
**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 7, 2019

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 7, 2019, 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, 2018 (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 7, 2019, 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 7, 2019
99.2	Corporate Presentation, dated January 7, 2019

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.

Date: January 7, 2019

Heron Therapeutics, Inc.

/s/ David L. Szekeres

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



Heron Therapeutics Highlights Progress in Pain Management and CINV Franchises

- Acceptance of HTX-011 NDA for Postoperative Pain Management with Priority Review Designation; PDUFA Date of April 30, 2019 -

- 90% of Patients Treated with HTX-011 Opioid-Free 72 Hours Post-Surgery in New Multi-center Clinical Study -

- Formal Development Initiated on HTX-034, Our Next-Generation Product for Postoperative Pain Management, Following Positive Preclinical Results -

- Fourth-Quarter 2018 Net Sales for CINV Franchise of Approximately \$28.1 Million, Up 180% Year-over-Year and Up 42% from the Third-Quarter of 2018 -

- Full-Year 2018 Net Sales for CINV Franchise of Approximately \$76.7 Million, versus Guidance of \$70 Million to \$72 Million -

- Full-Year 2019 Net Sales Guidance for CINV Franchise of \$115 Million to \$120 Million -

SAN DIEGO, Calif.-(PR NEWSWIRE)-January 7, 2019 — Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs, today highlighted progress in its pain management and chemotherapy-induced nausea and vomiting (CINV) franchises.

Recent Corporate Progress

Pain Management Franchise

- **Acceptance of HTX-011 NDA for Postoperative Pain Management with Priority Review Designation; PDUFA Date of April 30, 2019:** The U.S. Food and Drug Administration (FDA) recently accepted the new drug application (NDA) for Heron's investigational agent, HTX-011, and has granted it a Priority Review designation. The FDA set a Prescription Drug User Fee Act (PDUFA) goal date of April 30, 2019 and indicated that it is not currently planning an advisory committee meeting to discuss this application.
- **90% of Patients Treated with HTX-011 Opioid-Free 72 Hours Post-Surgery in New Multi-center Clinical Study:** In this study, 63 patients undergoing hernia repair surgery received HTX-011 together with a regimen of generic, over-the-counter (OTC), oral analgesics (acetaminophen and ibuprofen). Ninety percent (90%) of patients were opioid-free 72 hours post-surgery, and 81% were still opioid-free 28 days post-surgery.
- **Formal Development Initiated on HTX-034, Our Next-Generation Product for Postoperative Pain Management:** Based on the positive results of preclinical studies in which HTX-034 demonstrated significant pain reduction for 7 days, Heron has initiated formal development of this next-generation postoperative pain product.

CINV Franchise

- **Fourth-Quarter 2018 Net Sales:** Fourth-quarter 2018 net sales for the CINV franchise were approximately \$28.1 million, up 180% year-over-year and up 42% from the third quarter of 2018. This included net sales of approximately \$23.0 million for CINVANTI® (aprepitant) injectable emulsion and approximately \$5.1 million for SUSTOL® (granisetron) extended-release injection.
- **Full-Year 2018 Net Sales:** Full-year 2018 net sales for the CINV franchise were approximately \$76.7 million, versus guidance of \$70 million to \$72 million. This included net sales of approximately \$55.8 million for CINVANTI and approximately \$20.9 million for SUSTOL.
- **Full-Year 2019 Net Sales Guidance:** Heron expects full year 2019 net sales for the CINV franchise of \$115 million to \$120 million.

“2018 was a year of significant progress for Heron. On the commercial front, we are very pleased with the strong sales performance of our CINV franchise. On the development front, HTX-011 has now been shown to reduce pain significantly better than placebo or bupivacaine solution in five diverse surgical models, including studies that resulted in significantly more patients receiving HTX-011 who were opioid-free through 72 hours after surgery,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron. “In 2019, we look forward to working with the FDA to bring an important non-opioid pain management option to patients. We believe that HTX-011, if approved, could have a considerable impact on the opioid epidemic by significantly reducing the proportion of patients who experience severe pain and receive opioids after surgery.”

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 management 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. HTX-011 has been shown to reduce pain significantly better than placebo or bupivacaine solution in five diverse surgical models: hernia repair, abdominoplasty, bunionectomy, total knee arthroplasty and breast augmentation. HTX-011 was granted Fast Track designation from the FDA in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. Heron submitted an NDA to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. The FDA set a PDUFA goal date of April 30, 2019.

About CINVANTI (aprepitant) injectable emulsion

CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). CINVANTI 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 nausea and vomiting in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy). CINVANTI is the only IV formulation of an NK₁ receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of 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® 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 Heron Therapeutics, Inc.

Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to 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 pain or cancer.

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 full-year 2019 net sales guidance for the CINV franchise; whether the FDA approves the HTX-011 NDA as submitted; the timing of the FDA’s review process for HTX-011; whether the FDA will require an advisory committee meeting for HTX-011 in the future; the anticipated commercial launch of HTX-011; the timing and results of the studies in the HTX-034 development program; and other risks and uncertainties identified in the Company’s filings with the U.S. 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:

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858-251-4447

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Corporate Update

January 7, 2019

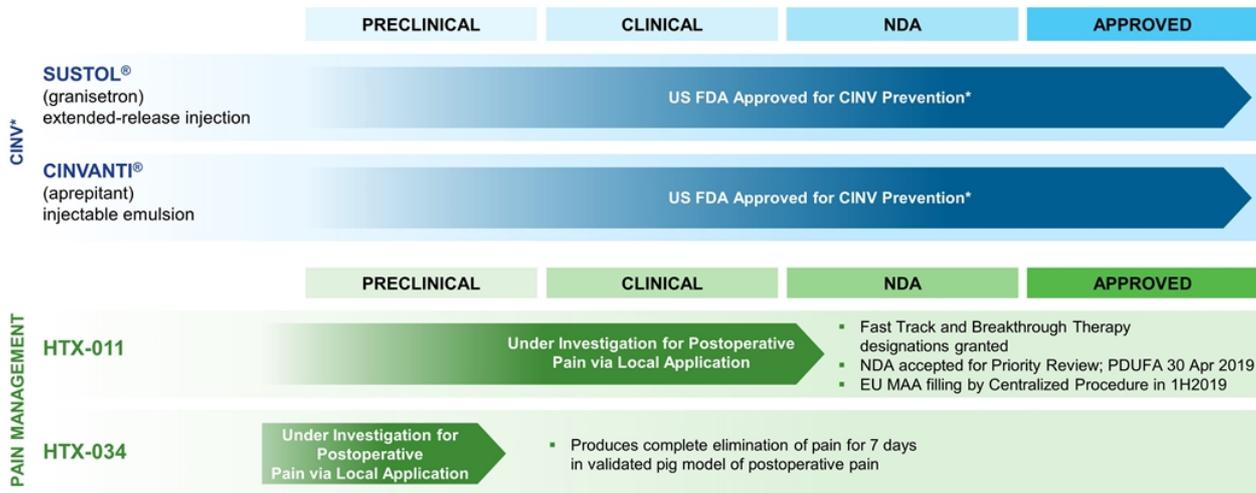


Forward-Looking Statements

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: the full-year 2019 net sales guidance for the CINV franchise; whether the FDA approves the HTX-011 NDA as submitted; the timing of the FDA's review process for HTX-011; whether the FDA will require an advisory committee meeting for HTX-011 in the future; whether the EMA accepts the HTX-011 MAA as submitted; whether the European Commission authorizes the MAA; the anticipated commercial launch of HTX-011; the potential market opportunity for HTX-011; the timing and results of the studies in the HTX-034 development program; and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and we take no obligation to update or revise these statements except as may be required by law.

Heron Pipeline

We are currently developing and commercializing pharmaceutical products for patients suffering from cancer or postoperative pain:



*CINV: Chemotherapy-induced nausea and vomiting. SUSTOL® (granisetron) extended-release injection is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. CINVANTI® (aprepitant) injectable emulsion, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). CINVANTI has not been studied for treatment of established nausea and vomiting.

