



JP Morgan Conference January 2018



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 potential market opportunity for SUSTOL®, CINVANTITM and HTX-011; the potential net sales for SUSTOL® and CINVANTITM; the timing of completion and results of the Phase 2 and Phase 3 trials for HTX-011; the timing of the NDA filing for HTX-011; the projected sufficiency of our capital position for future periods; the progress in the research and development of HTX-011 and our other programs, including the timing of clinical and manufacturing activities, and safety and efficacy results from our studies; 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.



Status of Product Portfolio



Pain

SUSTOL®

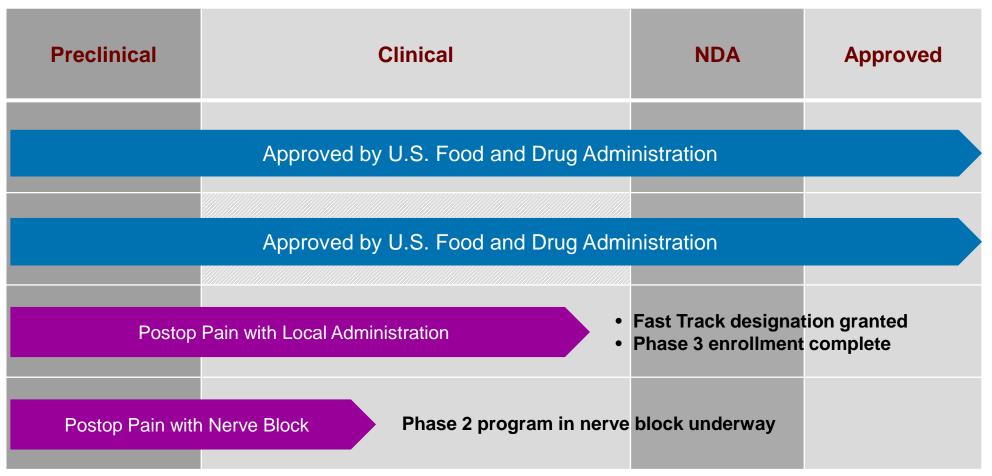
(granisetron) extendedrelease injection

CINVANTITM

(aprepitant) injectable emulsion

HTX-011 bupivacaine + meloxicam ER Local Administration

HTX-011 bupivacaine + meloxicam ER Nerve Block









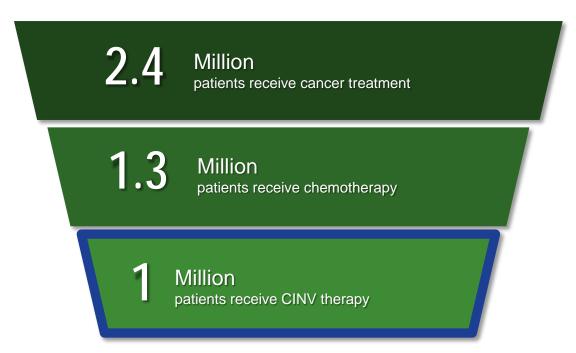
CINV Commercial Products



The Management of CINV Remains a Significant Clinical Challenge



> In the U.S., over 1 million people receive CINV therapy each year



Unmet Need

- Despite treatment with previously available therapies, many patients experience breakthrough CINV particularly in the delayed phase (days 2-5)
- CINV has a high clinical burden impacting patients' QOL and cancer treatment
- Prior to SUSTOL®, there were no single-agent 5-HT₃ antagonists indicated to prevent delayed CINV from a HEC regimen (including palonosetron)
- Prior to CINVANTI[®], there were no NK₁ receptor antagonists approved for both acute and delayed CINV that were free of synthetic surfactants
- HCPs cite the need for new therapies that deliver long-acting CINV prevention in both MEC and HEC

5-HT $_3$, serotonin; CINV, chemotherapy induced nausea and vomiting; HCP, health care professional; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; QoL, quality of life; NK $_1$, substance P neurokinin-1

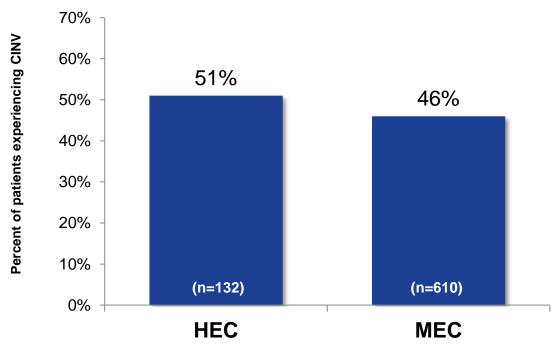


Despite Previously Available Therapies, a Large Percentage of Patients Experience Breakthrough CINV

V

% of MEC/HEC patients with breakthrough CINV despite prophylaxis

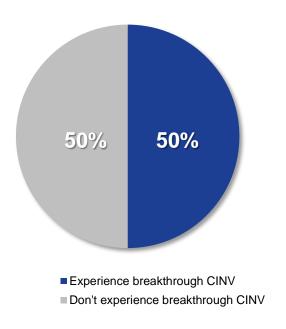
Community practice observational study



Data from a prospective observational study enrolling chemotherapy-naive patients who received single-day HEC or MEC at four oncology practice networks, all using electronic medical record (EMR) systems, in Georgia, Tennessee, and Florida. CINV = emesis or clinically significant nausea on days 1-5. Regimen for HEC was a 5-HT₃ + NK₁+ dexamethasone (CS) on Day 1; NK₁ on Days 2-3; CS on Days 2-4; For MEC it was 5-HT₃ + NK₁ + CS on Day 1; 5-HT₃, NK₁, or CS on Days 2-3

% of MEC/HEC patients with breakthrough CINV despite prophylaxis

Physician perception



Source: Instar Market Research, Dec 2015, N=75 oncologists

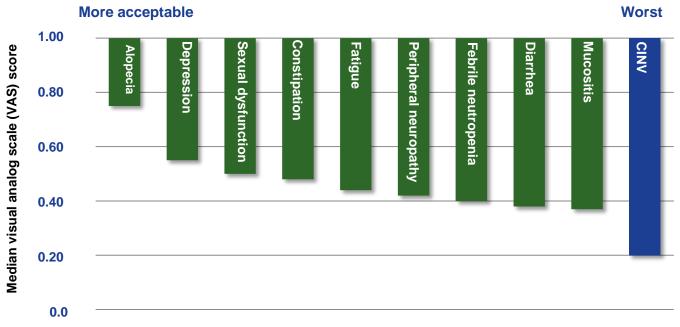


Source: Gilmore JW et al. J Oncol. 2014;10:68-74.

CINV Has a High Clinical Burden – Impacting Patients' QOL and Cancer Treatment

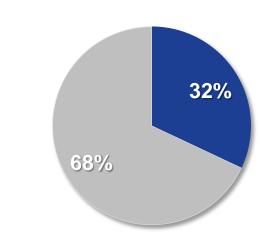


Patients identified CINV as the side effect of chemotherapy they most wanted to avoid



VAS scored from 0 to 1 where 0 is the least favorable and 1 is the most acceptable/favorable

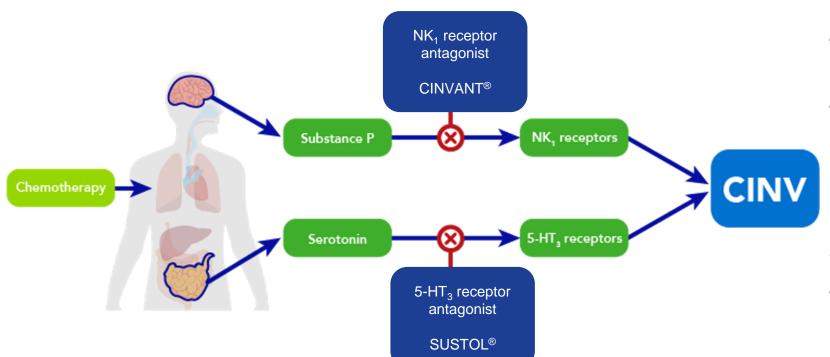
CINV commonly disrupts patients' cancer treatment



32% of oncology HCPs delayed or discontinued chemotherapy due to CINV within the prior year



