✔
  – Successfully completed
• Re-analysis of Phase 3 using new ASCO 2011 Guidelines  ✔
  – Re-analysis complete
  – Complete dataset and programs supplied to FDA and found acceptable
• NDA resubmission expected mid-year 2015 with positive MAGIC trial
HTX-019: Aprepitant IV

• HTX-019 is a proprietary IV formulation of aprepitant, an NK₁ receptor antagonist. NK₁ receptor antagonists are recommended to be used in combination with 5-HT₃ receptor antagonists for prevention of CINV.

• Primary Composition of Matter patent protection of aprepitant expired April 2015
  – Secondary patent on polymorphic form not relevant to intravenous formulation

• The other commercially available IV NK₁ receptor antagonist contains polysorbate 80, which has been shown to cause infusion site reactions, hypersensitivity and other reactions in some patients. HTX-019 is polysorbate 80 free and may avoid some of these adverse reactions.

• Product should receive a unique J-code and compete directly with EMEND® IV (fosaprepitant)

• Rapid development utilizing the 505(b)(2) registration pathway is anticipated to achieve NDA submission in 2H2016 based on bioequivalence (discussed with FDA)

1. LA Norris, et al. 2010 COMMUNITY ONCOLOGY; Polysorbate 80 hypersensitivity reactions: a renewed call to action
CINV FRANCHISE

COMMERCIAL OPPORTUNITY
Heron has the opportunity to establish a long-term, dominant position in a CINV market that has over 3.6M penetrable units.

**Injectable Drugs for the Prevention of CINV**

*Number of Package Units Sold by Quarter*

Data is Package Units; Ondansetron units reflect only 2 mg/ml and 32mg/50 ml strength sizes.
HEC Regimens Represent a Significant Market Opportunity for SUSTOL and HTX-019

Of All HEC Administrations, ~20% Are Given Without Concomitant IV 5-HT3 – Inconsistent With Clinical Guidelines

HEC Regimens Account For ~20% (500K) of Palonosetron Administrations

Source: IntrinsiQ data from July 2012 – June 2013
POST-OPERATIVE PAIN PROGRAM
Heron Post-Operative Pain Program

Target Product Profile for Best-in-Class Product:

♦ Maximal pain relief that lasts for 2-3 days
♦ Maximal reduction of opioid use
♦ Maximal reduction of length of hospital stay
♦ Elimination of dose-limiting peak of bupivacaine
♦ Easy to use for a large variety of procedures
♦ Does not require refrigeration or special handling

Introducing HTX-011:

♦ An injectable pain therapeutic that utilizes proprietary Biochronomer® polymer-based drug delivery platform technology
♦ Designed to deliver both bupivacaine (anesthetic) and meloxicam (anti-inflammatory) evenly over 2-3 days without a large initial peak

*HTX-011 builds on other innovations in the category and has best-in-class potential*
Local Anesthetics Exist in a Balance Between Water-Soluble and Lipid-Soluble Forms

- Local anesthetics have pKa values > 7.4, so at normal physiologic pH of 7.4, the majority of molecules exist as the water-soluble quaternary salt not able to penetrate nerve cell membrane.

Local anesthetic nerve penetration model adapted from Becker and Reed, Anesth Prog 53:98–109 2006
Local Anesthetics Exist in a Balance Between Water-Soluble and Lipid-Soluble Forms

Acidic Environment Shifts the Balance to Ionized Form Unable to Penetrate Nerve Cell Membrane

- The acidic environment associated with inflammation shifts the balance further to the left, resulting in far less drug penetrating the nerve membrane and reduced anesthetic effects.
- With a pKa of 8.1, bupivacaine is very sensitive to reduced pH

Local anesthetic nerve penetration model adapted from Becker and Reed, Anesth Prog 53:98–109 2006
HTX-011 Significantly Superior to EXPAREL at 24-72 Hours

1. Study #1; All studies used the post-operative pain model in pigs from Castle et al, 2013 EPJ
2. Study #2 compared <½ expected human dose of Biochronomer bupivacaine/meloxicam formulation to the human dose of EXPAREL® (40% smaller incision used with EXPAREL)

(n=4 pigs, except at 120 hrs for Study #2: preliminary results from 2 animals)
HTX-011 Shows Durable Response in Sciatic Nerve Block Model in Pigs

![Graph showing durable response in sciatic nerve block model in pigs with force in grams measured over different time periods (0.5H to 48H) for Saline, Bupivacaine 25 mg, Exparel 106 mg, and HTX-011 100 mg.](image-url)
HTX-011 Phase 1 Single-Ascending-Dose Study

**Design**
- Randomized, Single-Blind, Placebo-Controlled
- 3 Single Rising Dose Cohorts
- 144 hr pharmacokinetic & pharmacodynamic assessments

**Cohort 1**
- 100 mg HTX-011 (5 active:1 placebo)
- Min 7-day Observation Safety PK evaluation

**Cohort 2**
- 200 mg HTX-011 (5 active:1 placebo)
- Min 7-day Observation Safety PK evaluation

**Cohort 3**
- 400 mg HTX-011 (5 active:1 placebo)
Plasma Concentrations of Bupivacaine Observed with HTX-011
Mechanical Detection Threshold Using von Frey Fibers

Force where Subject No Longer Feels the Fiber

Force (mN) when Sensation Lost

HOURES

0 0.5 1 1.5 2 3 4 5 6 7 8 9 10 12 14 16 18 20 22 24 26 28 30

HTX-011 400 mg (n=5) Placebo (n=3)

*Combined placebo data from all cohorts
Pharmacodynamic Effects of HTX-011 Correlate with Pharmacokinetic Profile

*Combined placebo data from all cohorts
Safety

• No serious adverse events or premature discontinuations
• No clinically relevant ECG changes
• No clinically relevant laboratory changes
• Only adverse events considered possibly related to drug were associated with the subcutaneous administration of the product: mild redness and bruising at some injection sites
Next Steps for Post-Operative Pain Program

• SAD evaluation to complete in 1Q15 ✓
• Initiate Phase 2 in 2Q15
  – Bunionectomy study scheduled to start late 2Q
    • 20 patients will receive HTX-011 200 mg
    • 20 patients will receive HTX-011 400 mg
    • 20 patients will receive placebo
• Hernia and plastic procedures will likely follow bunion
• Completing toxicology for nerve-block and orthopedic indications to allow expansion of program
HTX-003
LONG-ACTING BUPRENORPHINE
FOR CHRONIC PAIN AND ADDICTION
30-Day Buprenorphine Comparison to Competitive Products in Development*

*RB Pharma is from US2013/0210853; Camurus data from US2013/0190341
# Financial Summary

## Summary Statement of Operations

<table>
<thead>
<tr>
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<th>Three Months Ended March 31, 2015</th>
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<tbody>
<tr>
<td><strong>Revenue</strong></td>
<td>$ _</td>
</tr>
<tr>
<td><strong>Operating expenses</strong></td>
<td>20,360</td>
</tr>
<tr>
<td><strong>Other income (expenses)</strong></td>
<td>(210)</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>$ (20,570)</td>
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<tr>
<td><strong>Net loss per share(^1)</strong></td>
<td>$ (0.70)</td>
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## Condensed Balance Sheet Data

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<th>March 31, 2015</th>
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<tbody>
<tr>
<td><strong>Cash and cash equivalents</strong></td>
<td>$ 55,556</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$ 59,627</td>
</tr>
<tr>
<td><strong>Total stockholders’ equity</strong></td>
<td>$ 48,001</td>
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</table>

\(^1\) Based on 29.4 million weighted average common shares outstanding for the period ended March 31, 2015