

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 8, 2018

Heron Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-33221
(Commission
File Number)

94-2875566
(I.R.S. Employer
Identification No.)

4242 Campus Point Court, Suite 200, San Diego, CA
(Address of principal executive offices)

92121
(Zip Code)

Registrant's telephone number, including area code (858) 251-4400

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 2.02 Results of Operations and Financial Condition.

On January 8, 2018, Heron Therapeutics, Inc. (the "Company") issued a press release announcing, among other things, certain of its financial results for the three and twelve months ended December 31, 2017 (the "Press Release"). A copy of the Press Release is furnished herewith as Exhibit 99.1.

This Item 2.02 and the Press Release attached hereto as Exhibit 99.1 are being furnished to the Securities and Exchange Commission.

Item 7.01 Regulation FD Disclosure.

Press Release.

On January 8, 2018, the Company issued the Press Release providing, among other things, a general update on corporate progress, as described in the Press Release.

Corporate Presentation.

A copy of presentation materials describing the business of the Company, all or a part of which may be used by the Company in investor or scientific presentations from time to time, is furnished herewith as Exhibit 99.2 (the "Corporate Presentation"). The Corporate Presentation has also been posted on the Company's website at www.heronix.com. The Company does not undertake any obligation to update the Corporate Presentation.

This Item 7.01, the Press Release and the Corporate Presentation are being furnished to the Securities and Exchange Commission.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, dated January 8, 2018
99.2	Corporate Presentation, dated January 2018

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Heron Therapeutics, Inc.

/s/ David L. Szekeres

David L. Szekeres
Senior Vice President, General Counsel,
Business Development and Corporate Secretary

Date: January 8, 2018



Heron Therapeutics Highlights Progress in CINV and Pain Management Franchises

- SUSTOL® Fourth-Quarter 2017 Net Sales of Approximately \$10 Million, Up 16% from Third-Quarter 2017 Net Sales of \$8.6 Million; Full-Year 2017 Net Sales of Approximately \$31 Million, versus Guidance of \$25 Million to \$30 Million -

- 2018 Net Sales Guidance for CINV Franchise of \$60 Million to \$70 Million -

- Enrollment Complete in Both Pivotal Phase 3 Studies for HTX-011; Top-line Results Expected in First Half of 2018 -

SAN DIEGO, Calif. – (BUSINESS WIRE) – January 8, 2018 – Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on developing novel, best-in-class treatments to address some of the most important unmet patient needs, today highlighted progress in the Company's pain management and CINV franchises.

CINV Franchise

- **SUSTOL® Sales.** SUSTOL (granisetron) extended-release injection fourth-quarter 2017 net product sales were approximately \$10 million, up 16% from third-quarter 2017 net product sales of \$8.6 million. SUSTOL full-year 2017 net product sales were approximately \$31 million, versus guidance of \$25 million to \$30 million.
- **2018 CINV Sales Guidance.** Net product sales guidance for full-year 2018 for the CINV franchise is \$60 million to \$70 million.
- **Permanent J-Code Now Effective.** On January 1, 2018, a product-specific billing code, or permanent J-code, for SUSTOL became available. The new J-code was assigned by the Centers for Medicare and Medicaid Services (CMS) and will help simplify the billing and reimbursement process for prescribers of SUSTOL.
- **CINVANTI™ Now Available.** In November 2017, the U.S. Food and Drug Administration (FDA) approved the Company's New Drug Application (NDA) for CINVANTI (aprepitant) injectable emulsion, the first and only polysorbate 80-free intravenous (IV) formulation of a neurokinin-1 (NK1) receptor antagonist indicated for the prevention of acute and delayed CINV. CINVANTI became commercially available in the United States on January 4, 2018.

Pain Management Franchise

Enrollment Complete in Phase 3 Pivotal Trials for HTX-011 in Postoperative Pain. Heron completed enrollment in its two pivotal Phase 3 efficacy studies in bunionectomy and hernia repair. Heron anticipates reporting top-line results in the first half of 2018 and expects to file an NDA with the FDA in the second half of 2018.

"Heron had a strong year in 2017, led by the advancement of the HTX-011 program toward an NDA filing, the success of our commercial team with SUSTOL and the expansion of our CINV franchise with the approval of CINVANTI," said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron. "We expect to build on our momentum in 2018 by reporting top-line pivotal Phase 3 results for HTX-011, filing an NDA for HTX-011 and growing our CINV franchise, which now includes two innovative products."

About HTX-011 for Postoperative Pain

HTX-011, which utilizes Heron's proprietary Biochronomer® drug delivery technology, is an investigational, long-acting, extended-release formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the prevention of postoperative pain. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction. The Phase 2 development program for HTX-011 was designed to target the many patients undergoing a wide range of surgeries who experience significant postoperative pain. Heron completed enrollment in its two pivotal Phase 3 efficacy studies in bunionectomy and hernia repair and anticipates reporting top-line results in the first half of 2018 and expects to file an NDA with the FDA in the second half of 2018.

About CINVANTI (aprepitant) injectable emulsion

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). CINVANTI is an intravenous formulation of aprepitant, a substance P/neurokinin-1 (NK1) receptor antagonist. CINVANTI is the first intravenous (IV) formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK1 receptor antagonist to significantly reduce CINV in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy). CINVANTI does not contain polysorbate 80 or any other synthetic surfactant. Pharmaceutical formulations containing polysorbate 80 have been linked to hypersensitivity reactions, including anaphylaxis and irritation of blood vessels resulting in infusion-site pain. FDA-approved dosing administration included in the United States prescribing information for CINVANTI is a 30-minute infusion.

Please see Full Prescribing Information at www.CINVANTI.com.

About SUSTOL (granisetron) extended-release injection

SUSTOL 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. SUSTOL is an extended-release, injectable 5-HT₃ receptor antagonist that utilizes Heron's Biochronomer® polymer-based drug delivery technology to maintain therapeutic levels of granisetron for 35 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL's efficacy and safety in more than 2,000 patients with cancer. SUSTOL's efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy).

Please see Full Prescribing Information at www.SUSTOL.com.

About Chemotherapy-Induced Nausea and Vomiting (CINV)

While chemotherapy is one of the most effective and commonly used therapies to help patients fight cancer, it is accompanied by debilitating side effects, including varying degrees of nausea and vomiting, often attributed as a leading cause of premature discontinuation of cancer treatment. The goal of antiemetic therapy is to prevent CINV in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy). The National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) have categorized chemotherapy regimens based on the degree to which they cause nausea and vomiting: low emetogenic chemotherapy (LEC); moderately emetogenic chemotherapy (MEC); and highly emetogenic chemotherapy (HEC).

About Heron Therapeutics, Inc.

Heron is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments that address some of the most important unmet patient needs. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents for patients suffering from cancer or pain. For more information, visit www.heronrx.com.

Forward-Looking Statements

This news release contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers that forward-looking statements are based on management's expectations and assumptions as of the date of this news release and are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, those associated with the potential market opportunities for SUSTOL and CINVANTI; the timing of completion and results of the Phase 3 studies for HTX-011; the timing of the NDA filing for HTX-011; 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 Heron takes no obligation to update or revise these statements except as may be required by law.

Investor Relations and Media Contact:

David L. Szekeres
Senior VP, General Counsel, Business Development and Corporate Secretary
dszekeres@herontx.com
858-251-4447

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Company Update

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[®], CINVANTI[™] and HTX-011; the potential net sales for SUSTOL[®] and CINVANTI[™]; 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

■ CINV
■ Pain

SUSTOL®
 (granisetron) extended-release injection

Approved by U.S. Food and Drug Administration

CINVANTI™
 (aprepitant) injectable emulsion

Approved by U.S. Food and Drug Administration

HTX-011 bupivacaine + meloxicam ER
 Local Administration

Postop Pain with Local Administration

- Fast Track designation granted
- Phase 3 enrollment complete

HTX-011 bupivacaine + meloxicam ER
 Nerve Block

Postop Pain with Nerve Block

Phase 2 program in nerve block underway



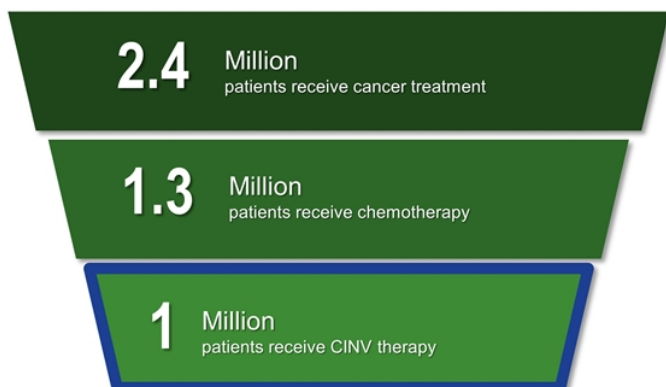


CINV Commercial Products

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-HT₃, serotonin; CINV, chemotherapy induced nausea and vomiting; HCP, health care professional; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; QoL, quality of life; NK₁, substance P neurokinin-1

Source: IPSOS Q2 2015 Cancer Tracking

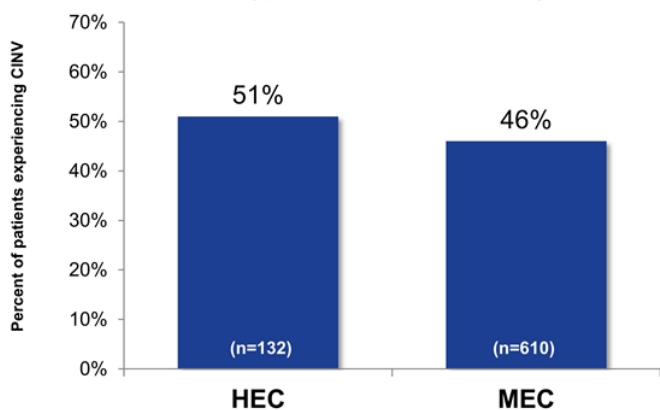


Despite Previously Available Therapies, a Large Percentage of Patients Experience Breakthrough CINV