CINV Prophylaxis Typically Requires Two Complimentary Mechanisms of Action



NK₁ receptor antagonists

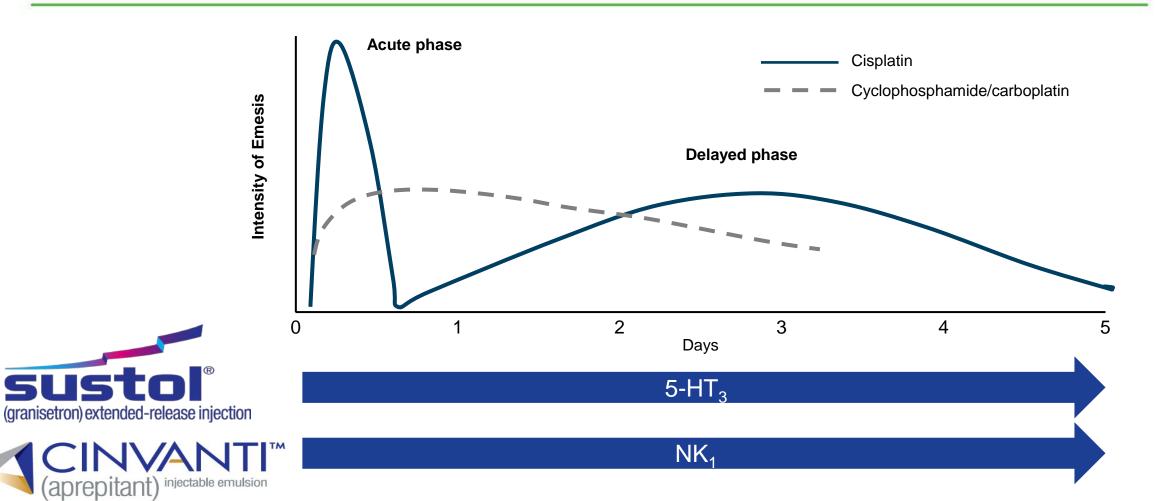
- Substance P is primary driver of delayed CINV, but related to ~15% of acute failures
- EMEND® IV (fosaprepitant), which has 90% share of the US NK₁ market, contains the synthetic surfactant polysorbate 80 that has been associated with hypersensitivity and infusion site reactions

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

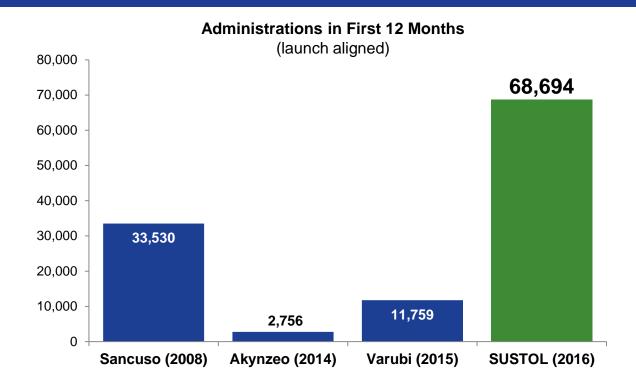


Heron Therapeutics Is the Only Company with Two Single-Agent Products Approved for Prevention of Acute and Delayed CINV



SUSTOL® Outperformed ALL Recent CINV New Brand Launches

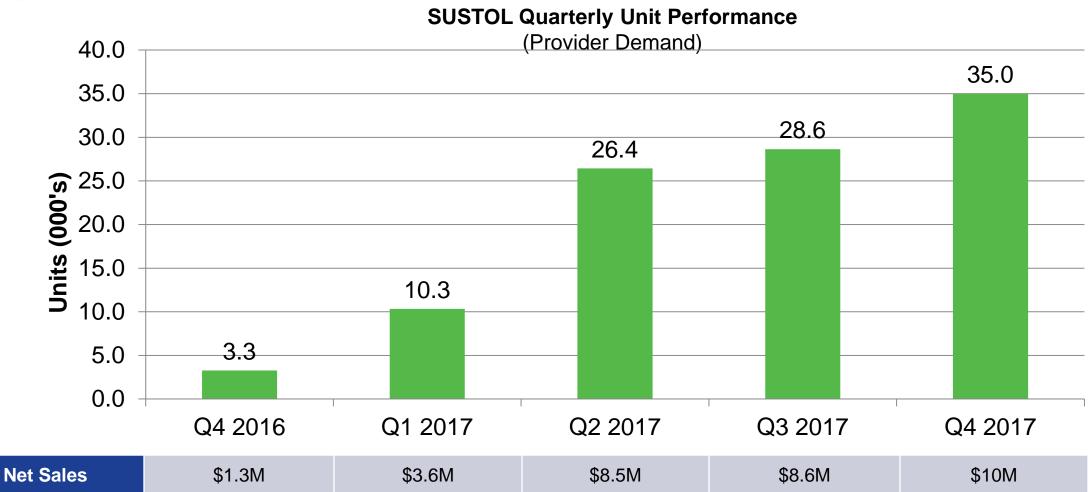
CINV New Brand Launches Since 2008



Sources: IMS DDD; Heron actuals (distributor 867 reports) are for 4Q2016 through 3Q2017; due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2.



SUSTOL® Net Revenue Up 16% to \$10 Million in Q4 Over 100,000 Units of SUSTOL Sold to Practices in 2017 Full Year 2017 Net Revenue Was Approximately \$31M



Source: Heron 867 data

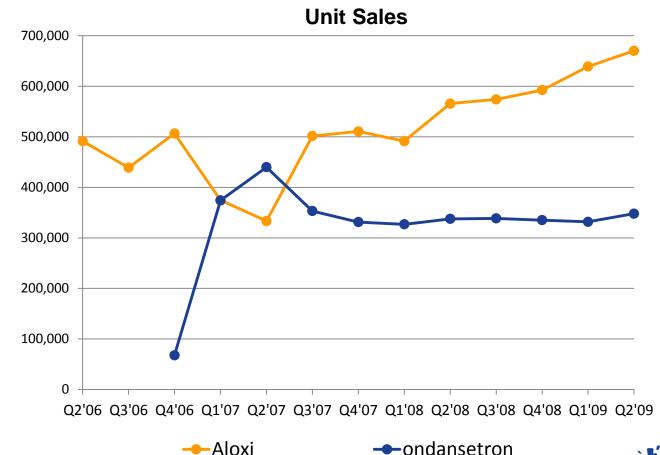
16%↑ —



Market Insights Suggest SUSTOL® May Decline Modestly Through the Arbitrage and Grow Thereafter – Consistent with Aloxi® Analogue

Recent Market Insights

- Practices that are converting to SUSTOL are likely to maintain use¹
- ~67% of current "dabblers" likely to stop or reduce use of SUSTOL during arbitrage²
- ~20% of SUSTOL non-users would consider initiating SUSTOL during arbitrage²
 - "If generic Aloxi is available, it's going to allow me to start using SUSTOL without having to worry about maintaining my Aloxi contract"
 PM
- ~55% of HCPs said they would be interested in using SUSTOL post-arbitrage (equating to an addressable market of ~650K units)²
 - "When ASP [erodes], we would switch all patients from generic Aloxi to SUSTOL." – PM
 - "SUSTOL usage would increase. There's no reason to keep people on generic Aloxi." – PM



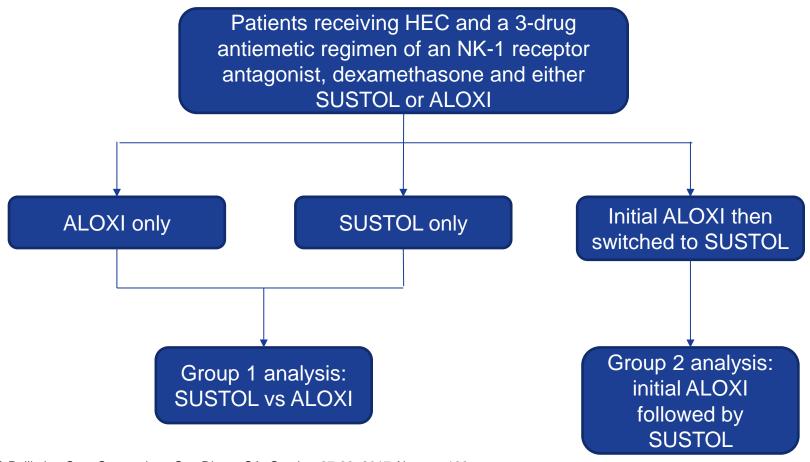


¹ Customer discussions

² Putnam Associates Qual Research Findings, June 2017

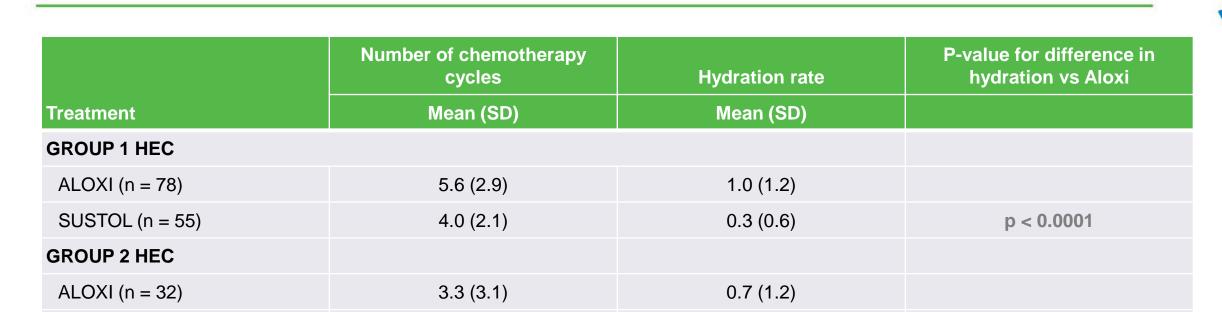
Study Conducted to Evaluate Hydration Rates With SUSTOL® vs ALOXI® Based on Prior Observation of Fewer Unscheduled Visits Due to CINV by HEC Patients Receiving SUSTOL