HTX-011 and HTX-034 are an investigational new drugs and are not approved by the FDA or other regulatory authority

HTX-011 NDA for Postoperative Pain Management Has Received Priority Review

- FDA granted Priority Review to HTX-011 NDA with a PDUFA goal date of April 30, 2019
- HTX-011 received Fast Track designation in 4Q 2017 and Breakthrough Therapy designation in 2Q 2018
 - Fast Track and Breakthrough Therapy products eligible for priority review if supported by clinical data at time of NDA submission
- Priority Review designation
 - for drugs that, if approved, would be significant improvements in safety or effectiveness of the treatment or prevention of serious conditions
 - intended to direct overall attention and resources of FDA to evaluation of such applications

Postoperative Pain and its Impact on the Opioid Crisis



The Cost of Opioids

How Postoperative Opioids Can Be a Doorway to Addiction

MORE THAN 50 MILLION surgical procedures happen in the United States.¹
90% of patients undergoing a surgical procedure are prescribed opioids for pain management.²



As many as **6.5%** of patients who take opioids to manage pain after surgery may become persistent opioid users.¹



Of these 2.6 million persistent opioid users, approximately

~500,000 will become addicted to opioids.³

That equals about **2.9 MILLION PEOPLE.¹**



In addition, opioid discharge prescriptions filled by recovering surgical patients result in more than **1 billion unused pills.^{4,5}**

70% of all these opioid tablets go unused.² **90%** of these pills remain inside the home in unsecured locations.⁶ **32%** of all opioid addicts report first opioid exposure through leftover pills.⁷

More than **\$13 billion** of the annual healthcare costs associated with addiction can be attributed to postoperative pain management.^{1,3,8}



References: 1. Brummett, Chad M., et al. 2017. "New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults." *JAMA Surgery* 152 (6): e170504. doi:10.1001/jamasurg.2017.0504.
2. Hill, Maureen V., et al. 2017. "Wide Variation and Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures." *Annals of Surgery* 265 (4): 709-714. 3. Banta-Green, et al (2009). Opioid use behaviors, mental health and pain—Development of a typology of chronic pain patients. *Drug and Alcohol Dependence* 104(1-2), 34-42. <https://doi.org/10.1016/j.drugalcdep.2009.03.021>. 4. CDC 2017. Centers for Disease Control and Prevention. Opioid Overdose: U.S. Prescribing Rates Map. Available at <https://www.cdc.gov/drugoverdose/maps/prescribe-maps.html>. Accessed 8 March 2018. 5. Levy et al. "Trends in Opioid Analgesic-Prescribing Rates by Specialty, U.S., 2007-2012." *Am J Prev Med*. 2015;49(3):409-413. 6. Sales, et al. 2011. "Overprescription of Postoperative Narcotics: A Look at Postoperative Pain Medication Delivery, Consumption and Disposal in Urological Practice." *The Journal of Urology* 185 (2): 551-55. doi:10.1016/j.juro.2010.09.088. 7. Canfield, Maria C., et al. 2010. "Prescription Opioid Use Among Patients Seeking Treatment for Opioid Dependence." *Journal of Addiction Medicine* 4 (2): 108-13. doi:10.1097/ADM.0b013e3181b5a713. 8. The Council of Economic Advisers, 2017. *The Underestimated Cost of the Opioid Crisis*.

Heron's Goals For Postoperative Pain Program

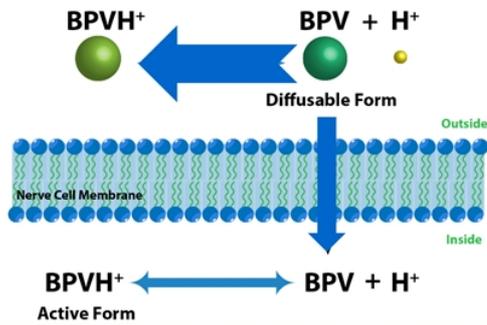
- Our philosophy is that:
 1. Opioids play an important role for reduction of severe pain, but should be used as a last resort, rather than the first step in pain management
 2. Reduction in the use of opioids should not come at the cost of patients experiencing more pain
 3. Using our technology as part of a multi-modal postoperative pain regimen, our goal is to:
 - Eliminate the need for opioids to control postoperative pain in as close to 100% of patients as possible, making discharge prescriptions for opioids unnecessary in the outpatient setting
 - Provide better pain control than conventional reliance on opioids

HTX-011 Mechanism of Action



A Potential Hypothesis: Inflammation, pH, and Local Anesthetic Failure

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



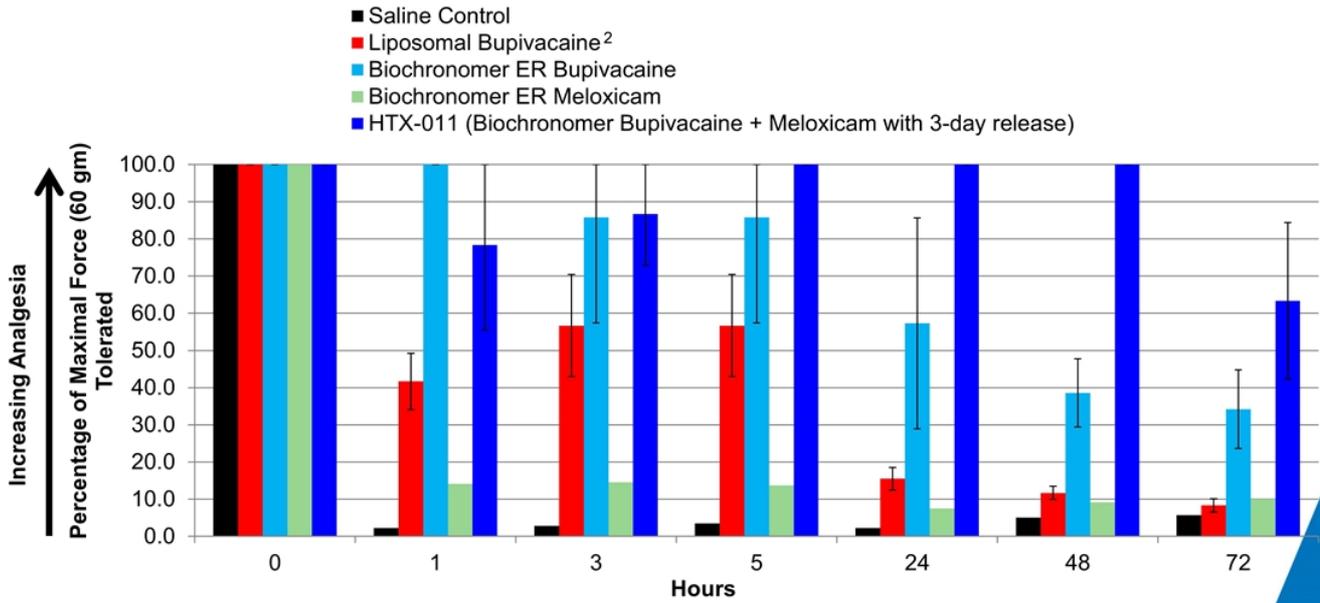
Inflammation produces an acidic environment

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

- With a pKa of 8.1, bupivacaine is sensitive to reduced pH
- The acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects^{1,2}

1. Hargreaves, K, Keiser, K, Local anesthetic failure in endodontics: Mechanisms and Management , *Endodontic Topics* 1:26–39 2002
2. Local anesthetic nerve penetration model adapted from Becker and Reed. *Anesth Prog* 53:98–109 2006

HTX-011 is Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery as Demonstrated in this Preclinical Model¹



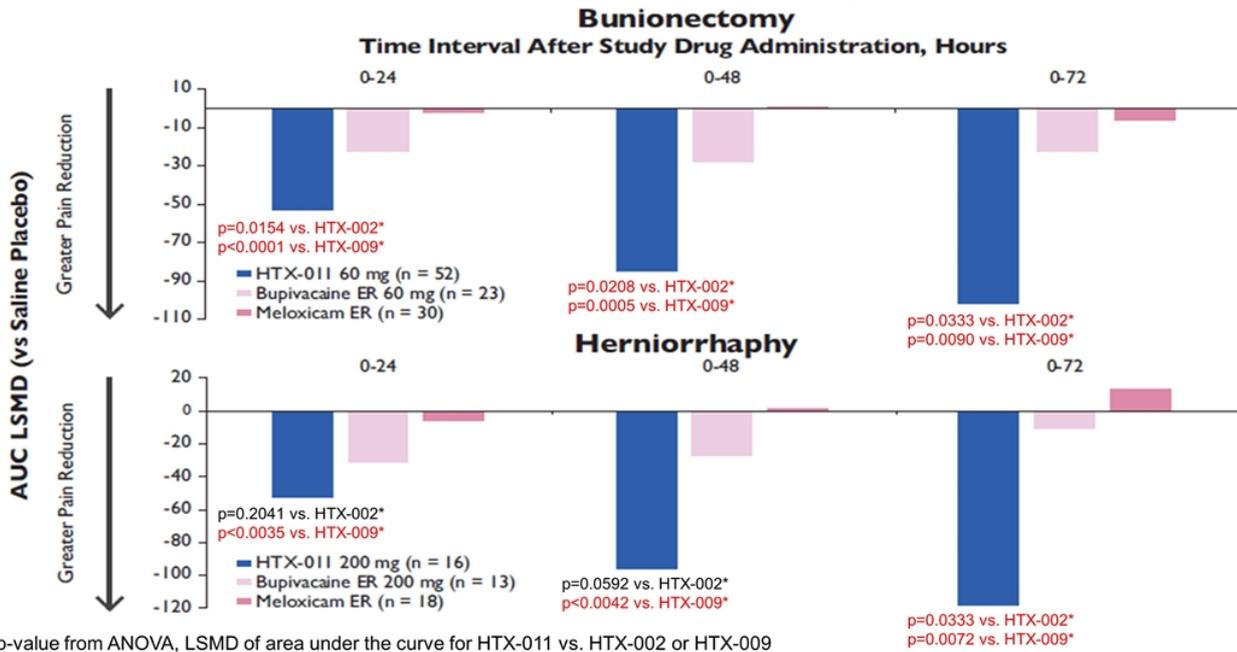
¹ Postoperative pain model in pigs from Castle et al, 2013 EPJ

² Human dose of liposomal bupivacaine with 40% smaller incision

(n=4 pigs in each arm)



HTX-011 Reduces Pain Better Than the Individual Components in Both Bunionectomy and Herniorrhaphy Phase 2 Studies



*p-value from ANOVA, LSMD of area under the curve for HTX-011 vs. HTX-002 or HTX-009

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



HTX-011 is Applied into the Surgical Site at the End of Surgery Without a Needle

HTX-011 is a single-dose application administered via a needle-free syringe to directly coat the affected tissue within the surgical site prior to suturing



Reference: Data on file.