% of MEC/HEC patients with breakthrough CINV despite prophylaxis

Community practice observational study

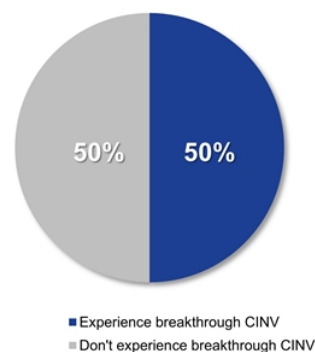


Data from a prospective observational study enrolling chemotherapy-naive patients who received single-day HEC or MEC at four oncology practice networks, all using electronic medical record (EMR) systems, in Georgia, Tennessee, and Florida. CINV = emesis or clinically significant nausea on days 1-5. Regimen 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

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

% of MEC/HEC patients with breakthrough CINV despite prophylaxis

Physician perception



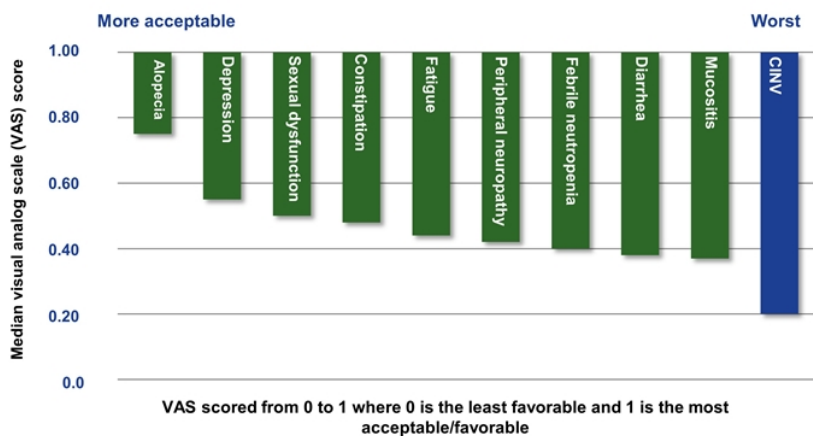
Source: Instar Market Research, Dec 2015, N=75 oncologists



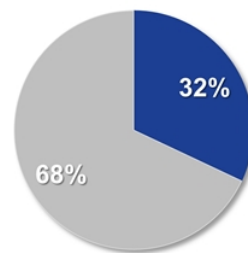
CINV Has a High Clinical Burden – Impacting Patients’ QOL and Cancer Treatment



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



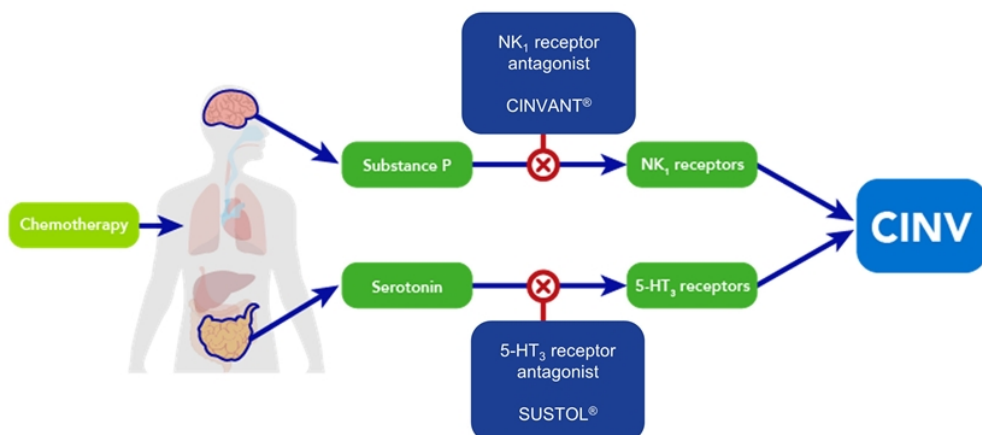
CINV commonly disrupts patients’ cancer treatment



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

Sun CC et al. *Support Care Cancer*. 2005;13:219-227.
 Van Laar ES et al. *Support Care Cancer*. 2015;23:151-7

CINV Prophylaxis Typically Requires Two Complimentary Mechanisms of Action



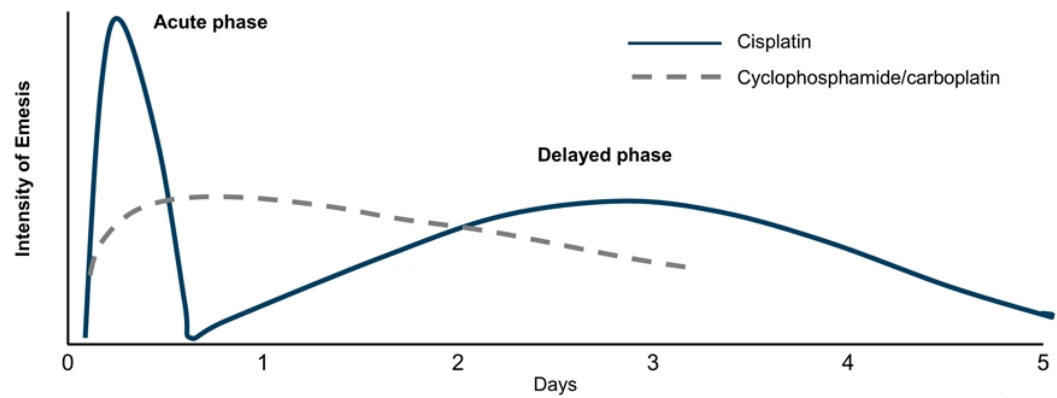
NK₁ receptor antagonists

- 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[®]
(granisetron) extended-release injection

5-HT₃

CINVANTI[™]
(aprepitant) injectable emulsion

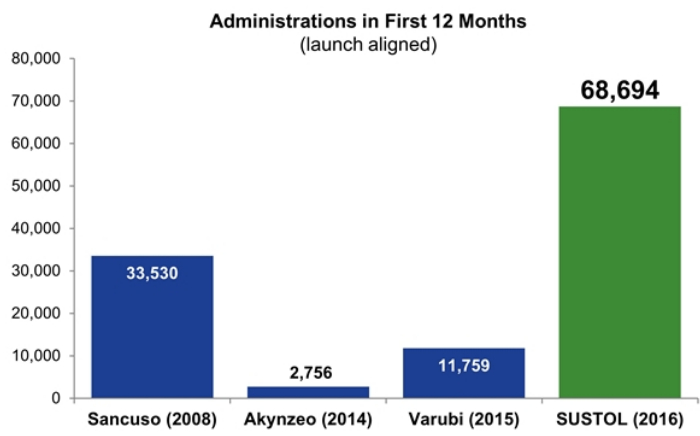
NK₁

HERON
THERAPEUTICS
Developing Best-in-Class Medicine. Improving Lives.™

SUSTOL® Outperformed ALL Recent CINV New Brand Launches



CINV New Brand Launches Since 2008



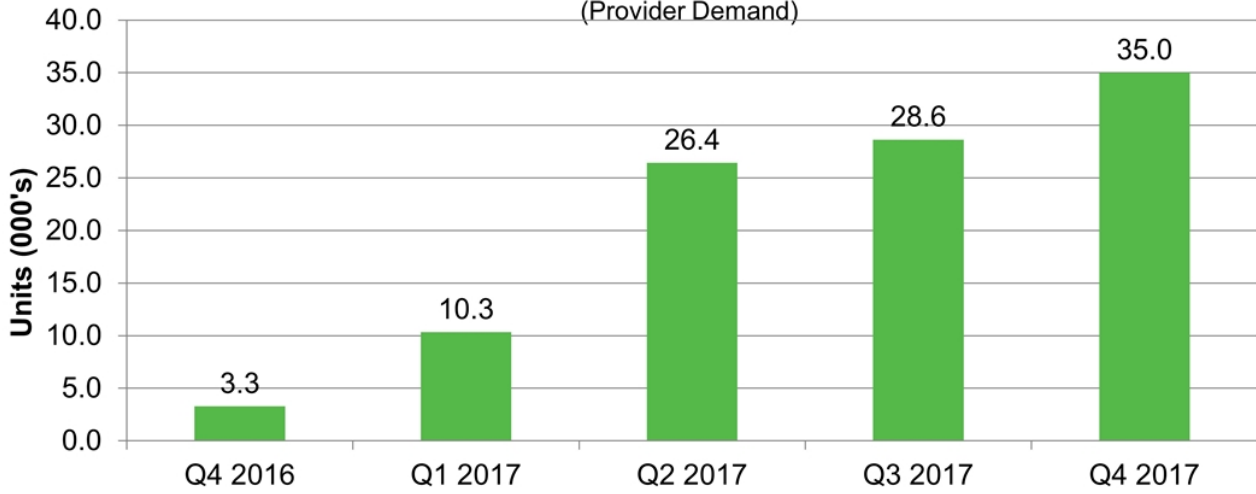
Sources: IMS DDD; Heron actuals (distributor 867 reports) are for 4Q2016 through 3Q2017; due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2.