STUDY DESIGN





HEC Patients Treated With SUSTOL Experienced Significantly Lower Requirements For Hydration Compared to ALOXI



0.5 (1.0)

• In Group 1, **40**% of patients treated with SUSTOL required hydration compared to **81**% of patients treated with ALOXI.

2.9 (2.0)



p = 0.028

SUSTOL (n = 32)

CINVANTI™ Now Launched

 CINVANTI™ is the first and only polysorbate 80-free IV NK₁ receptor antagonist approved for the prevention of <u>both</u> acute and delayed CINV



CINVANTI™ is indicated in adults, in combination with other antiemetic agents, 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).

Please see Full Prescribing Information on www.CINVANTI.com

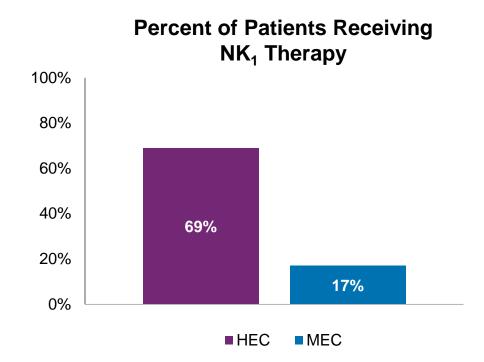


Despite an NCCN Category 1 Recommendation, NK₁'s are Underutilized



HEC ■ 5-HT₃ ■ dexamethasone ■ NK₁ ± olanzapine ■ MEC ■ 5-HT₃ ■ dexamethasone ± NK₁ ± olanzapine

NCCN 2017



IPSOS "US Tandem Oncology Monitor Anti-Emetics Report" is based on chart audit data of 68,437 patient records between 2015 and 2016



Aprepitant Has Provided Trusted Efficacy for CINV Prevention for Nearly 15 Years

Overview of Aprepitant

FDA approved	2003
NCCN Category 1 recommendation	Yes
Phase 3/4 clinical trials*	22
Patients studied in clinical trials*	7100+

~1.4 million administrations per year*^ ~90% of which is IV fosaprepitant

Aprepitant is the only single-agent NK₁ that:

- Is FDA-approved for prevention of CINV in both acute and delayed phases
- Can be administered to patients receiving chemotherapy regardless of cycle length

No other NK₁ has been proven more effective than aprepitant



CINVANTI™ Is the First and Only Polysorbate 80-Free IV NK₁ Approved for the Prevention of Both Acute and Delayed CINV

	CINVANTI™ IV	EMEND® IV	Varubi [®] IV	
	aprepitant emulsion	fosaprepitant	rolapitant	
Indicated for prevention of both acute and delayed CINV	Yes	Yes	No	
Can be administered regardless of chemo cycle length	Yes	Yes	No	
Preliminary data supports administration by IV push	Yes¹	No	No	
Polysorbate 80-free formulation	Yes	No	Yes	
Emulsion formulation requires no reconstitution	Yes	No	Yes	
Aloxi® and dexamethasone are stable when added to the product ²	Yes	No	Yes	
Can be stored at room temperature for 60 days	Yes	No	Yes	

^{1.} FDA-approved dosing administration included in the US prescribing information (PI) for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.

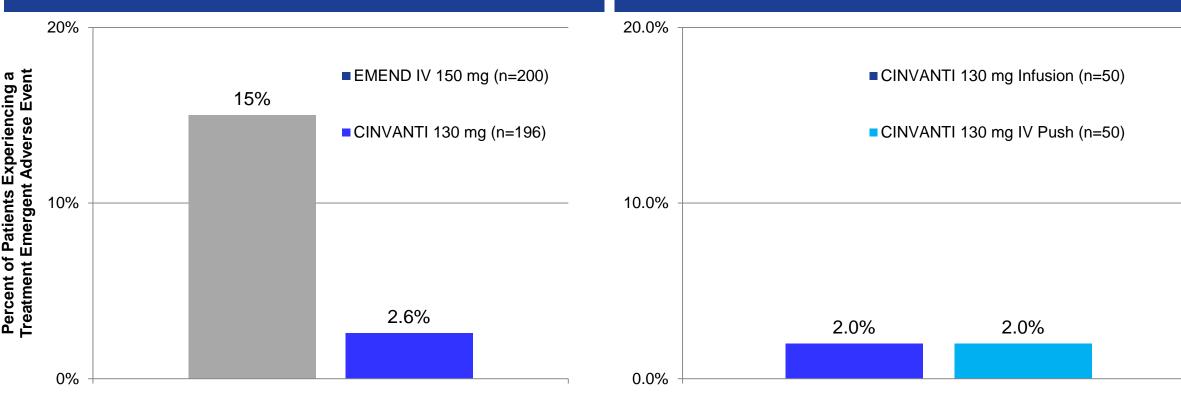


^{2.} Aloxi® PI states that it should not be mixed with other drugs

CINVANTI® Was Well Tolerated Given as an Infusion or as an IV Push

CINVANTI Produced Fewer TEAEs Within 30 Minutes of Infusion Than EMEND IV¹

CINVANTI Was Well Tolerated When Given by Both 30-minute Infusion and 2-minute IV Push²



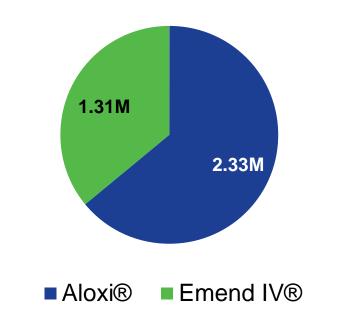
- 1. Data on file.
- 2. FDA-approved dosing administration included in the US prescribing information for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.

With CINVANTI™, Heron Adds a Second Best-In-Class Therapy to Compete in a Branded CINV Market with ~3.6M Annual Units





Leading Branded CINV Products (Annual Units)





2018 CINV Franchise Outlook



SUSTOL®: We continue to expect core SUSTOL business to hold firm and with possibility of modest decline during arbitrage and growth thereafter

- Even with the potential for generic palonosetron, 4th quarter unit sales grew 22%
- Approximately \$31M in net product sales in 2017
- Permanent J-code 1627 granted by CMS; effective January 1, 2018



CINVANTI®

- Commercially available in the US
- We believe it has the best overall profile compared to the other available NK₁ antagonists
- Offers strong strategic and operational fit with existing commercial organization to win in a branded
 CINV market with ~3.6M annual units

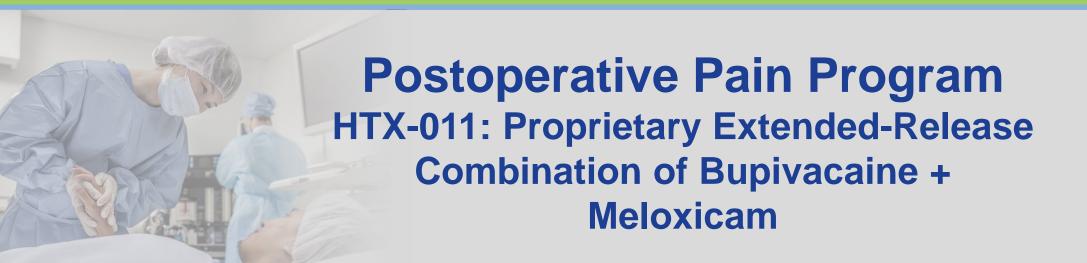


CINV Franchise

CINV franchise 2018 guidance of \$60M-\$70M in net product sales









Postoperative Opioids: A Doorway to Addiction



surgical procedures happen in the United States.