Seven Active-Controlled Studies Showing Significantly Better Pain Reduction With HTX-011 Than Bupivacaine Included in NDA

Study	Phase	Surgical Model	Tissue Type	Significant for Pain Reduction vs. PBO	Significant for Pain Reduction vs. BPV	Significant Reduction in Opioid Use
202	2	Herniorrhaphy	Soft	✓	✓	✓
203	2	Abdominoplasty	Soft	✓	✓	✓
208	2	Bunionectomy	Bony	✓	✓	✓
209	2b	TKA	Bony	✓	✓	✓
211	2b	Breast Augmentation	Soft	✓	✓	✓
301	3	Bunionectomy	Bony	✓	✓	✓
302	3	Herniorrhaphy	Soft	✓	✓	✓

PBO = placebo; BPV = bupivacaine solution; TKA = total knee arthroplasty

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

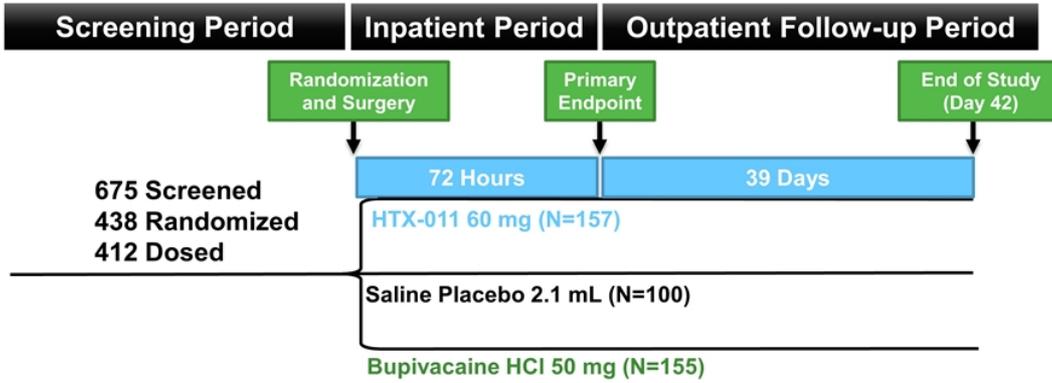
HTX-011 Clinical Development

EPOCH 1: Bunionectomy Results
(Study 301)



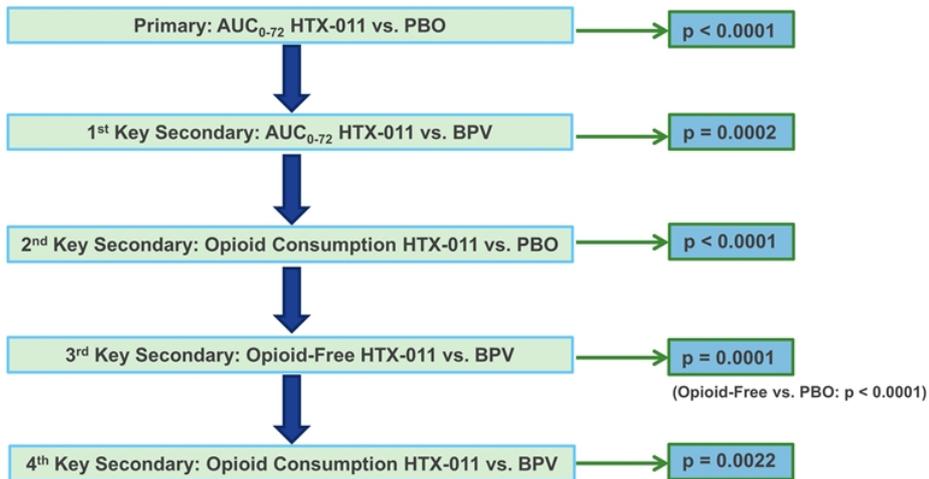
EPOCH 1 (Study 301) Bunionectomy: Study Design

- N = 412 (3:2:3 to HTX-011 60 mg, saline placebo, or bupivacaine HCl 50 mg)
- 438 subjects were randomized and 412 were dosed (ITT Population)
- 13 sites in the United States



1 subject (006-1018) was randomized to Bupivacaine HCl but received saline placebo