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



SUSTOL Quarterly Unit Performance
(Provider Demand)



Net Sales

\$1.3M

\$3.6M

\$8.5M

\$8.6M

\$10M

Source: Heron 867 data

16%↑



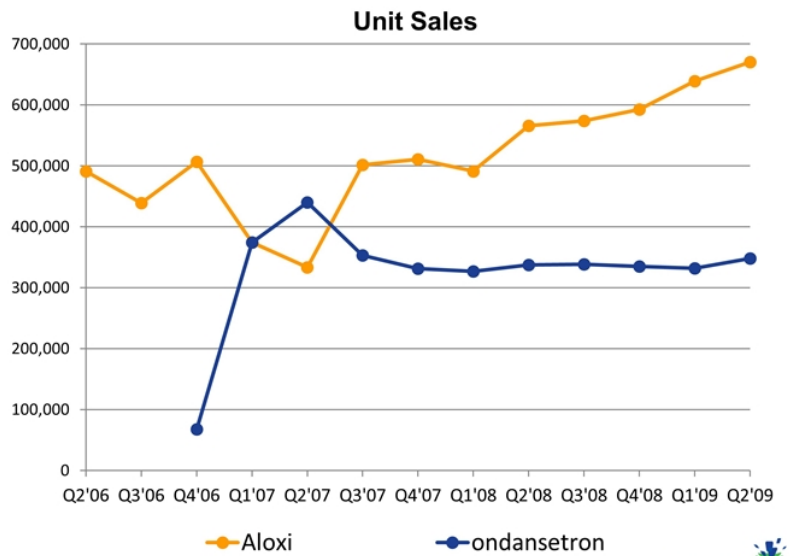
Market Insights Suggest SUSTOL® May Decline Modestly Through the Arbitrage and Grow Thereafter – Consistent with Aloxi® Analogue

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

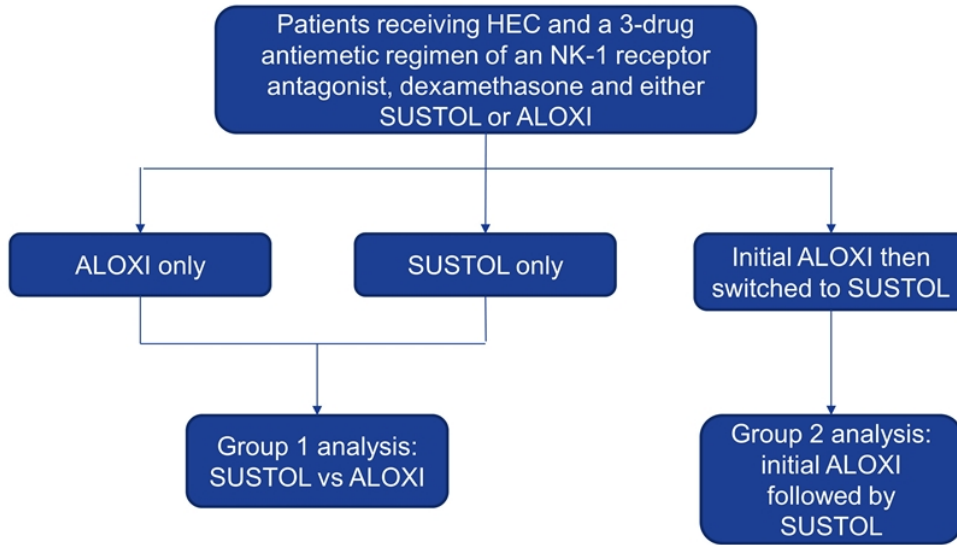
2 Putnam Associates Qual Research Findings, June 2017



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



Vacirca, et. Al., ASCO Palliative Care Symposium, San Diego, CA; October 27-28, 2017 Abstract 108.



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



Treatment	Number of chemotherapy cycles	Hydration rate	P-value for difference in hydration vs Aloxi
	Mean (SD)	Mean (SD)	
GROUP 1 HEC			
ALOXI (n = 78)	5.6 (2.9)	1.0 (1.2)	p < 0.0001
SUSTOL (n = 55)	4.0 (2.1)	0.3 (0.6)	
GROUP 2 HEC			
ALOXI (n = 32)	3.3 (3.1)	0.7 (1.2)	p = 0.028
SUSTOL (n = 32)	2.9 (2.0)	0.5 (1.0)	

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

HEC: Highly emetogenic chemotherapy; max: Maximum; min: Minimum; SD: Standard deviation.

Vacirca, et. Al., ASCO Palliative Care Symposium, San Diego, CA; October 27-28, 2017 Abstract 108.



CINVANTI™ Now Launched

- CINVANTI™ is the first and only polysorbate 80-free IV NK₁ receptor antagonist approved for the prevention of **both** 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



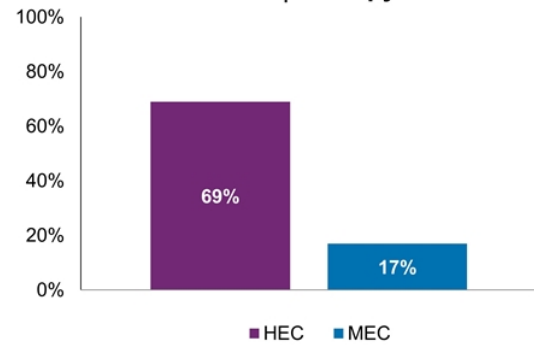
Despite an NCCN Category 1 Recommendation, NK₁'s are Underutilized

NCCN Antiemetic Guidelines

HEC	MEC
<ul style="list-style-type: none">▪ 5-HT₃▪ dexamethasone▪ NK₁± olanzapine	<ul style="list-style-type: none">▪ 5-HT₃▪ dexamethasone± NK₁± olanzapine

NCCN 2017

Percent of Patients Receiving NK₁ Therapy



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

*Both oral aprepitant and IV fosaprepitant combined

17 ^Source: IMS NPA 2016-2017

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	Yes ¹	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

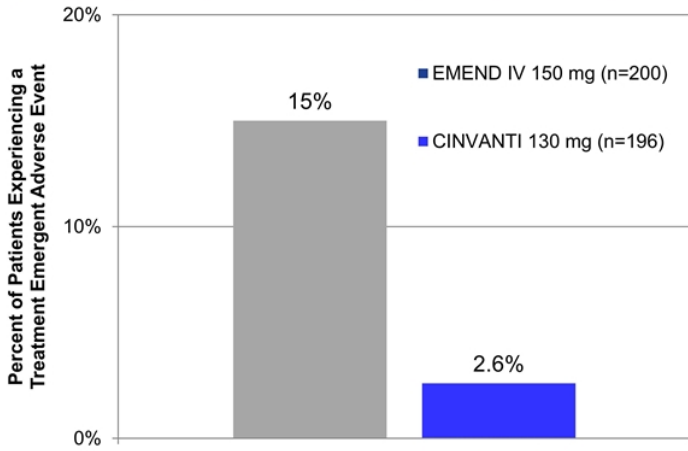
1. FDA-approved dosing administration included in the US prescribing information (PI) for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.

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

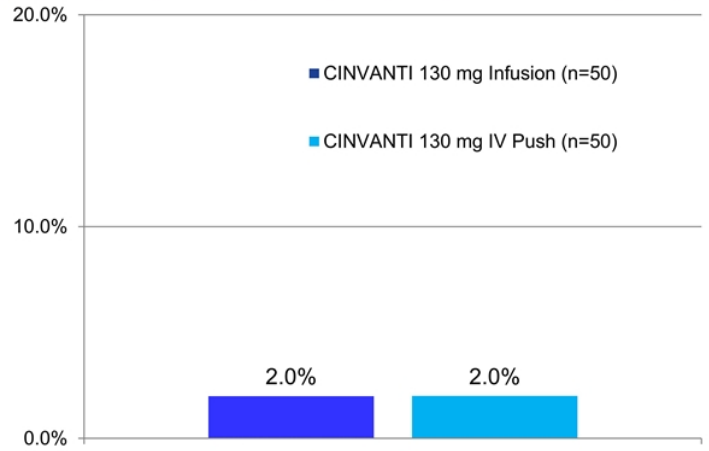
CINVANTI® Was Well Tolerated Given as an Infusion or as an IV Push



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.

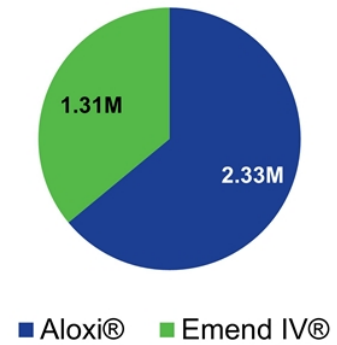
2. FDA-approved dosing administration included in the US prescribing information for CINVANTI (aprepitant) injectable emulsion is a 30-minute infusion.