80%

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

As many as

6.5%

of patients that take
opioids to manage pain
after surgery may become persistent opioid
users.

That equals about

2.6 MILLION PEOPLE

Of these 2.6 million persistent opioid users.

26% or 676,000

will become addicted to opioids.







70% of all these opioid tablets go unused

In addition, hundreds of millions of

LEFTOVER PILLS

are then brought home from the hospital after surgery

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

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

43%

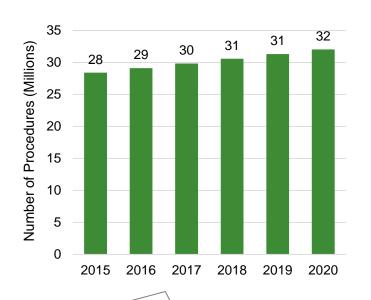
(\$14.2 billion)
of the healthcare costs
associated with addiction can
be attributed to postoperative
pain management.





Market Is Large and Local Anesthetic Use Is Common, but Current Extended Release Anesthetics Have Not Fulfilled the Promise of Long-Acting Pain Relief

Procedures Requiring Postoperative Pain Relief, 2015-2020¹

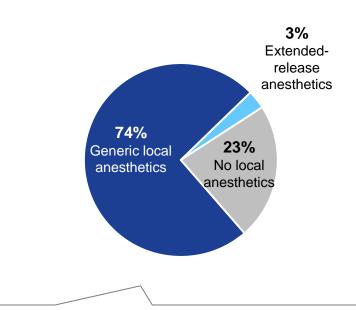


~28M surgeries in 2015 required postoperative pain management with non-OTC pain medications and had sufficient pain to warrant an extended-release local anesthetic

Sources:

- ¹ DRG claims analysis (2015), DRG Postoperative Pain Pharmacor
- ² DRG physician and P&T member interviews (2016; n=106)
- *Based on analysis of current postoperative pain management across 40 target procedures (~28M procedures)

Local Anesthetic Usage Across Key Surgeries, 2015^{1*}



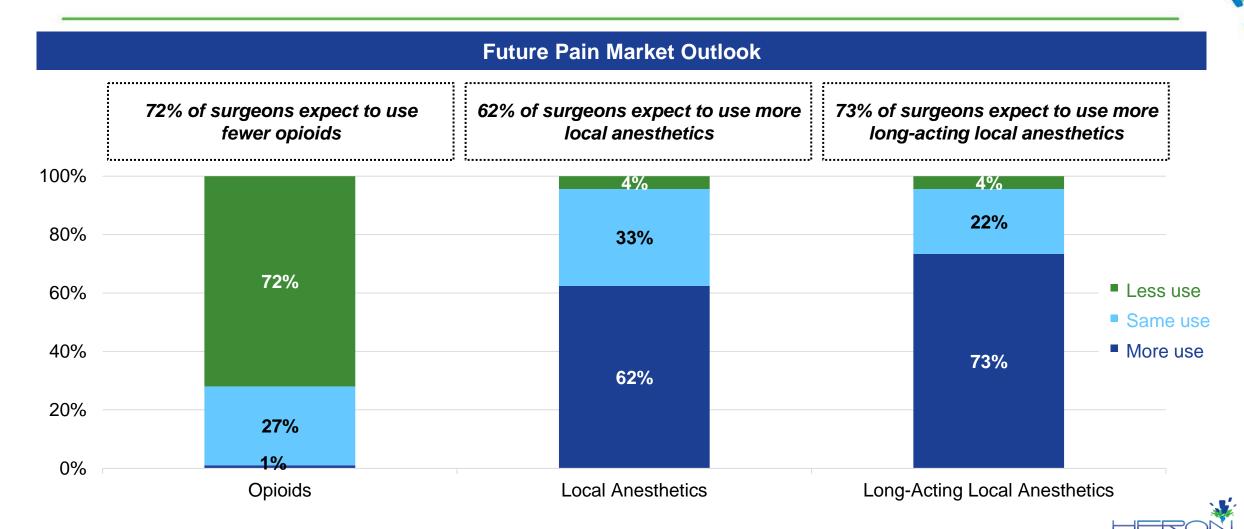
Local anaesthetics (LAs) are used to manage postoperative pain in ~21M procedures in 2015; bupivacaine is the most commonly used LA for local administration with **11M** procedures/year for postop pain

Key Limiters of Liposomal Bupivacaine Market Penetration

- Perceived inability to achieve marketed duration of efficacy²
- No large scale studies have reproducibly shown superiority versus bupivacaine solution
- HCPs not persuaded that incremental efficacy is worth the cost
- Because of the above, there are significant formulary access restrictions²
 - Restricted by Specialty
 - Restricted by Procedure
 - Not on Formulary
 - Very low penetration in ASC and outpatient settings¹



Surgeons Expect to Use Less Opioids and More Long-Acting Local Anesthetics as Better Options Become Available



Large US Market Opportunity

Theoretical and Target Market

~28M Annual US Surgical Procedures Requiring Postoperative Pain Management (\$7.0 – 8.4B)

~15M procedures	~6M procedures	~7M procedures	
Initial Targets Higher volume procedures across 4 major specialties ~ 6.5M Orthopedic procedures ~ 4.3M General Surgery procedures ~ 3.3 M OB/GYN procedures ~ 1.1M Plastic Surgery procedures	Secondary Targets Higher volume procedures in non-core specialties (e.g., ENT, urology, hand, others)	Tertiary Targets Lower volume procedures and procedures where local anesthetics are not widely used today	
\$3.8 – 4.5B	\$1.6 – 1.9B	\$1.7 – 2.1B	

Theoretical Market Size



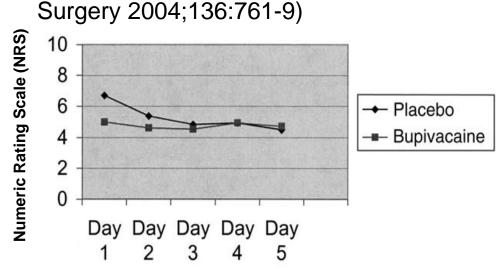
High Procedure Volume in Target Markets Provides a Robust ROW Market Opportunity

Country	Total Surgical Procedures	Total Procedures Requiring Postop Pain Management	Initial Target Procedures	Remaining Secondary, Lower Volume & Procedures Currently Not Using Local Anesthetics
Germany	22,545,000	6,838,000	3,649,000	3,189,000
France	14,545,000	4,357,000	2,292,000	2,065,000
UK UK	13,882,000	3,835,000	1,790,000	2,045,000
Italy	5,637,000	2,530,000	1,919,000	611,000
Canada	3,416,000	1,638,000	1,282,000	356,000
Japan	25,959,000	6,600,000	2,668,000	3,932,000
Total	85,984,000	25,798,000	13,600,000	12,198,000

Why Haven't Extended Release Local Anesthetics Penetrated This Large Market

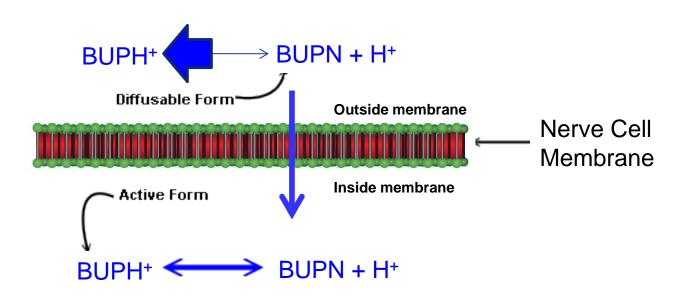
- Regardless of delivery technology, extended release bupivacaine products do not reduce pain sufficiently beyond 24 hours to beat bupivacaine HCI:
 - Exparel[®] (liposomal ER bupivacaine)
 - Xaracoll[™] (bupivacaine collagen matrix)
 - Posimur[™] (SABER-bupivacaine)
 - HTX-002 (Biochronomer ER bupivacaine)
 - ON-Q[®] bupivacaine pump (continuous infusion)

60-Hour Continuous Infusion of Bupivacaine With On-Q Pump in Hernia Repair Was Significantly Different From Placebo for Only 24 hr (Schurr et. al.