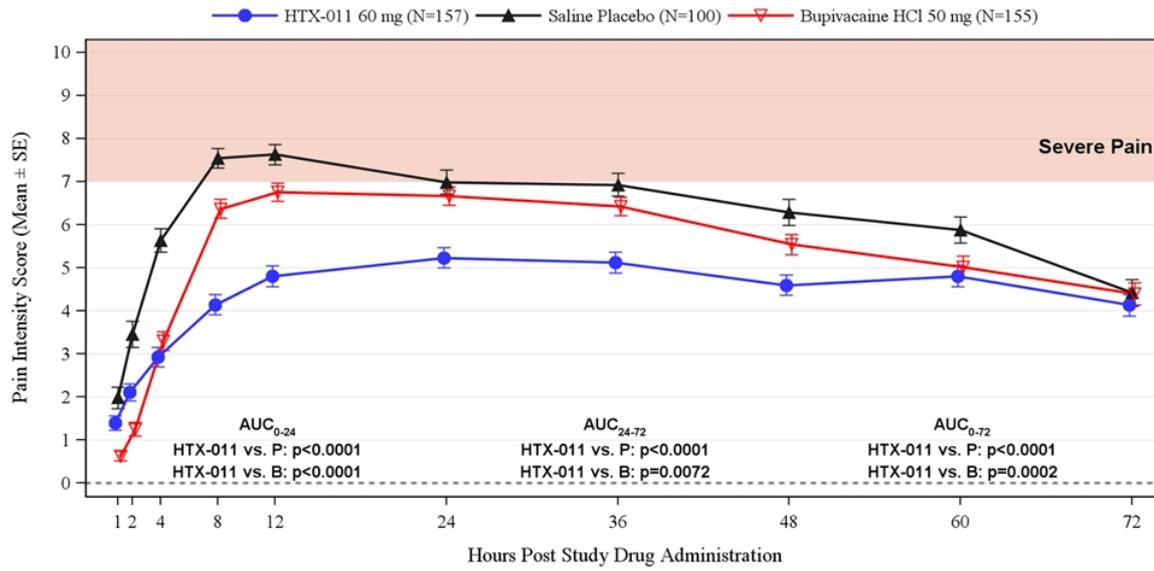
EPOCH 1 Bunionectomy: Results Hierarchy



PBO: saline placebo; BPV: bupivacaine HCl

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

EPOCH 1 Bunionectomy: Mean Pain Intensity



17

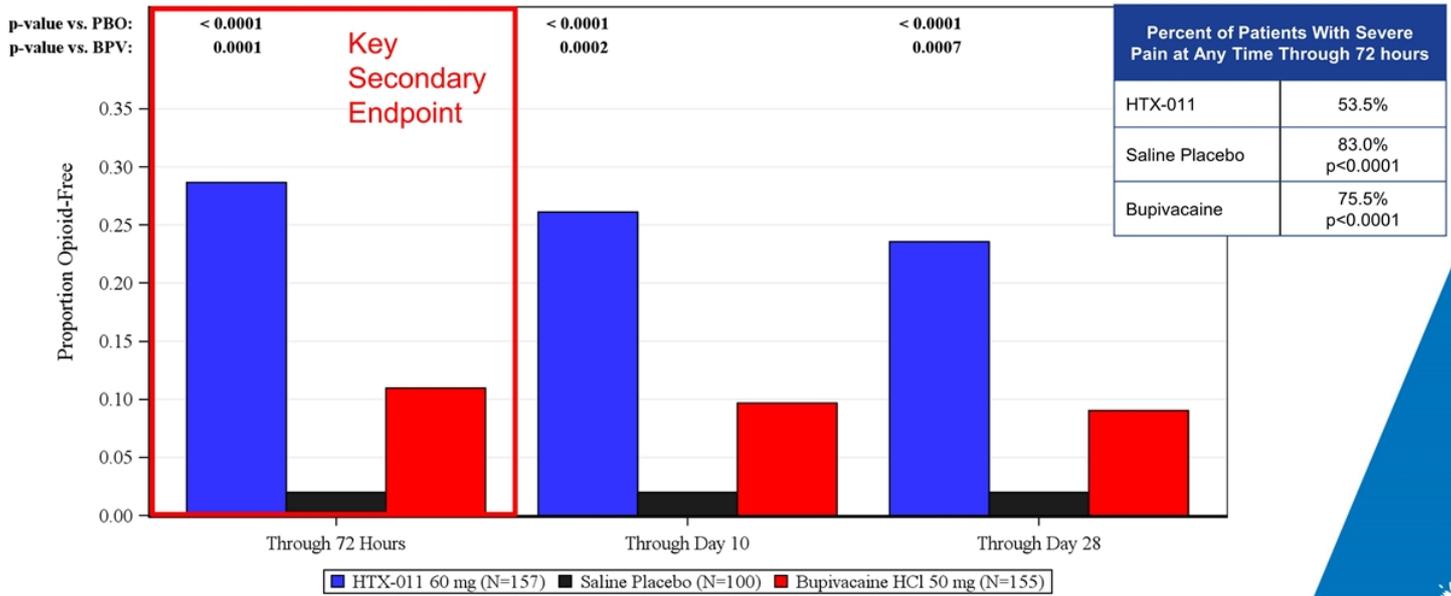
wWOCF – window worst observation carried forward

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

Source: Figure 14.2.7



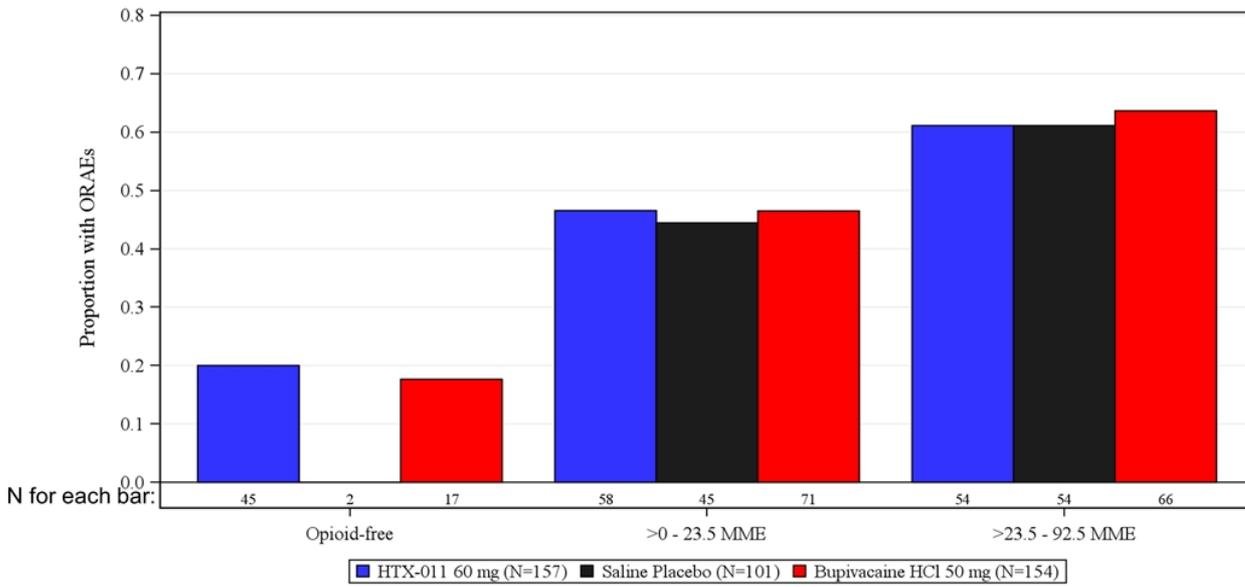
EPOCH 1 Bunionectomy: Percentage of Subjects Who Are Opioid-Free Through 72 hours and Through Days 10 and 28



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



EPOCH 1 Bunionectomy: HTX-011 Opioid-Free Subjects Have the Lowest Rate of Opioid-Related Adverse Events (ORAEs)

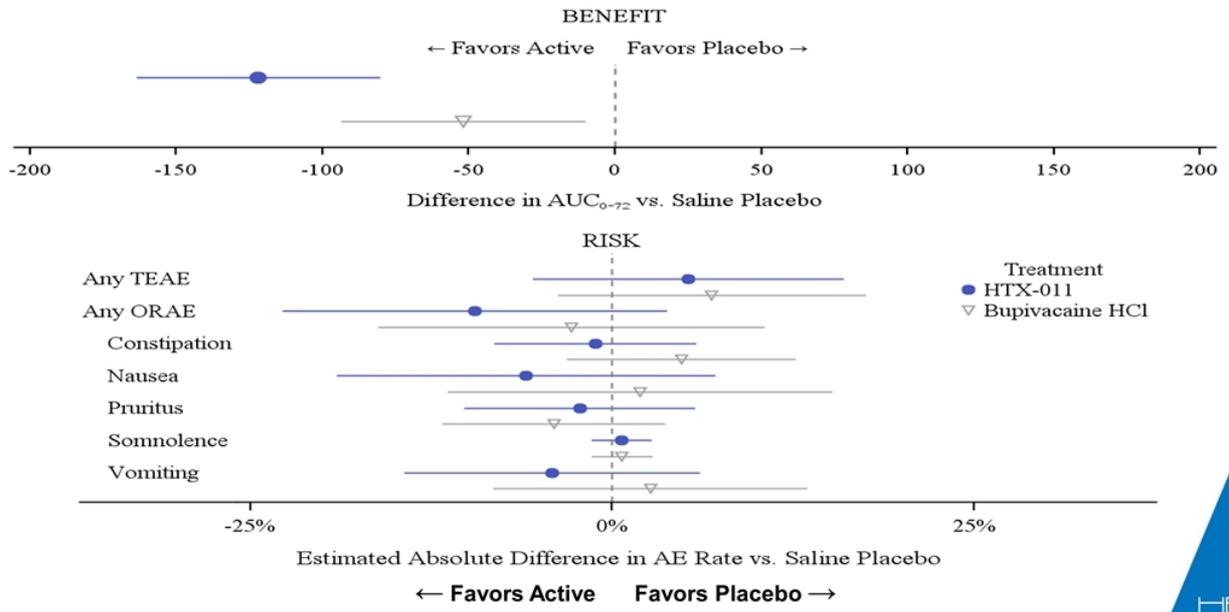


Opioid consumption is measured in milligram morphine equivalents (MME)

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



EPOCH 1 Bunionectomy: Benefit – Risk for HTX-011



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

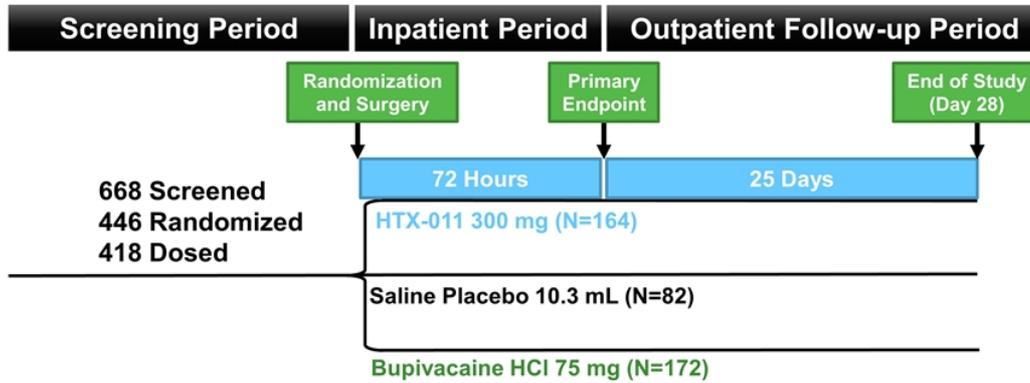
HTX-011 Clinical Development

EPOCH 2: Herniorrhaphy Results
(Study 302)