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)



Source: IMS TTM Q3'17



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

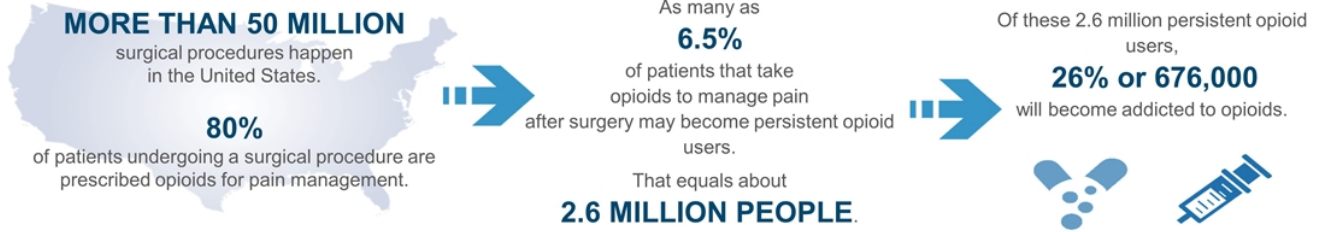
- **CINV franchise 2018 guidance of \$60M–\$70M in net product sales**





Postoperative Pain Program
HTX-011: Proprietary Extended-Release
Combination of Bupivacaine +
Meloxicam

Postoperative Opioids: A Doorway to Addiction



In addition, hundreds of millions of **LEFTOVER PILLS** are then brought home from the hospital after surgery

70% of all these opioid tablets go unused

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

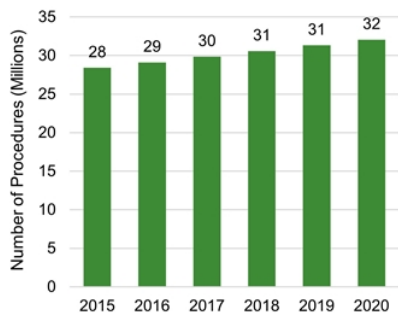
32% of all opioid addicts report first opioid exposure through leftover pills

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

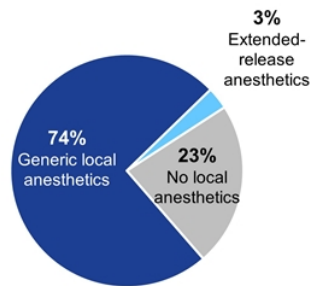
Sources:

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, 2015¹



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

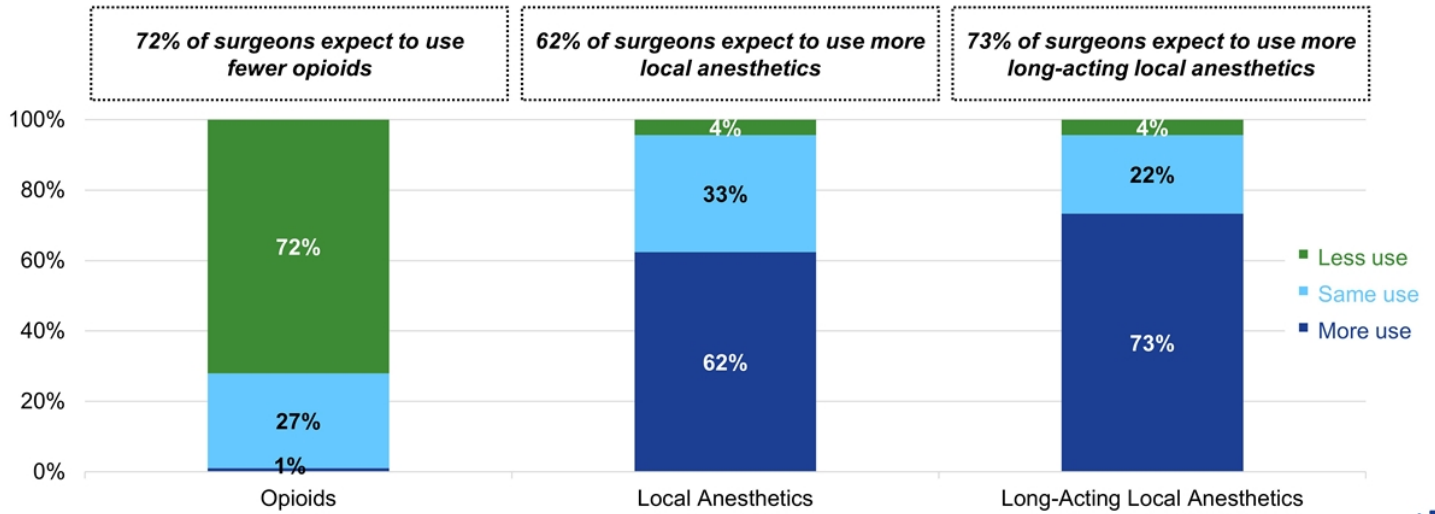
Key Limiters of Liposomal Bupivacaine Market Penetration

- 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

Future Pain Market Outlook



Source: DRG Physician Survey (2016)

Large US Market Opportunity

Theoretical and Target Market

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



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

\$3.8 – 4.5B

Secondary Targets

Higher volume procedures in non-core specialties (e.g., ENT, urology, hand, others)

\$1.6 – 1.9B

Tertiary Targets






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

\$1.7 – 2.1B

Theoretical Market Size

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

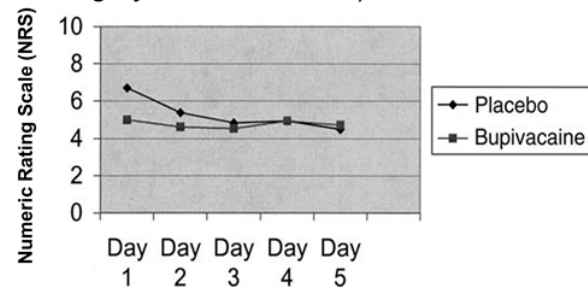


Country	Total Surgical Procedures	Total Procedures Requiring Postop Pain Management	Initial Target Procedures	Remaining Secondary, Lower Volume & Procedures Currently Not Using Local Anesthetics
 Germany	22,545,000	6,838,000	3,649,000	3,189,000
 France	14,545,000	4,357,000	2,292,000	2,065,000
 UK	13,882,000	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

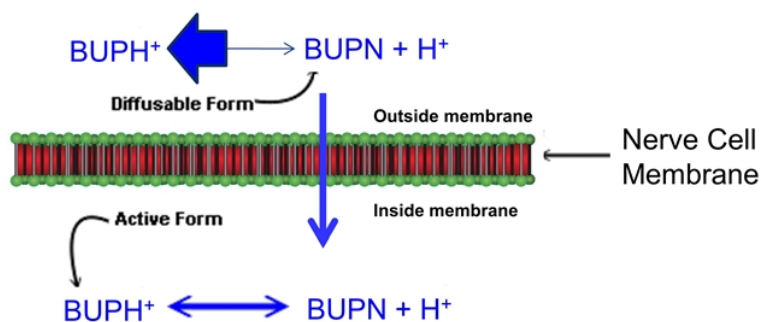
- Regardless of delivery technology, extended release bupivacaine products do not reduce pain sufficiently beyond 24 hours to beat bupivacaine HCl :
 - Exparel® (liposomal ER bupivacaine)
 - Xaracoll™ (bupivacaine collagen matrix)
 - Posimur™ (SABER-bupivacaine)
 - HTX-002 (Biochronomer ER bupivacaine)
 - 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. Surgery 2004;136:761-9)



Inflammation Plays a Key Role in Pain Management

(Current local anesthetics do not address this)



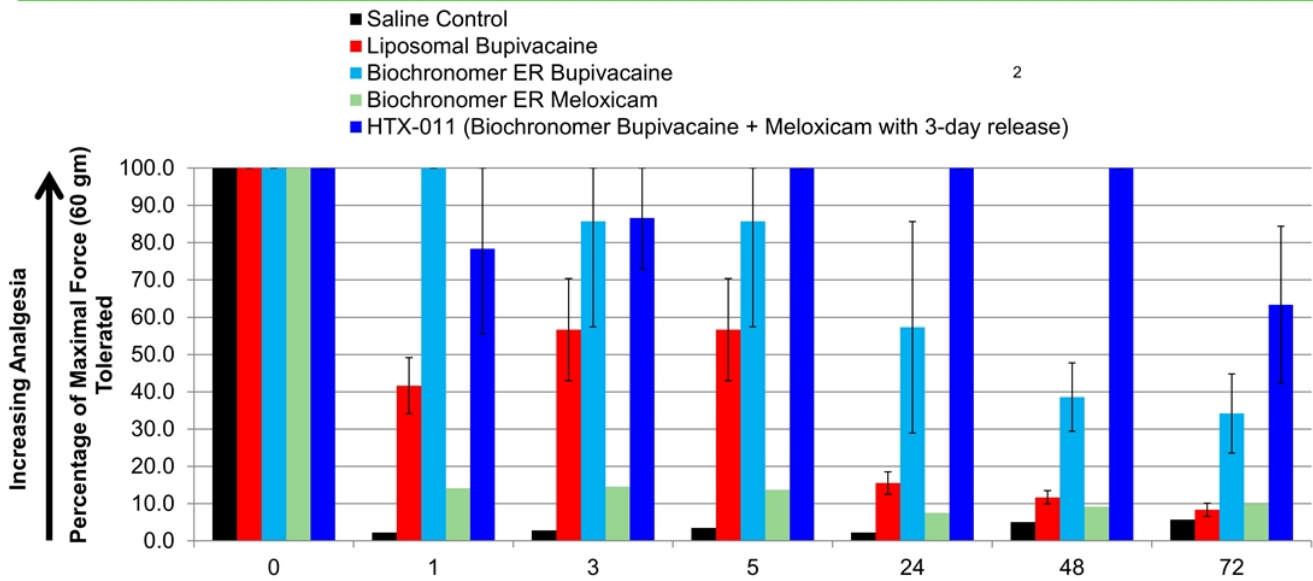
- Surgical insult produces an immediate drop in pH
- As inflammatory cytokines are released and inflammation sets in, the acidic environment is maintained for many days
- The acidic environment shifts the balance to the ionized form, which is unable to enter the nerve