Inflammation Plays a Key Role in Pain Management

(Current local anesthetics do not address this)



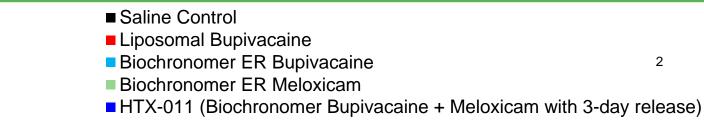
- Surgical insult produces an immediate drop in pH
- As inflammatory cytokines are released and inflammation sets in, the acidic environment is maintained for many days
- The acidic environment shifts the balance to the ionized form, which is unable to enter the nerve
- Acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects^{1,2}
- Bupivacaine is very sensitive to reduced pH
- Addition of meloxicam is designed to help reduce local inflammation and allow bupivacaine to work better in the first several days after surgery

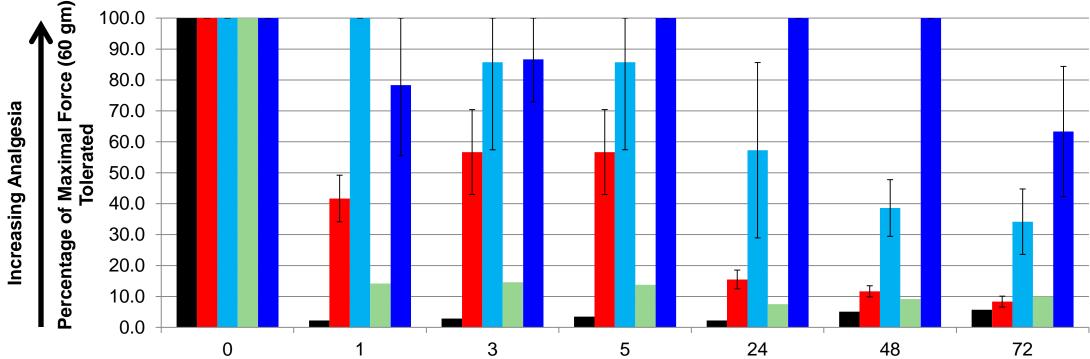


^{1.} Ueno, et al. J of Inflammation Research 1:41-48 2008.

^{2.} Local anesthetic nerve penetration model adapted from Becker and Reed, Anesth Prog 53:98–109 2006

HTX-011 Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery¹





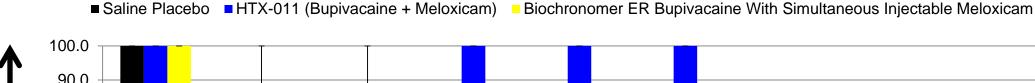
¹ Postoperative pain model in pigs from Castle et al, 2013 EPJ

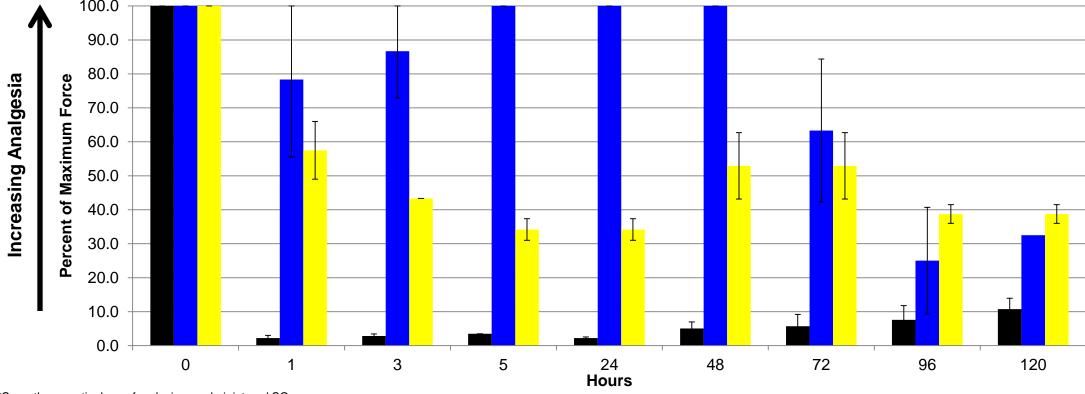


² Human dose of liposomal bupivacaine with 40% smaller incision (n=4 pigs in each arm)

Activity of HTX-011 Cannot Be Replicated By Systemic Administration of Meloxicam Along With ER Bupivacaine

Pig Post-Operative Pain Model

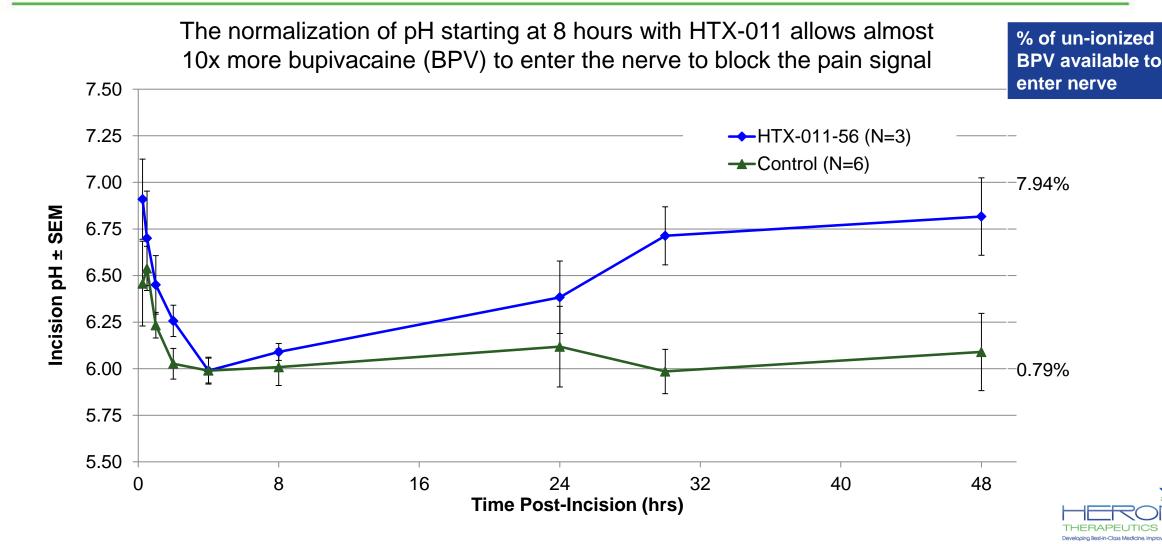




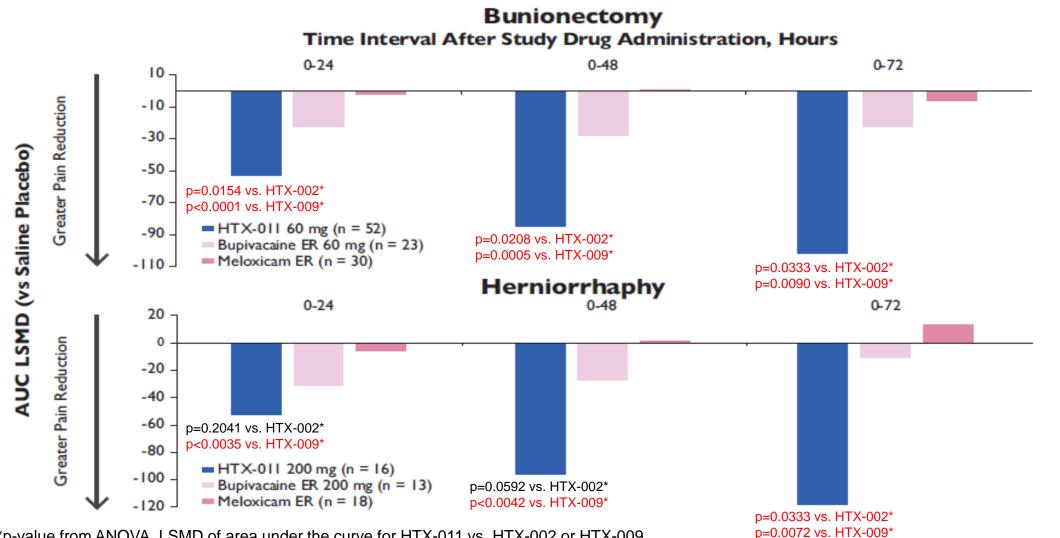
^{*}Supratherapeutic dose of meloxicam administered SQ Post-operative pain model in pigs from Castle et al, 2013 EPJ



The Unique Mechanism of Action of HTX-011 Has Been Demonstrated in the Pig Post-Op Pain Model

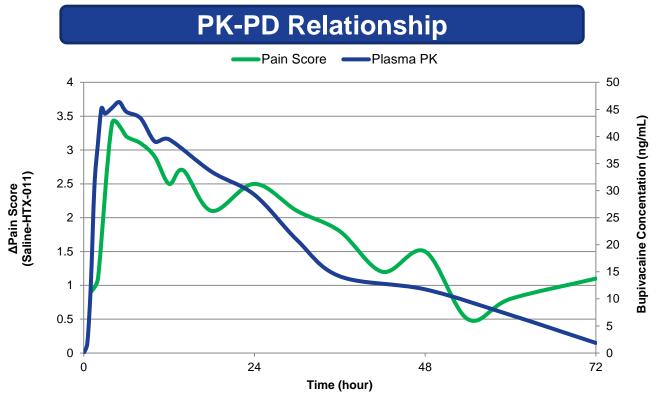


Unique MOA of HTX-011 Produces Significantly Greater Pain Reduction Than ER Versions of Bupivacaine or Meloxicam