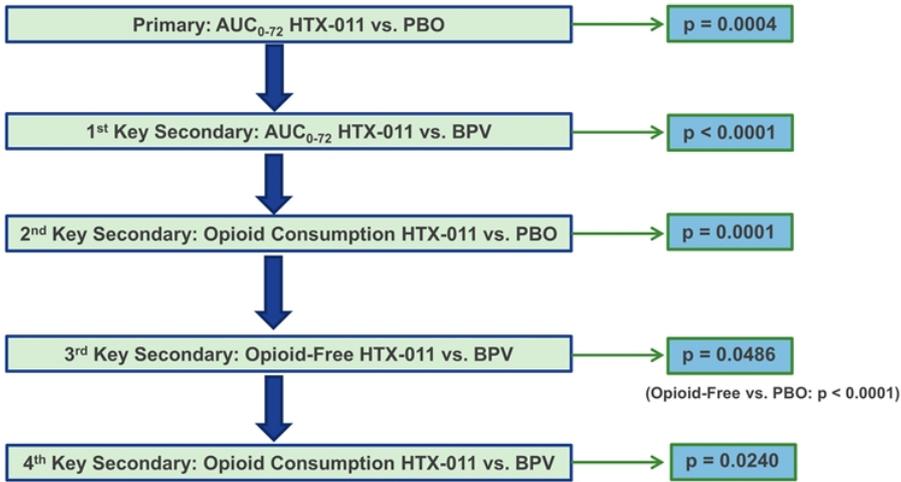
EPOCH 2 (Study 302) Herniorrhaphy: Study Design

- N= 418 (2:1:2 to HTX-011 300 mg, saline placebo, or bupivacaine HCl 75 mg)
- 446 subjects were randomized and 418 were dosed (ITT Population)
- 17 sites in 2 countries (United States, Belgium)



1 subject (005-2018) was randomized to HTX-011 but received Bupivacaine HCl

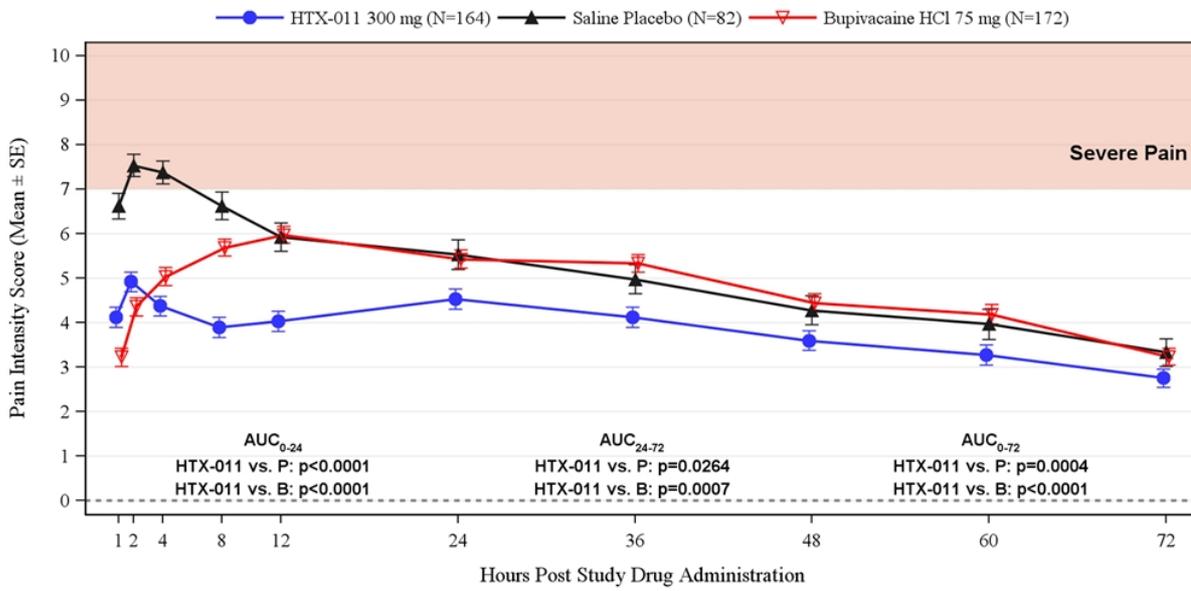
EPOCH 2 Herniorrhaphy: Results Hierarchy



PBO: saline placebo; BPV: bupivacaine HCl

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

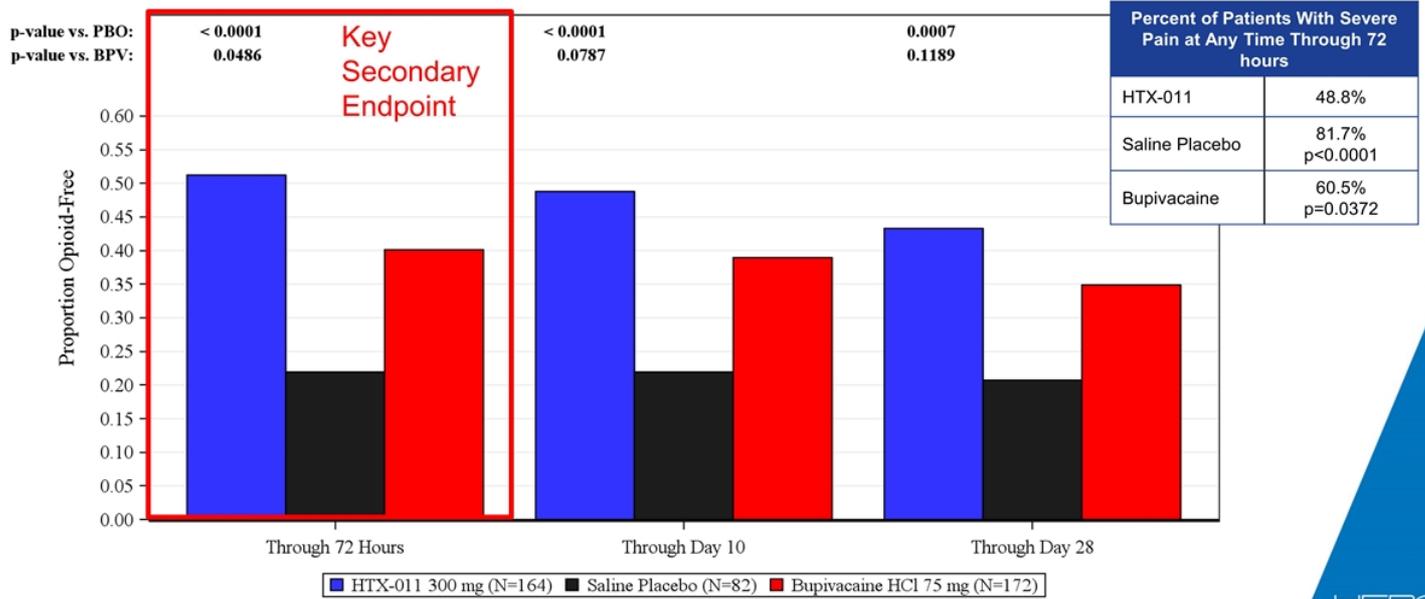
EPOCH 2 Herniorrhaphy: Mean Pain Intensity



24 Source: Figure 14.2.7

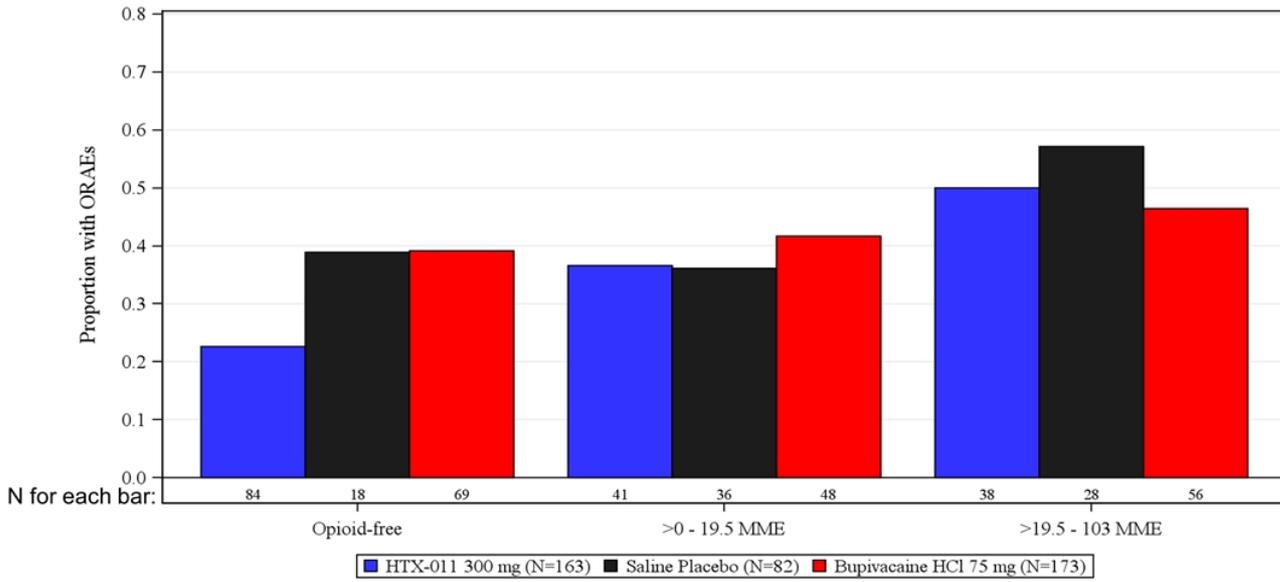
HTX-011 is an investigational new drug and not approved by the FDA