- 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

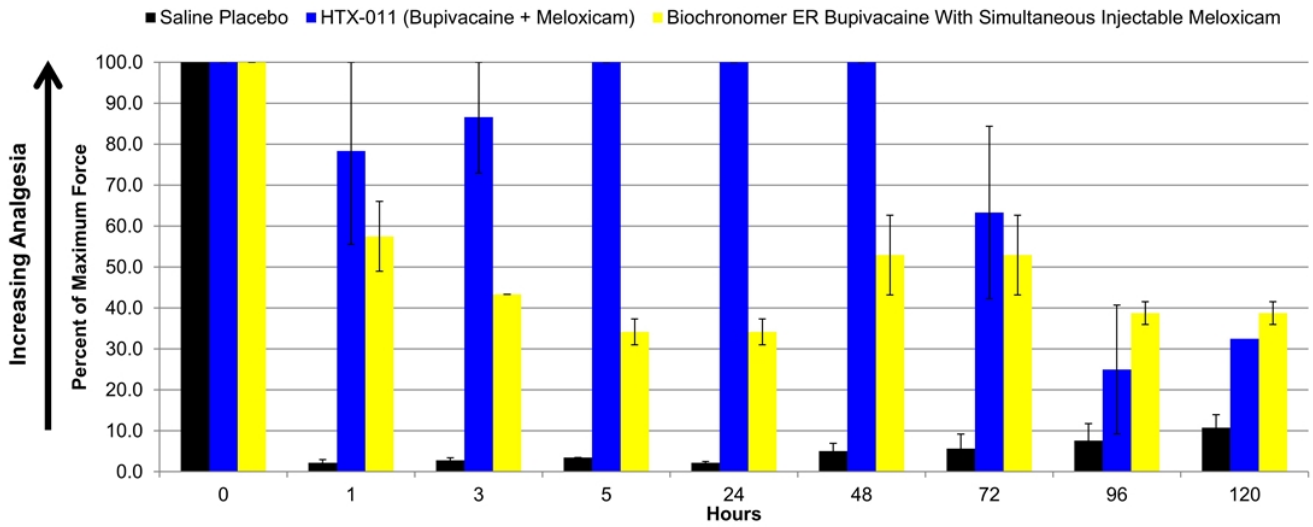


¹ Postoperative pain model in pigs from Castle et al, 2013 EPJ
² Human dose of liposomal bupivacaine with 40% smaller incision (n=4 pigs in each arm)

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

(n=4 pigs in each arm)

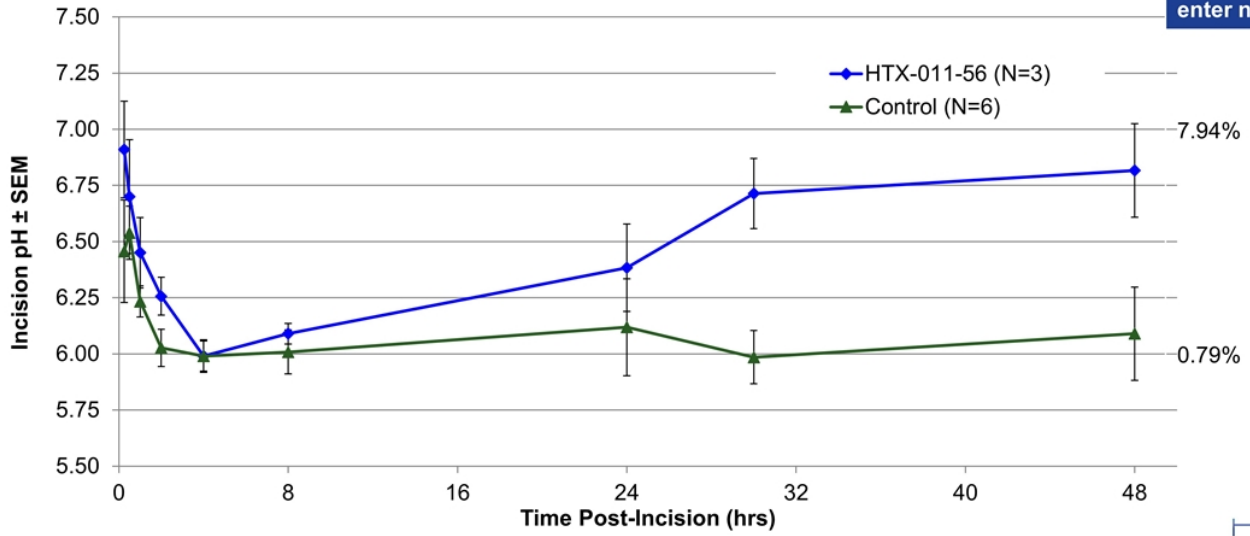


The Unique Mechanism of Action of HTX-011 Has Been Demonstrated in the Pig Post-Op Pain Model

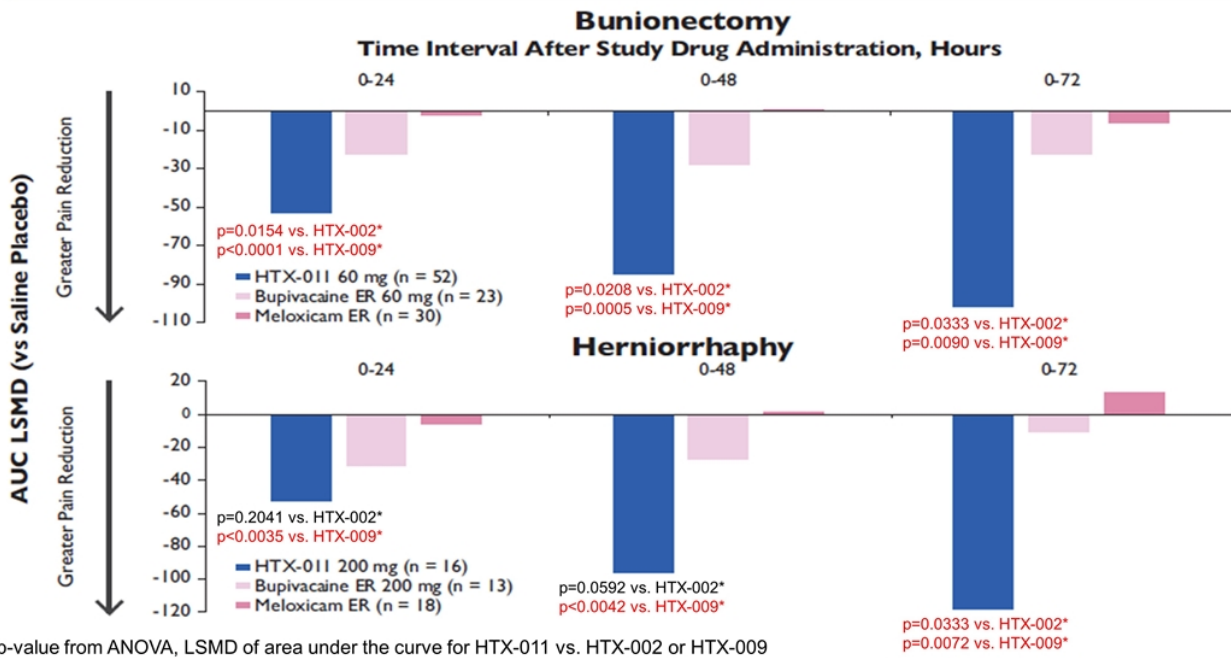


The normalization of pH starting at 8 hours with HTX-011 allows almost 10x more bupivacaine (BPV) to enter the nerve to block the pain signal

% of un-ionized BPV available to enter nerve



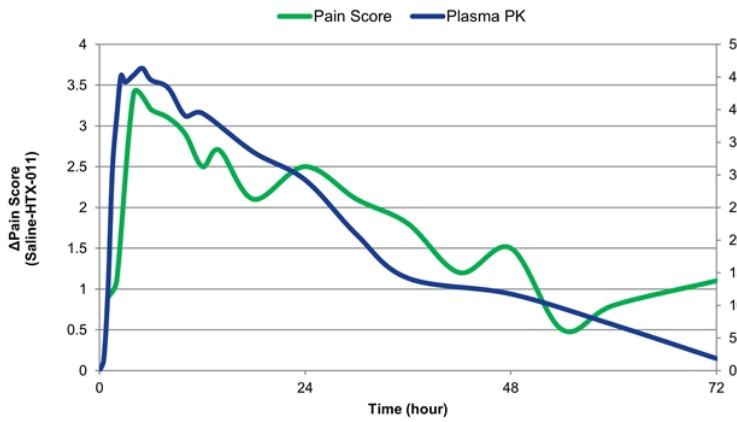
Unique MOA of HTX-011 Produces Significantly Greater Pain Reduction Than ER Versions of Bupivacaine or Meloxicam



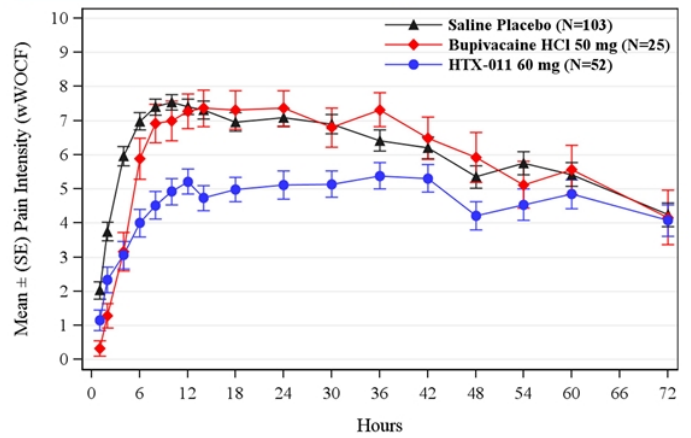
Unique MOA of HTX-011 Results in an Excellent PK-PD Relationship Relationship Not Seen With Other ER Bupivacaine Formulations

HTX-011 (bupivacaine + meloxicam)

PK-PD Relationship



Mean Pain Intensity vs Time



AUC_{0-24 hr}
60 mg vs P: p < 0.0001
60 mg vs B: p = 0.0020

AUC_{0-48 hr}
60 mg vs P: p < 0.0001
60 mg vs B: p = 0.0020

AUC_{0-72 hr}
60 mg vs P: p = 0.0003
60 mg vs B: p = 0.0166

Source: Data on File, Heron Therapeutics, Inc.