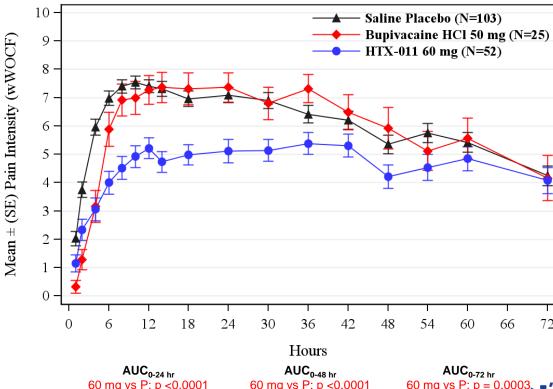


Unique MOA of HTX-011 Results in an Excellent PK-PD Relationship Not Seen With Other ER Bupivacaine Formulations

HTX-011 (bupivacaine + meloxicam)



Mean Pain Intensity vs Time



60 mg vs P: p < 0.0001

60 mg vs B: p = 0.0020

60 mg vs B: p = 0.0020

60 mg vs P: p = 0.0003

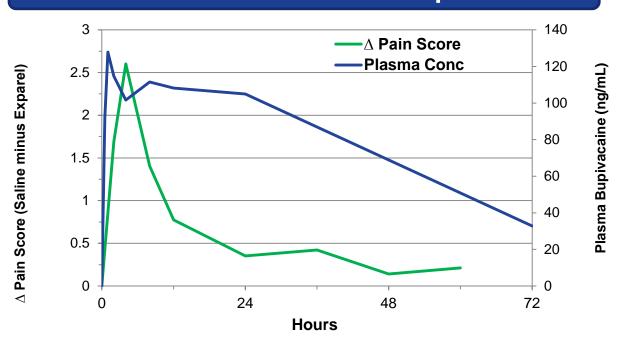
Source: Data on File, Heron Therapeutics, Inc.

*LOCF method used to account for missing data, with wWOCF adjustment for use of rescue medications

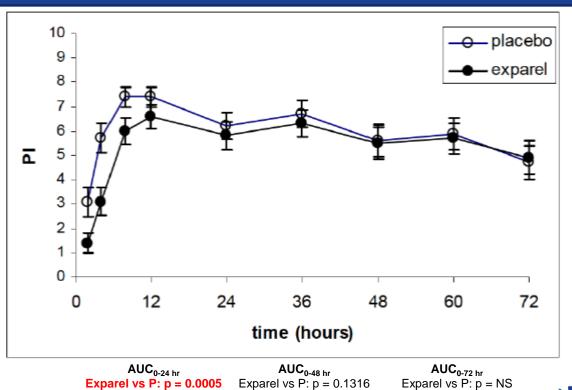
Exparel® Does Not Demonstrate a PK-PD Relationship



No PK-PD Relationship



Mean Pain Intensity vs Time

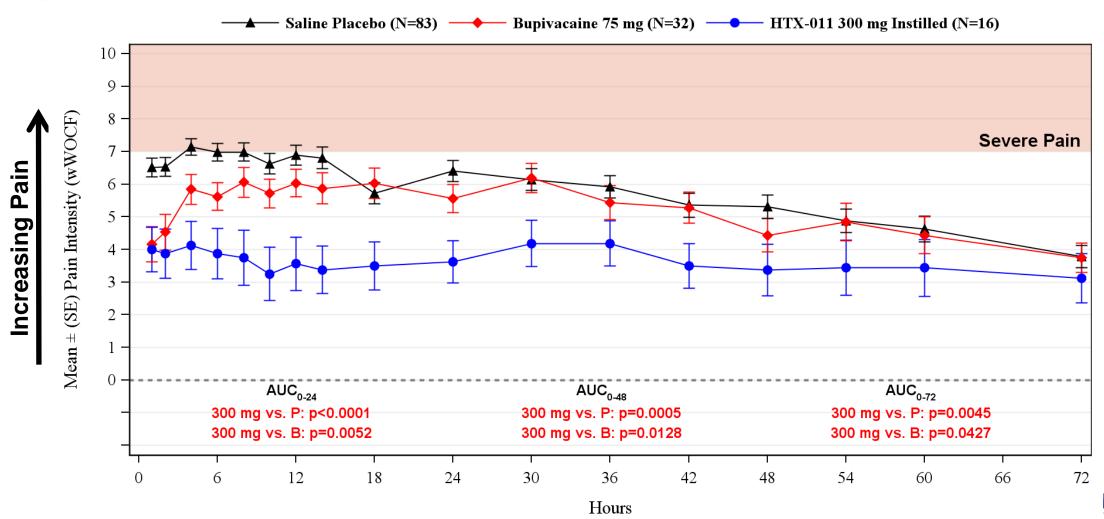


HERON THERAPEUTICS

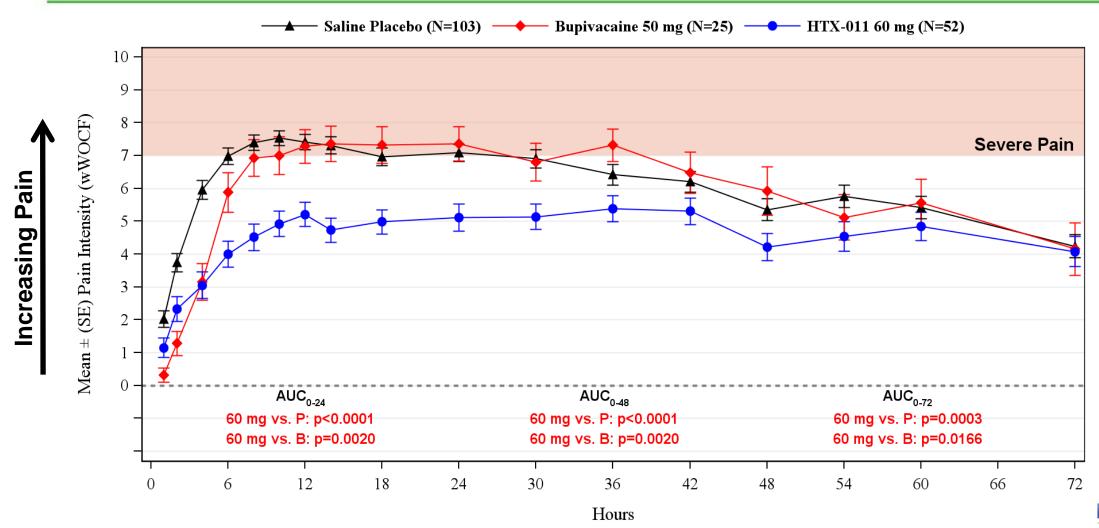
HTX-011 PHASE 2 RESULTS



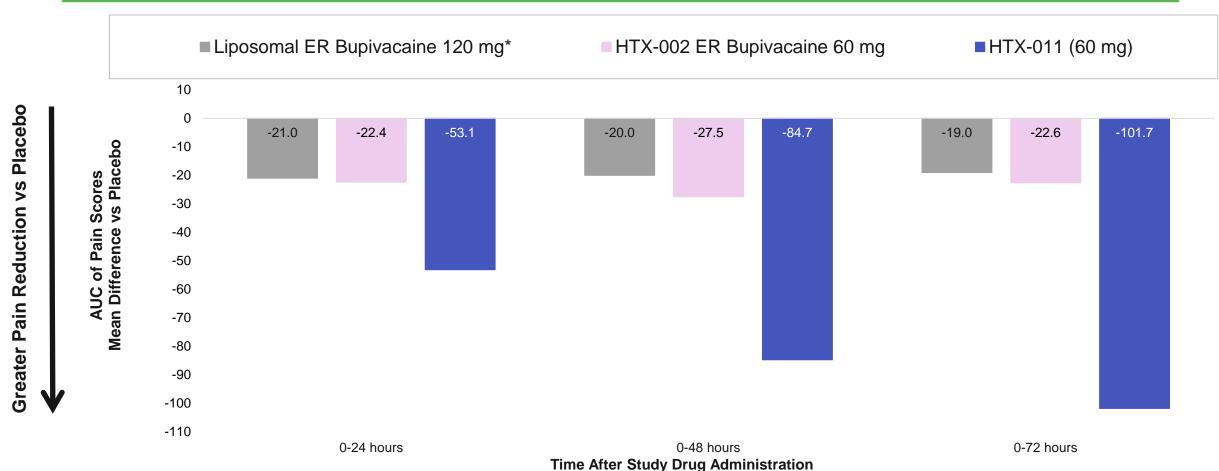
Study 202: HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Herniorrhaphy