EPOCH 2 Herniorrhaphy: Percentage of Subjects Who Are Opioid-Free Through Day 28



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

EPOCH 2 Herniorrhaphy: HTX-011 Opioid-Free Subjects Have the Lowest Rate of Opioid-Related Adverse Events (ORAEs)

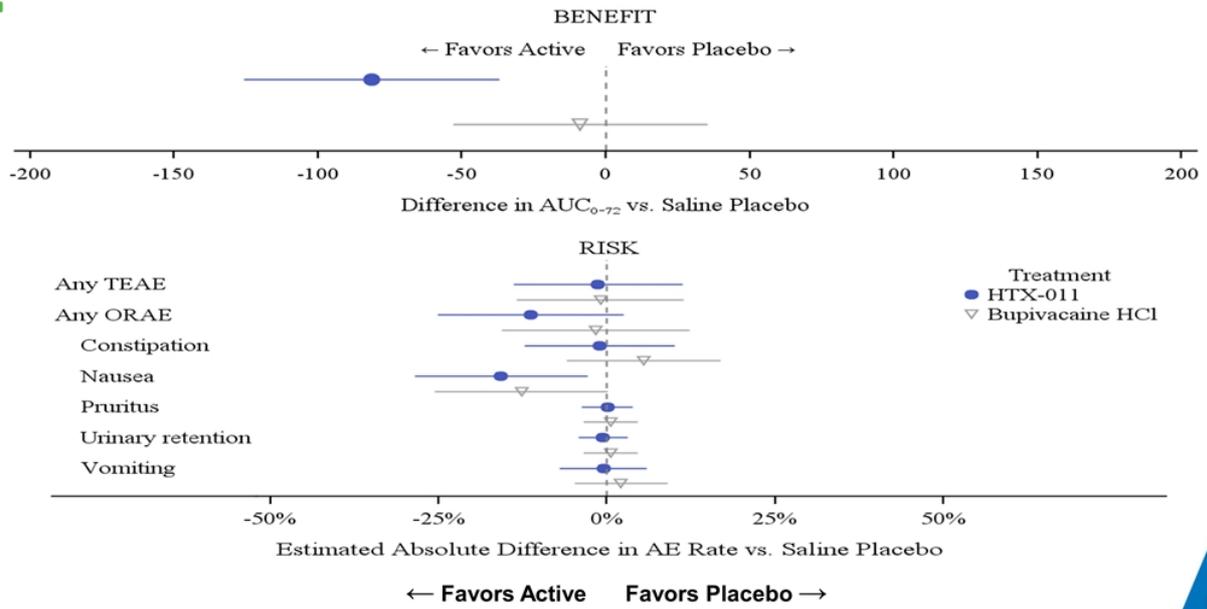


Opioid consumption is measured in milligram morphine equivalents (MME)

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



EPOCH 2 Herniorrhaphy: Benefit – Risk for HTX-011



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

HTX-011 Clinical Development

Phase 2b Total Knee Arthroplasty
(TKA) Study
(Study 209)



Study 209 Phase 2b: Total Knee Arthroplasty

HTX-011 400 mg
Instillation
N = 58

HTX-011 400 mg
Instillation, plus ropivacaine
50 mg injected to posterior
capsule
N = 56

Saline Placebo
Injection
N = 53

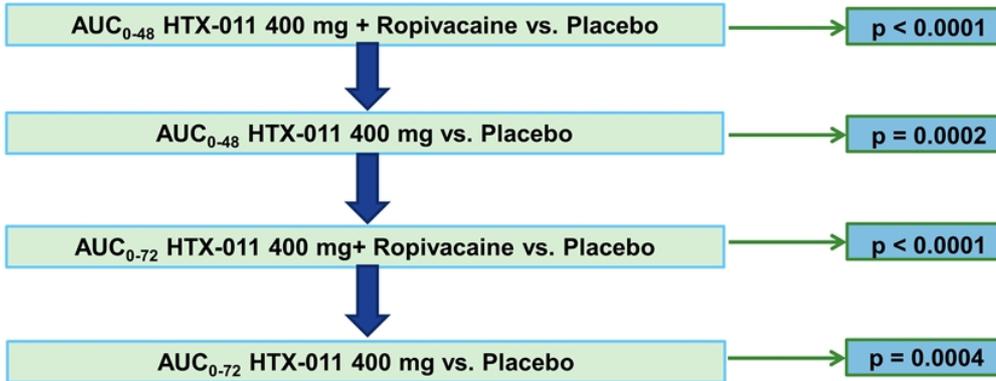
Bupivacaine 125 mg
Injection
N = 55

- Pre-op Medication: acetaminophen (IV) 1 g, pregabalin (oral) 150 mg
- HTX-011 Administration Technique: needle-free instillation of 100 mg for posterior capsule & 300 mg for remaining tissue
- Ropivacaine Administration Technique: 50 mg injected into posterior capsule
- Post-op Medication: only opioid rescue medication available

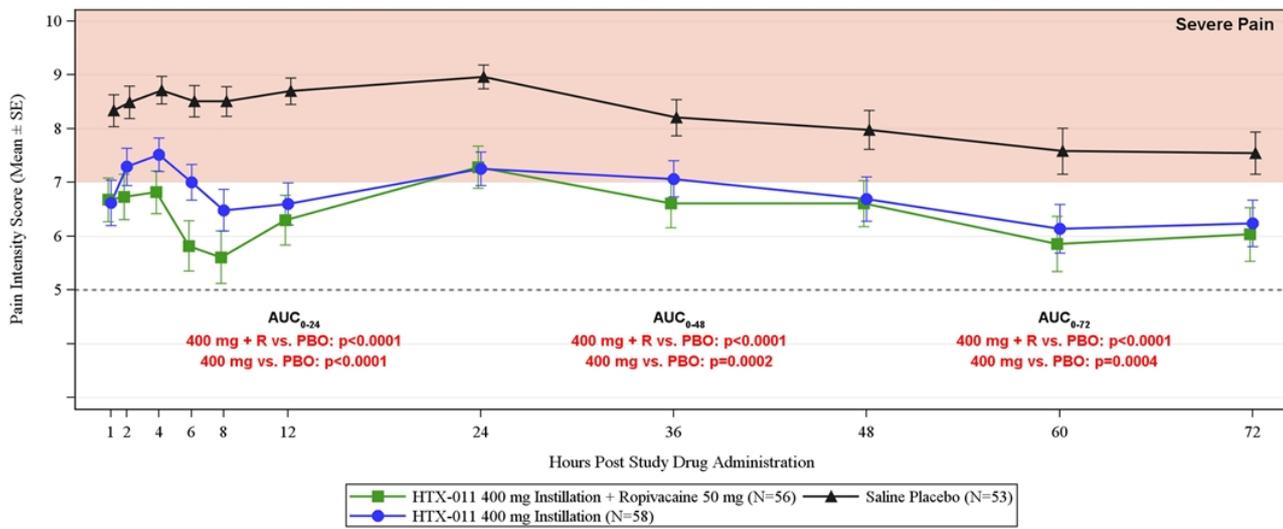
HTX-011 is an investigational new drug and not approved by the FDA

Study 209 TKA: Results Hierarchy

HTX-011 via instillation achieved primary and key secondary endpoints for reduction in pain intensity scores at rest (NRS-R)