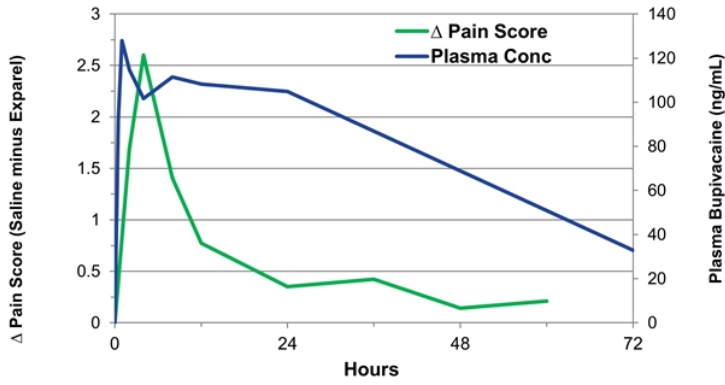
*LOCF method used to account for missing data, with wWOCF adjustment for use of rescue medications



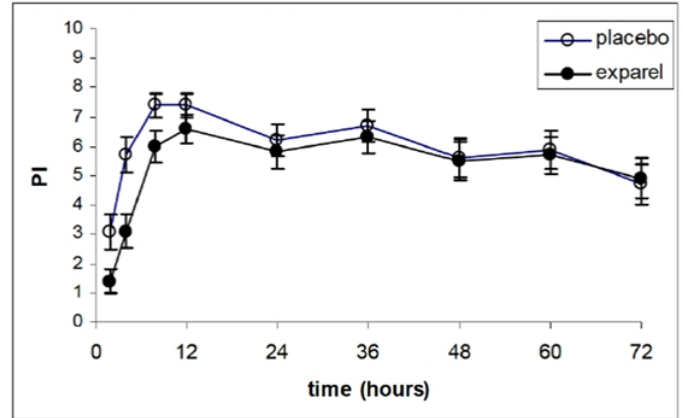
Exparel® Does Not Demonstrate a PK-PD Relationship

Exparel® (liposomal bupivacaine)

No PK-PD Relationship



Mean Pain Intensity vs Time



$AUC_{0-24 \text{ hr}}$ Exparel vs P: $p = 0.0005$
 $AUC_{0-48 \text{ hr}}$ Exparel vs P: $p = 0.1316$
 $AUC_{0-72 \text{ hr}}$ Exparel vs P: $p = \text{NS}$

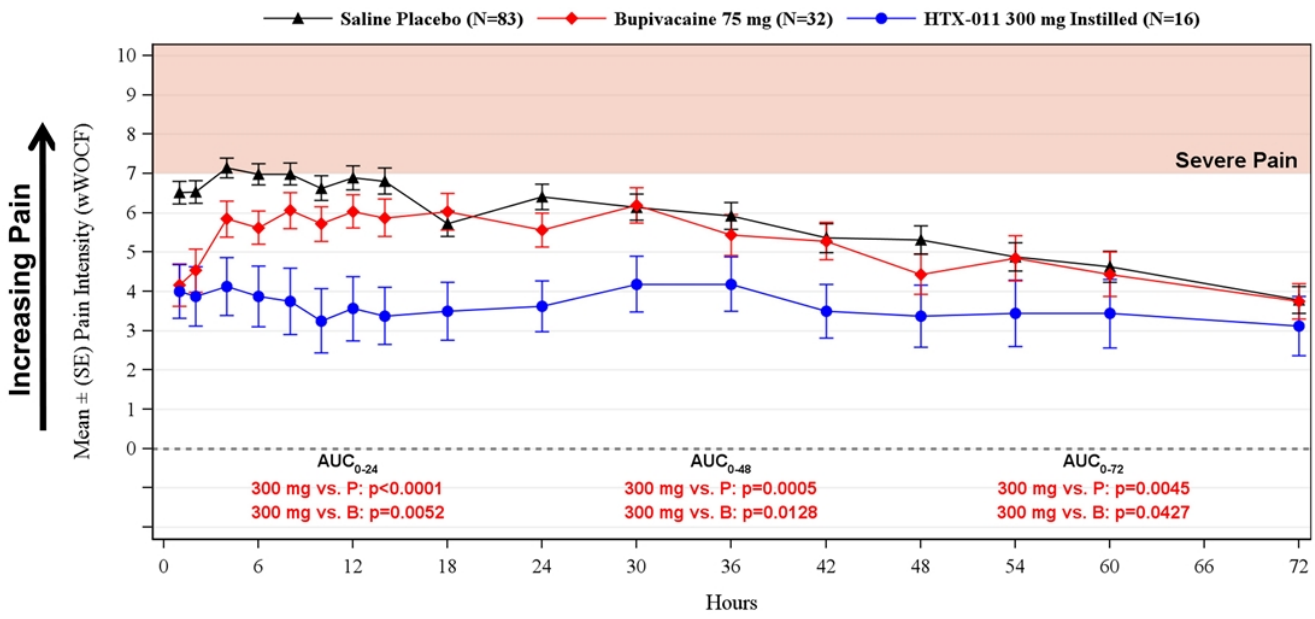
Source: EXPAREL FDA Clinical Pharmacology and Biopharmaceutics Review; Golf, et al. Adv Ther (2011) 28(9):776-788.



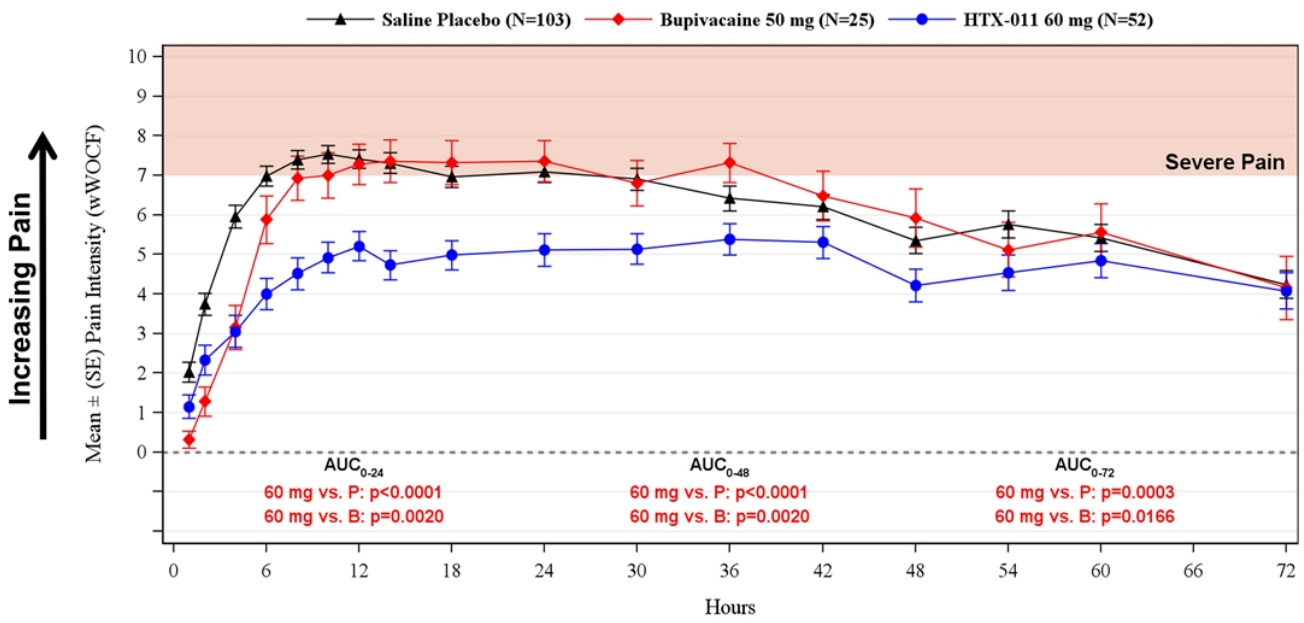


HTX-011 PHASE 2 RESULTS

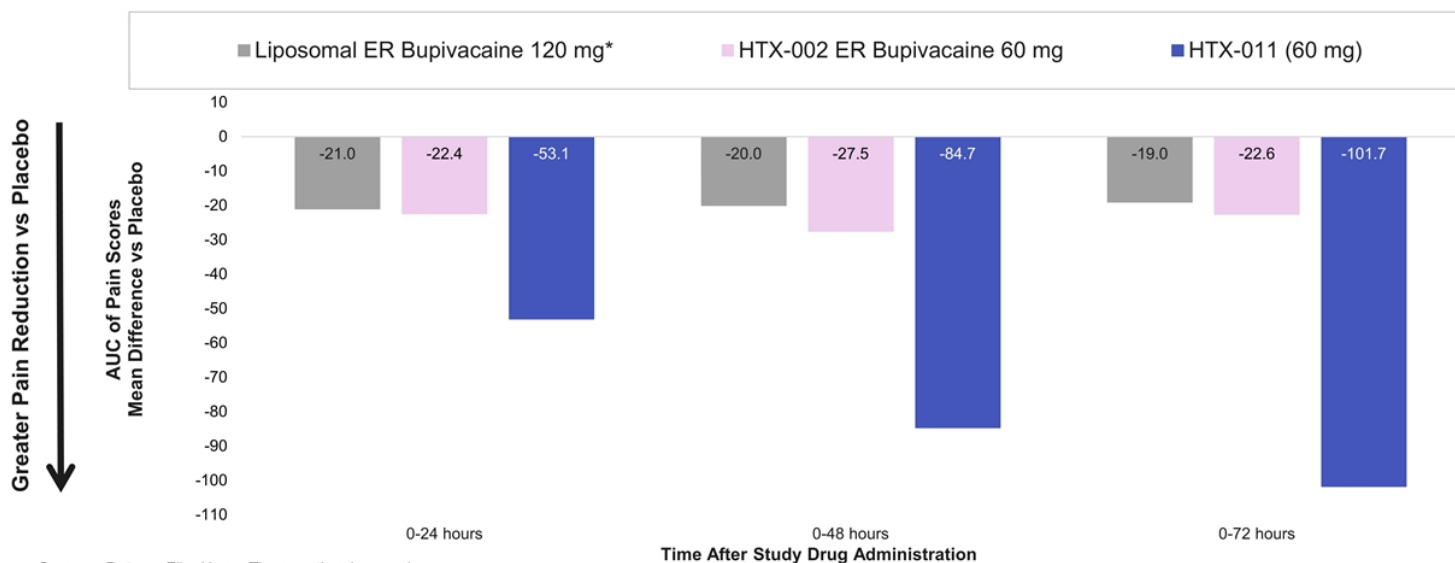
Study 202: HTX-011 Reduces Pain Significantly Better Than Placebo or Bupivacaine (Standard-of-Care) After Herniorrhaphy



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.