Study 208: HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Bunionectomy



In a Cross-Study Comparison of a Standardized Bunionectomy Model Two Forms of Extended-Release Bupivacaine Produced Remarkably Similar Results



Sources: Data on File, Heron Therapeutics, Inc., and

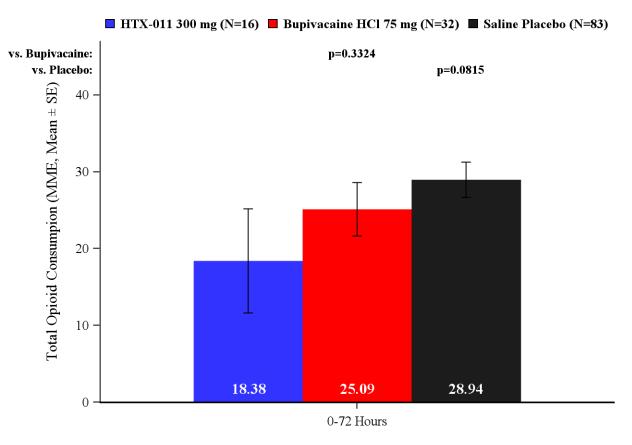
*Onel E, Daniels S, Golf M, Patou G. A phase 3, randomized, placebo-controlled trial of Exparel ®, an extended release bupivacaine local analgesic, in bunionectomy. Presented at the 2011 AAOS Annual Meeting in San Diego, CA.

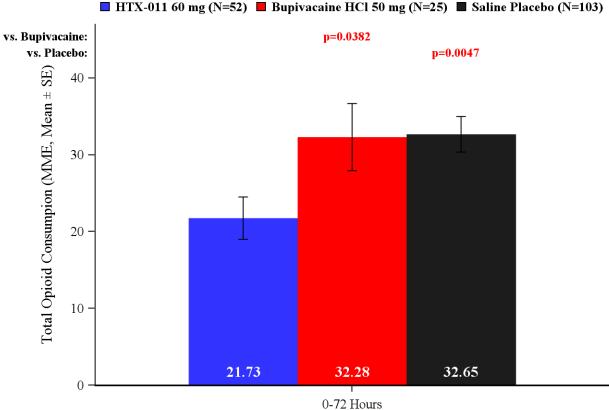


HTX-011 Reduces Total Opioid Use vs Bupivacaine and Placebo in Phase 2

Study 202 - Herniorrhaphy Study

Study 208 - Bunionectomy Study



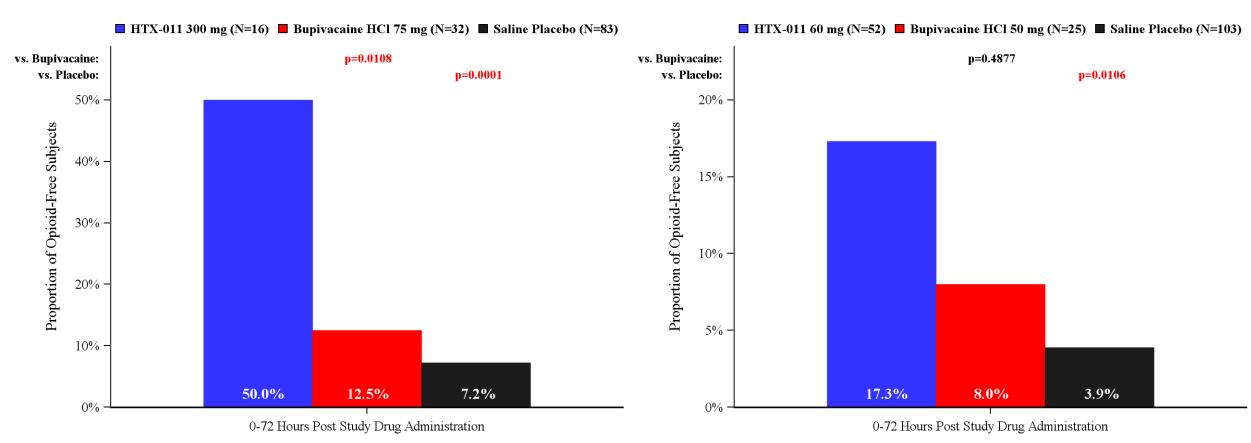




HTX-011 Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo in Phase 2

Study 202 - Herniorrhaphy Study

Study 208 - Bunionectomy Study



Source: Data on File, Heron Therapeutics, Inc.

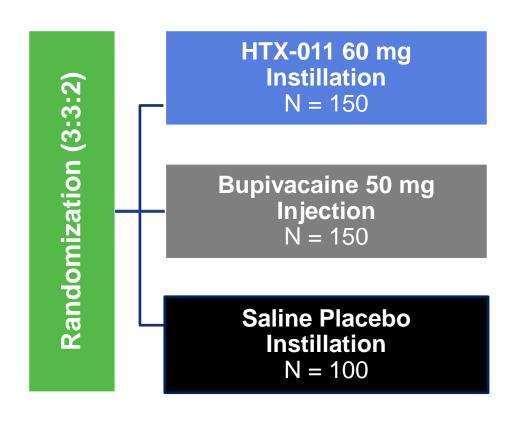




ENROLLMENT COMPLETED IN BOTH PHASE 3 PIVOTAL TRIALS



Study 301: Phase 3 Bunionectomy Study Design



Study 301 Endpoints

Primary: Pain Intensity AUC₀₋₇₂ vs. placebo

1st Key Secondary: Pain Intensity AUC₀₋₇₂ vs.

bupivacaine

2nd Key Secondary: Opioid use vs. placebo

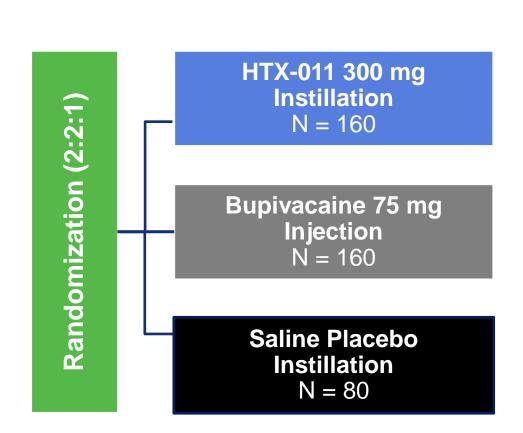
3rd Key Secondary: Opioid-free vs. bupivacaine

4th Key Secondary: Opioid use vs. bupivacaine

The trial design provides at least 90% power to detect a statistically significant difference between HTX-011 and each of the control groups for primary and all key secondary endpoints



Study 302: Phase 3 Herniorrhaphy Study Design



Study 302 Endpoints

Primary: Pain Intensity AUC₀₋₇₂ vs. placebo

1st Key Secondary: Pain Intensity AUC₀₋₇₂ vs.

bupivacaine

2nd Key Secondary: Opioid use vs. placebo

3rd Key Secondary: Opioid-free vs. bupivacaine

4th Key Secondary: Opioid use vs. bupivacaine

The trial design provides at least 90% power to detect a statistically significant difference between HTX-011 and each of the control groups for primary and all key secondary endpoints