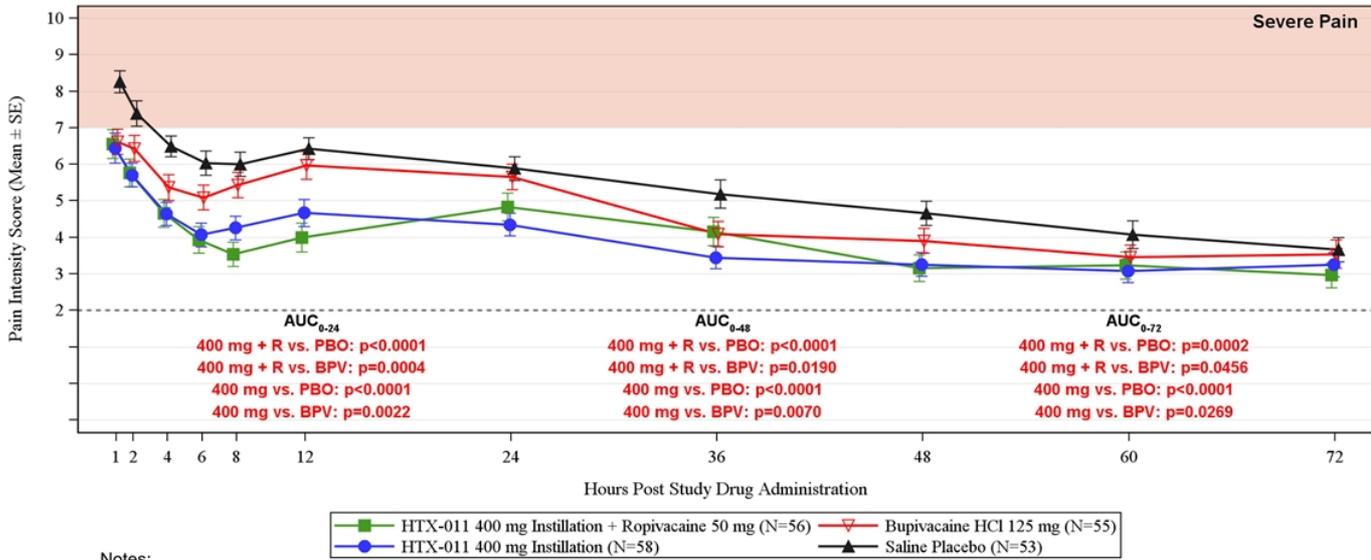
Study 209 TKA: Significant Separation between HTX-011 Arms and Placebo through 72 Hours (Primary Endpoint)



WOCF for use of opioid rescue medication and LOCF for missing pain data

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

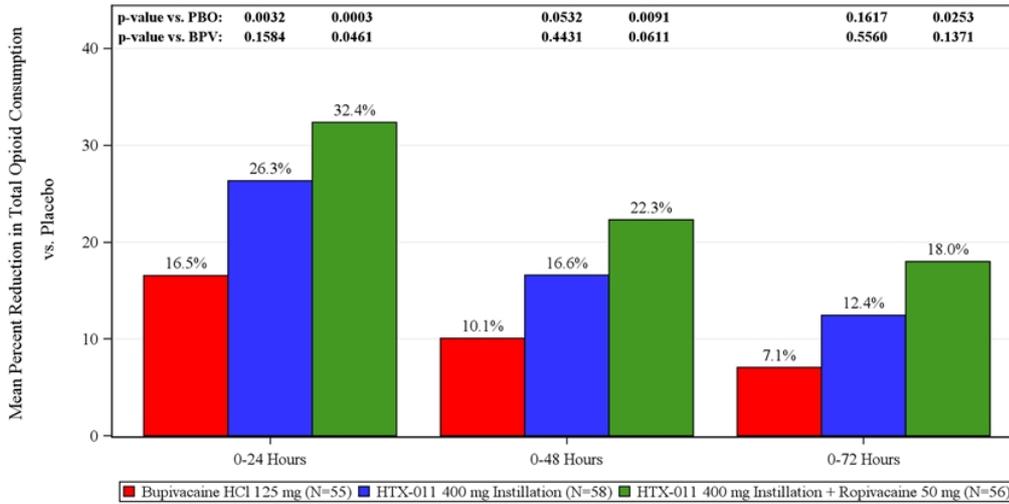
Study 209 TKA: HTX-011 Significantly Superior to Both Placebo and Bupivacaine Through 72 Hours Without Adjusting for Opioid Use



Notes:
 Pain intensity collected at rest
 LOCF for missing data and no adjustment for use of opioid rescue medication



Study 209 TKA: HTX-011 Reduces Opioid Use through 72 Hours

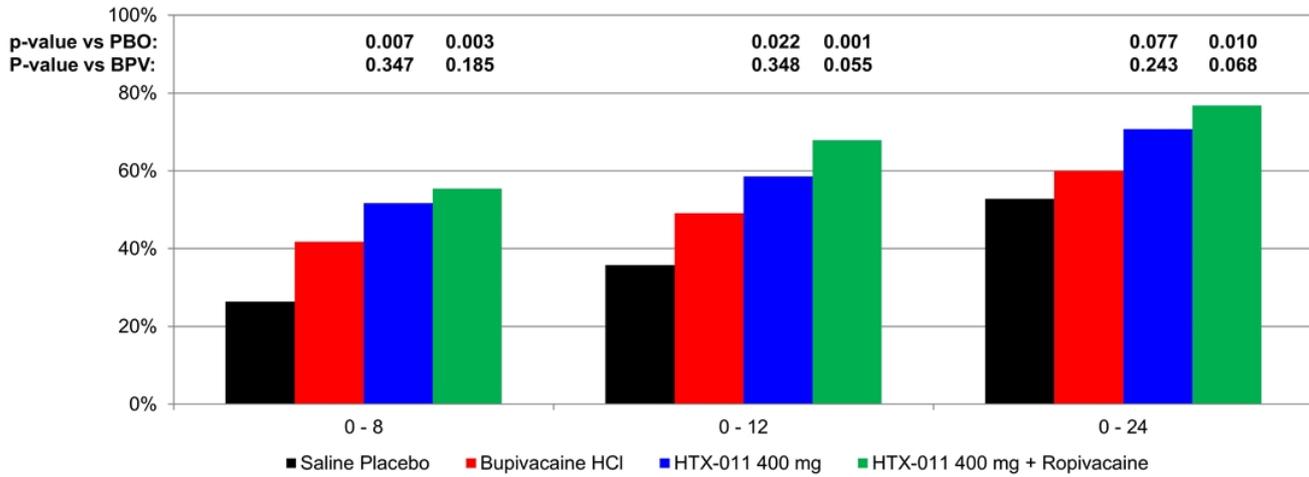


Opioid consumption is measured in milligram morphine equivalents (MME)

Source: Figure 14.2.2.2

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

Study 209 TKA: Significant Increase Compared to Placebo in Patients Achieving “Discharge Ready” MPADSS Criteria* with HTX-011



*MPADSS, modified postanaesthetic discharge scoring system. The proportion of subjects who first achieve an MPADSS score ≥ 9 at each timepoint was analyzed cumulatively. P-values from Fisher's exact test.

Source: Table 14.2.13.2

Safety Summary

HTX-011 was generally well tolerated across all Phase 2 and Phase 3 studies with no clinically meaningful differences in:

- Overall adverse events
- The incidence of serious adverse events
- Premature discontinuations due to adverse events
- Potential local anesthetic systemic toxicity (LAST) adverse events
- Potential wound healing related adverse events
- No deaths on HTX-011 (one on bupivacaine)

HTX-011 Clinical Development

Phase 2 Opioid Elimination Study in
Herniorrhaphy
(Study 215)



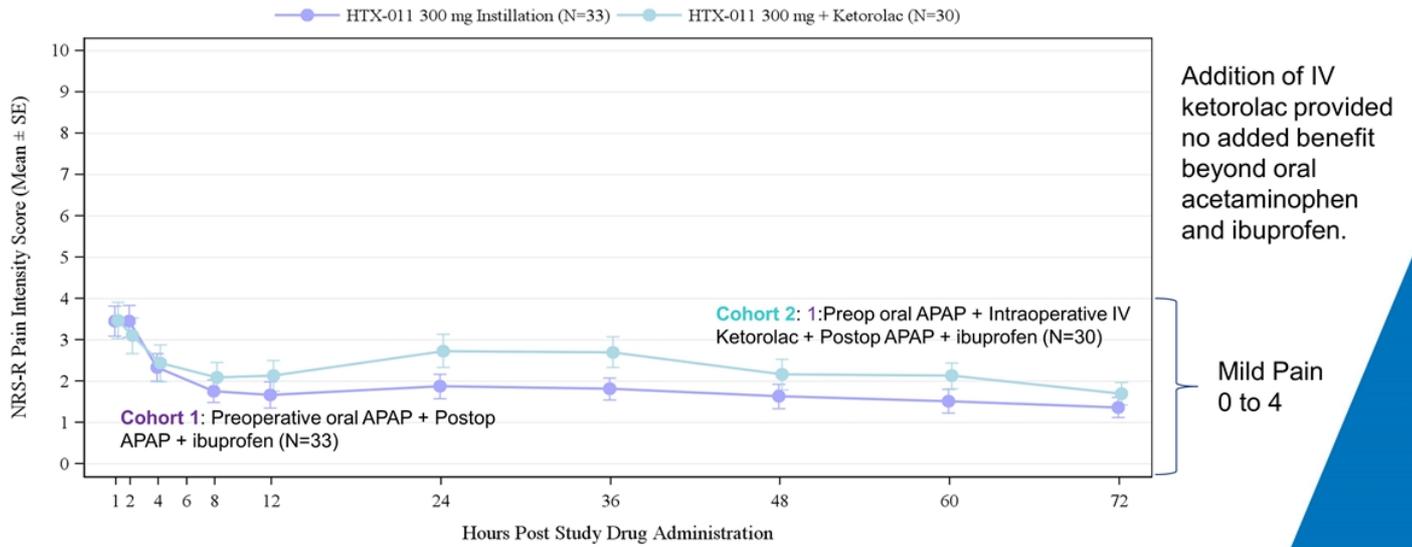
Study 215 Herniorrhaphy: Pilot Opioid Elimination Study

Study Rationale: Pilot study to evaluate use of HTX-011 with a standard background multimodal regimen.