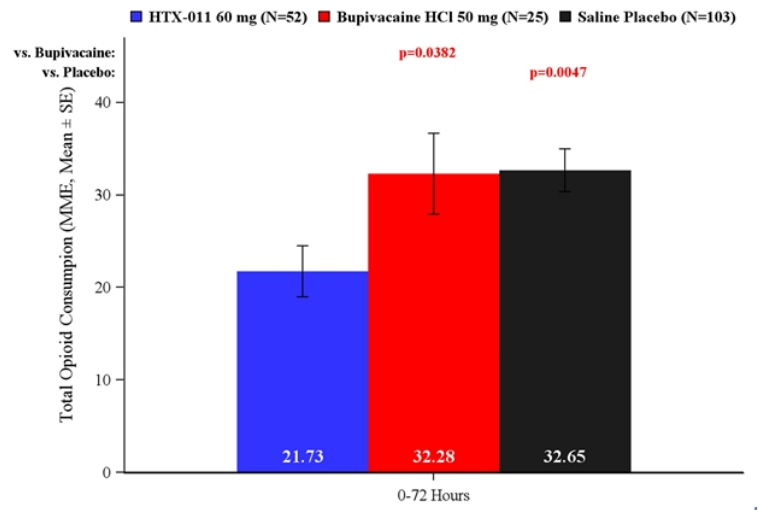
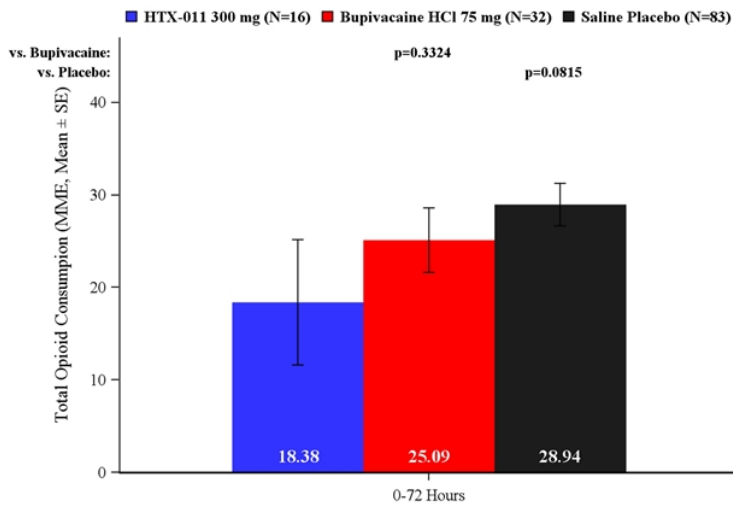


HTX-011 Reduces Total Opioid Use vs Bupivacaine and Placebo in Phase 2



Study 202 - Herniorrhaphy Study

Study 208 - Bunionectomy Study



Source: Data on File, Heron Therapeutics, Inc.

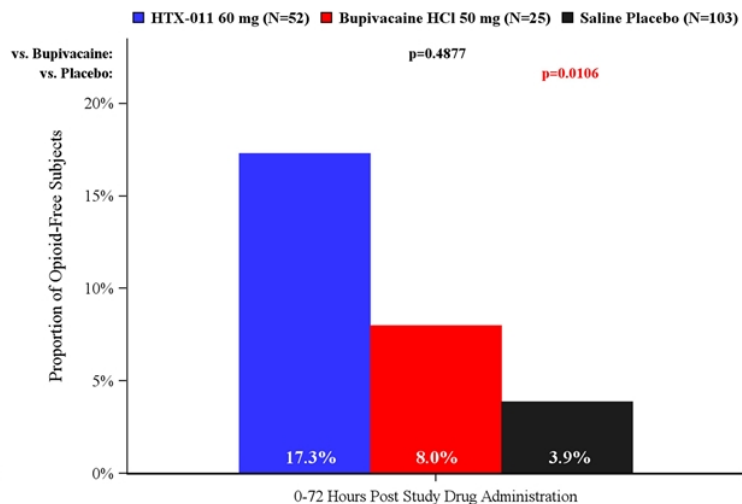
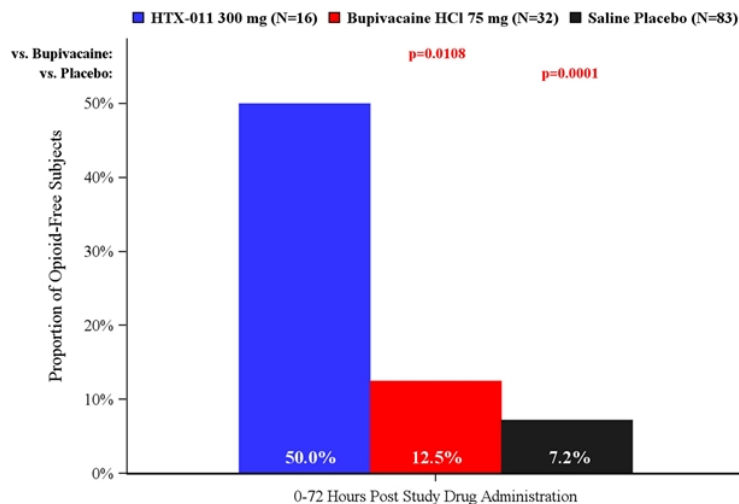


HTX-011 Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo in Phase 2



Study 202 - Herniorrhaphy Study

Study 208 - Bunionectomy Study



Source: Data on File, Heron Therapeutics, Inc.

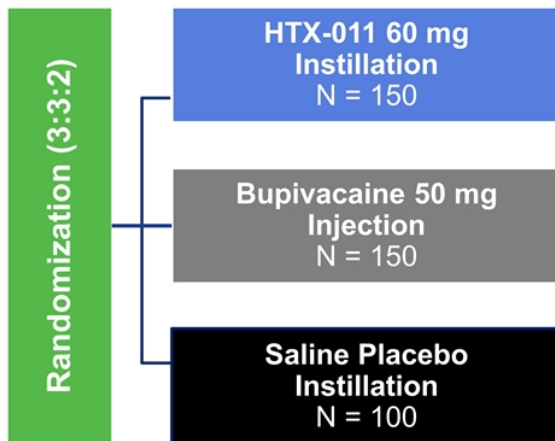




ENROLLMENT COMPLETED IN BOTH PHASE 3 PIVOTAL TRIALS

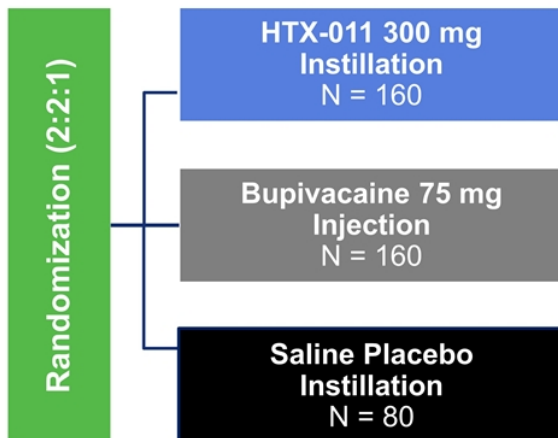
Study 301: Phase 3 Bunionectomy

Study Design



Study 301 Endpoints
Primary: Pain Intensity AUC_{0-72} vs. placebo
1 st Key Secondary: Pain Intensity AUC_{0-72} vs. bupivacaine
2 nd Key Secondary: Opioid use vs. placebo
3 rd Key Secondary: Opioid-free vs. bupivacaine
4 th 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

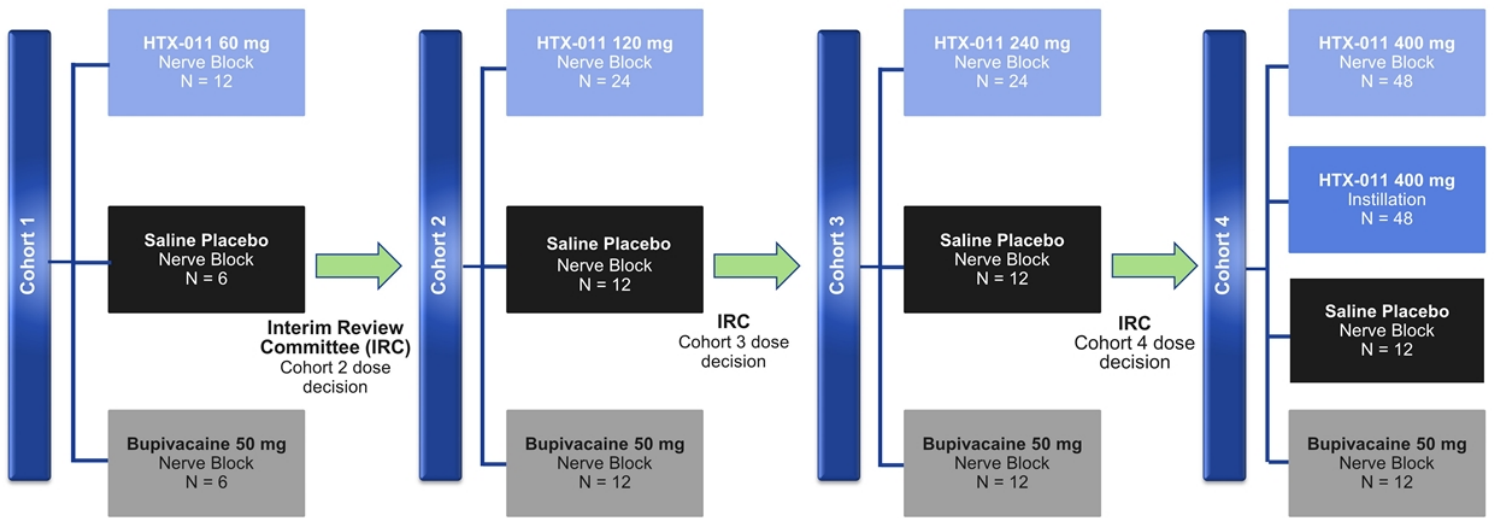
Study 302: Phase 3 Herniorrhaphy Study Design