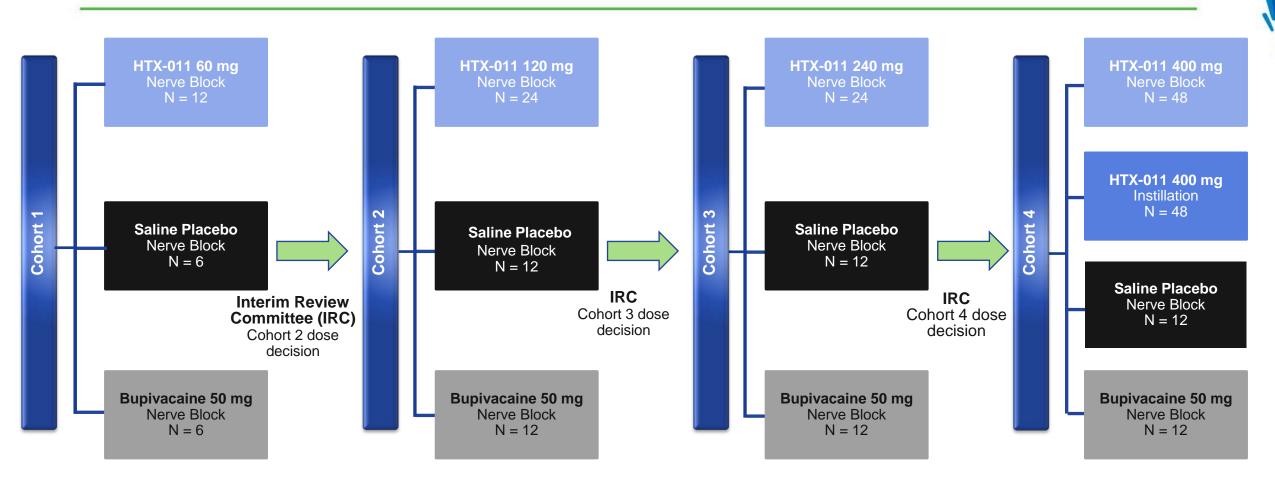




On-Going Phase 2b Studies



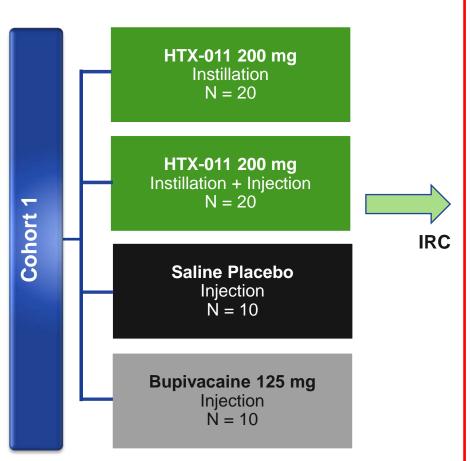
Phase 2b Study 211: Nerve Block in Breast Augmentation Study Design

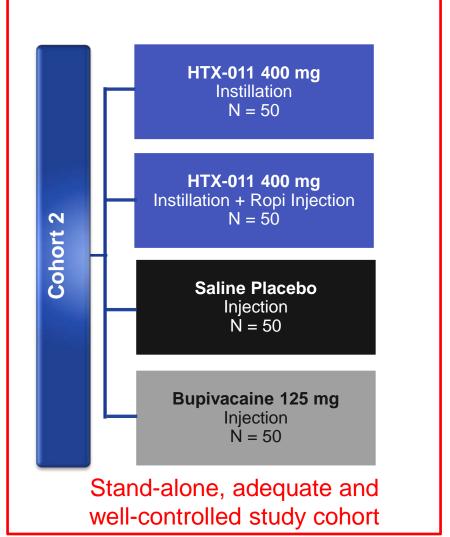


Protocol includes additional optional cohorts to evaluate other doses and administration techniques.



Phase 2b Total Knee Arthroplasty Study Design





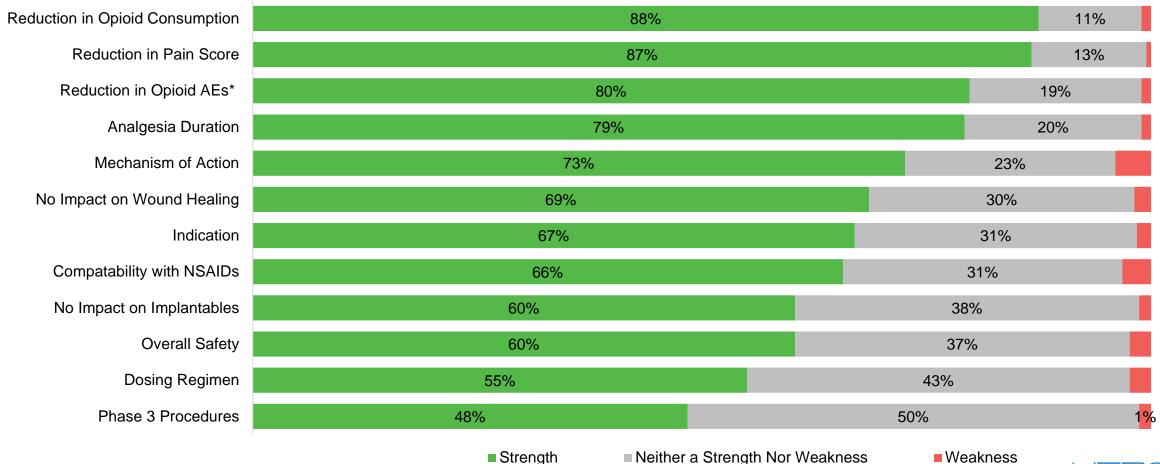


Summary: HTX-011 Is Poised to Fulfill the Promise of a Long-Acting Extended-Release Local Anesthetic

Large, growing market opportunity	\checkmark
Differentiated, synergistic mechanism addresses inflammation – a key inhibitor of both generic and long-acting local anesthetics	✓
Demonstrated superiority vs. generic bupivacaine solution in 3 diverse surgical models in Phase 2; both pivotal Phase 3 trials include a comparison to bupivacaine	✓
Consistent 72-hour efficacy - Pain reduction - Opioid reduction	✓
Applicable in large and small procedures without admixture with bupivacaine solution – reducing chance of dosing errors and systemic toxicity	✓
Simple administration with potential safety advantages	✓
Potential to address most pressing unmet needs cited by key stakeholders – patients, surgeons, anesthesiologists & formulary decision makers	✓
Extensive patent protection through 2035	✓

Overwhelmingly Positive Response by Physicians and Pharmacists to HTX-011's Target Product Profile

HTX-011 Target Product Profile: Strengths

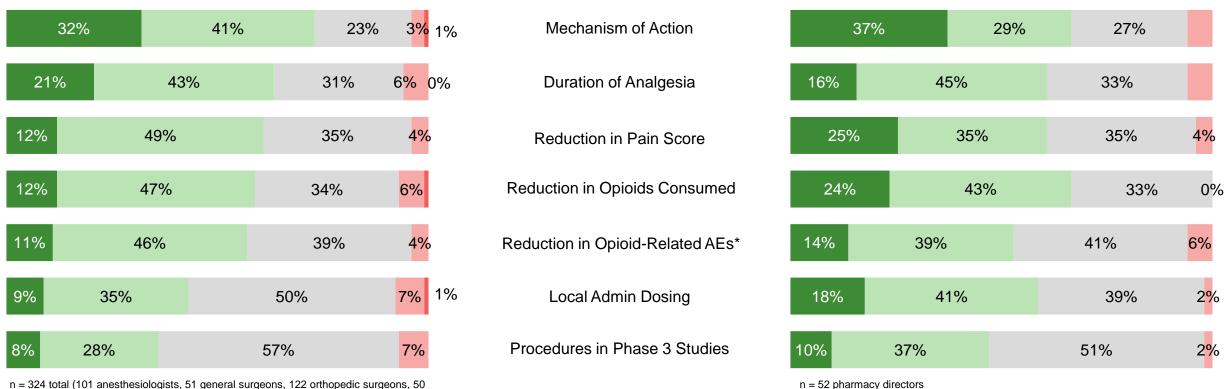




Pharmacy Directors Strongly Preferred HTX-011 over Exparel® Based on MOA, Reduction in Pain, and Reduction in Opioids

Preference for HTX-011 vs. Exparel Based on Product Attributes

<u>Physician Responses</u>



n = 324 total (101 anesthesiologists, 51 general surgeons, 122 orthopedic surgeons, 50 plastic surgeons)

Shading Legend:

Strongly favors HTX- Somewhat favors HTX- Product X and Exparel generally Somewhat favors Strongly favors
011 011 equivalent Exparel Exparel



Financial Summary

Condensed Balance Sheet Data (In thousands)	September 30, 2017
Cash, cash equivalents and short-term investments	\$ 74,016
Accounts receivable, net	\$ 28,851
Total assets	\$ 118,196
Promissory note payable	\$ 25,000
Total stockholders' equity	\$ 40,053

In December 2017, we issued 9.7 million shares of common stock for net proceeds of \$142.7 million. Including the net proceeds, pro forma cash, cash equivalents and short-term investments totaled \$216.7 million at September 30, 2017



Key Catalysts in Pain Management & CINV Franchises

HTX-011 for Postoperative Pain	CINVANTI™ and SUSTOL® for CINV
✓ Fast Track designation granted	2018 net sales guidance for CINV franchise: \$60M - \$70M
✓ Completed enrollment in Phase 3 pivotal trials	
Top-line Pivotal Phase 3 results 1H 2018	
NDA filing 2H 2018	