Study 302 Endpoints
Primary: Pain Intensity AUC_{0-72} vs. placebo
1 st Key Secondary: Pain Intensity AUC_{0-72} vs. bupivacaine
2 nd Key Secondary: Opioid use vs. placebo
3 rd Key Secondary: Opioid-free vs. bupivacaine
4 th 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

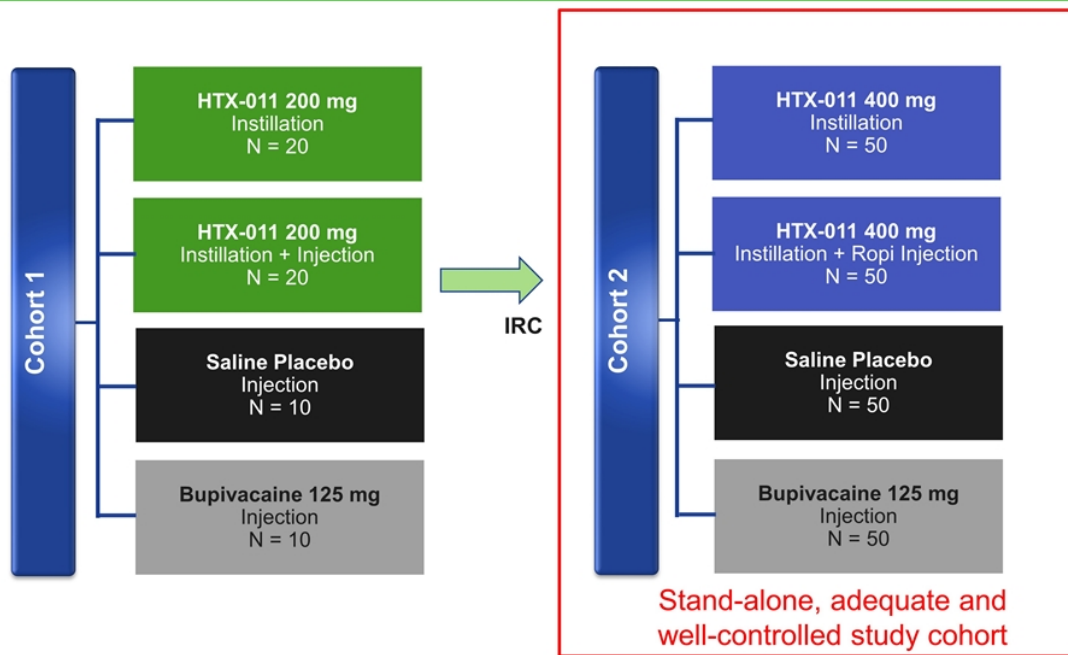
On-Going Phase 2b Studies

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



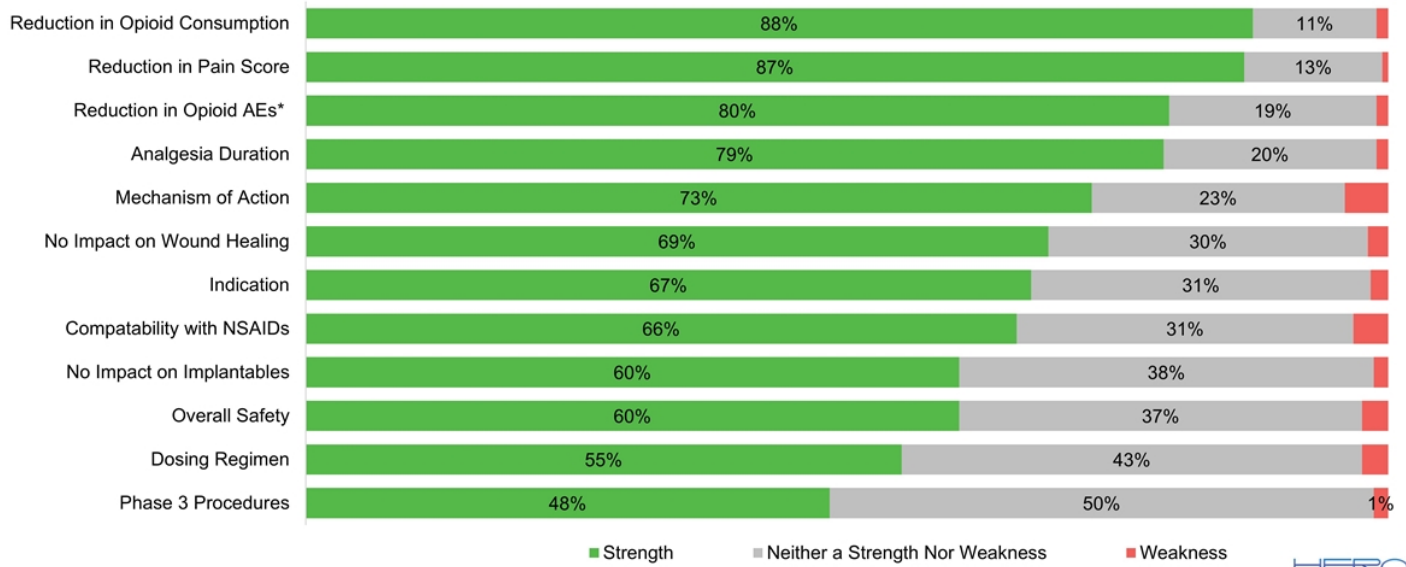
Large, growing market opportunity	✓
Differentiated, synergistic mechanism addresses inflammation – a key inhibitor of both generic and long-acting local anesthetics	✓
Demonstrated superiority vs. generic bupivacaine solution in 3 diverse surgical models in Phase 2; both pivotal Phase 3 trials include 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



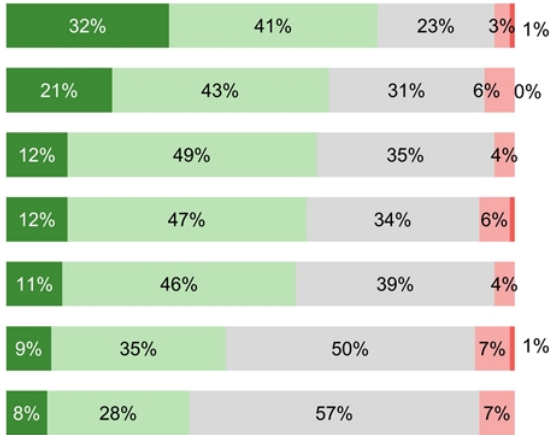
n = 376 total (101 anesthesiologists, 51 general surgeons, 122 orthopedic surgeons, 50 plastic surgeons, 52 pharmacy directors)
 *Opioid AE's are assumed to be reduced with significant reduction in use



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

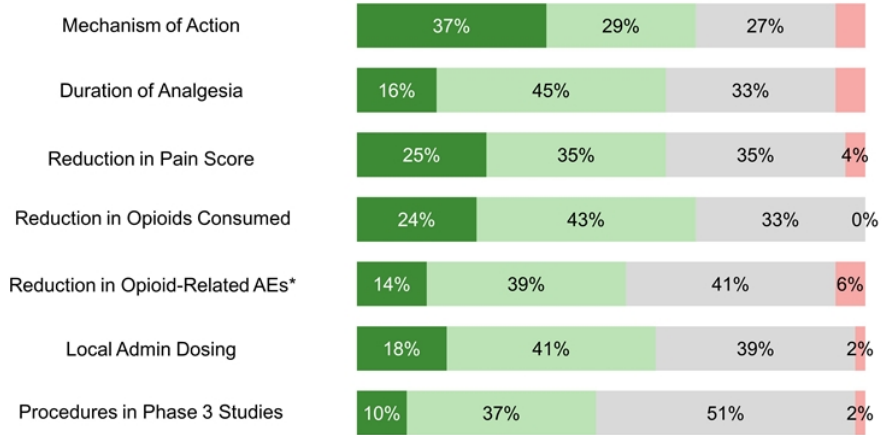
Preference for HTX-011 vs. Exparel Based on Product Attributes

Physician Responses



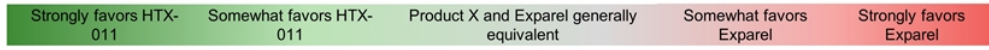
n = 324 total (101 anesthesiologists, 51 general surgeons, 122 orthopedic surgeons, 50 plastic surgeons)

Pharmacy Director Responses



n = 52 pharmacy directors

Shading Legend:



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

Common shares outstanding at December 31, 2017 totaled 64.6 million



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	