Study Design:

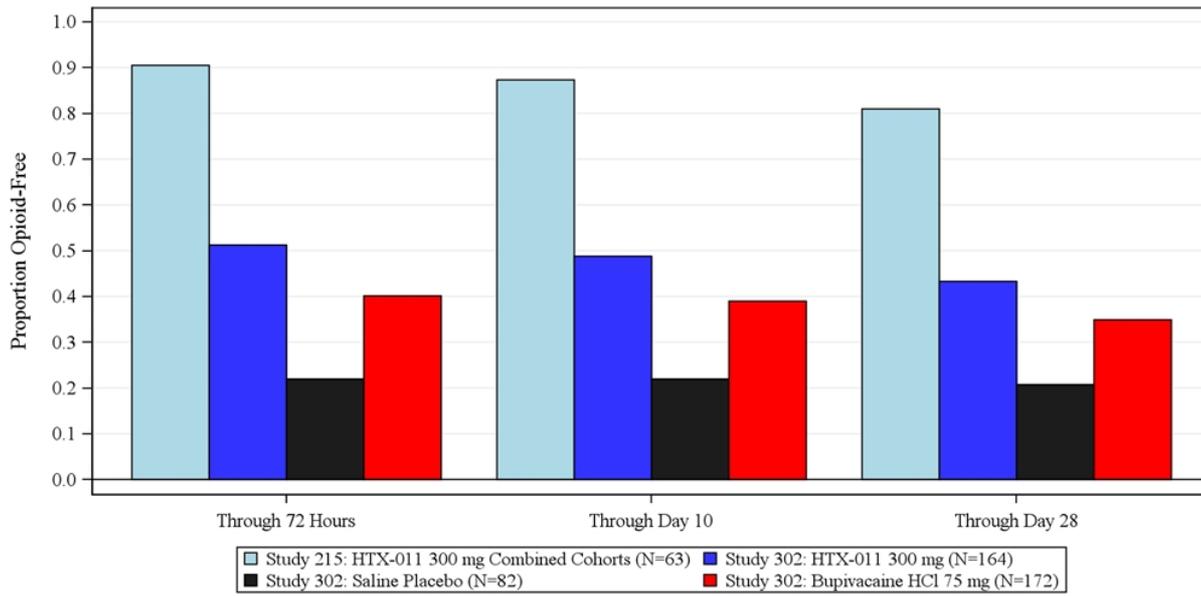
Treatment	Cohort	
	1	2
Number of Subjects Dosed	33	30
HTX-011 300 mg	√	√
+ Preoperative oral acetaminophen (APAP)	√	√
+ Postoperative acetaminophen q 6h + ibuprofen q6h	√	√
+ Intraoperative IV ketorolac		√

Study 215 Herniorrhaphy: HTX-011 Plus Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours



WOCF for use of opioid rescue medication and LOCF for missing pain data

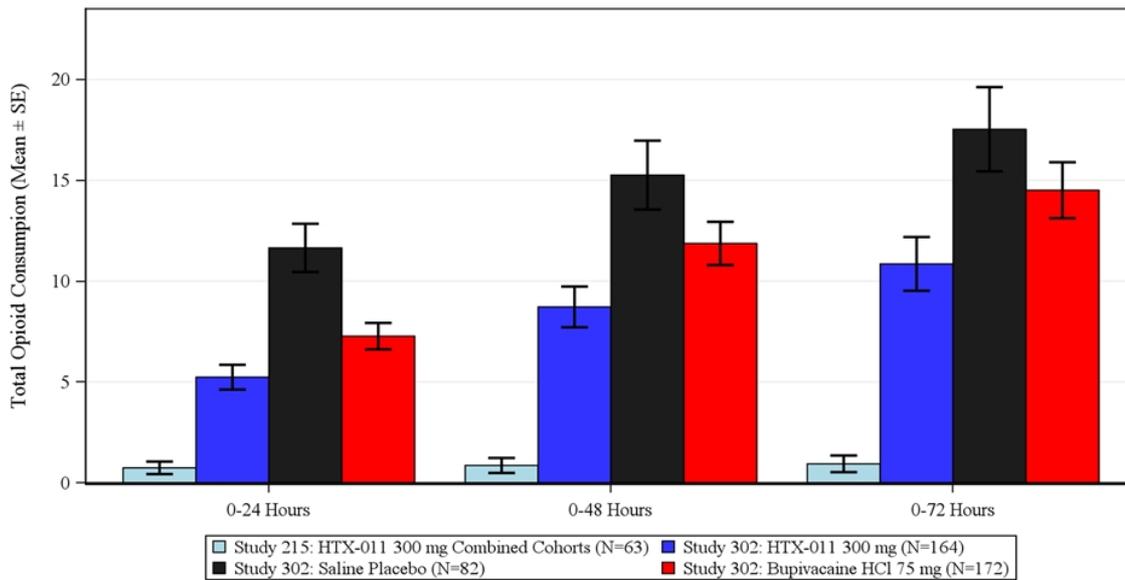
Study 302 and Study 215 Herniorrhaphy: Proportion of Patients Opioid-Free



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



Study 302 and Study 215 Herniorrhaphy: Mean Consumption of Opioid Rescue Medication



Opioid consumption is measured in milligram morphine equivalents (MME)

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

Proposed Standardized Protocol for Outpatient Open Inguinal Hernia Repair Surgery

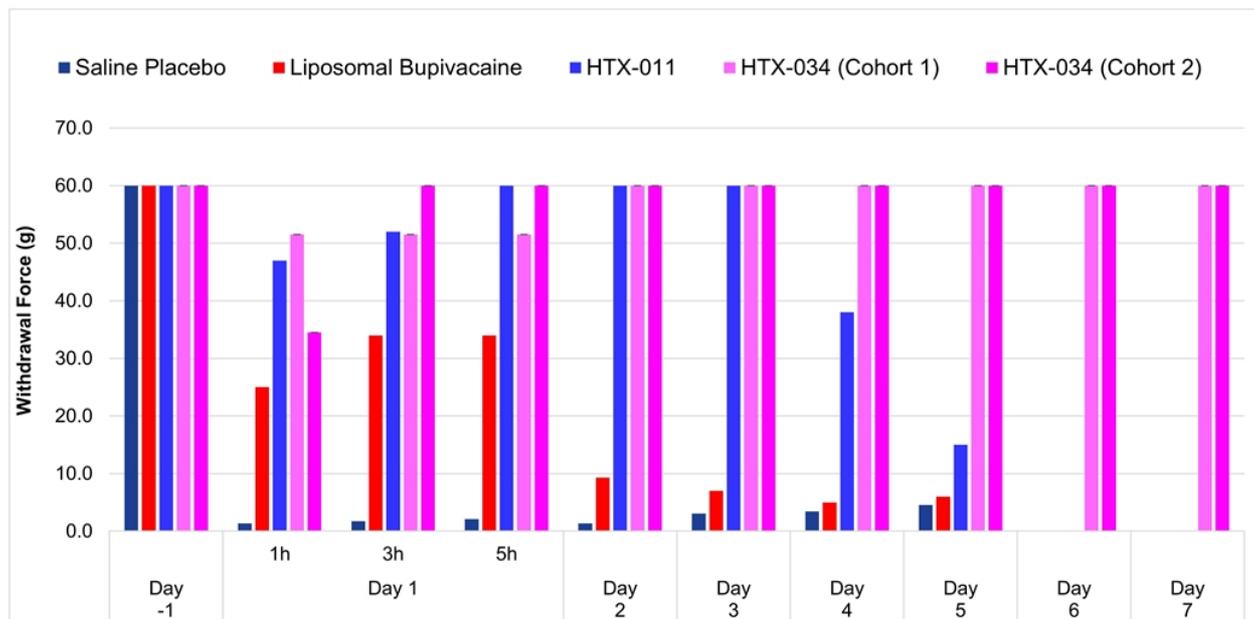
- HTX-011 at the end of surgery
- Scheduled acetaminophen and ibuprofen for 5 days; PRN after that
- For discharge 2 hours post surgery, only patients who have experienced a pain score of 6 or more should be given discharge opioids
 - 80% of patients would not need a discharge prescription
 - 5 pills of oxycodone would have been sufficient to avoid calls to the surgeon
- Use of this protocol in the approximately one million such procedures/year in US would decrease outpatient opioids by >90% from the current estimate of approximately 30M pills/year

HTX-034 Development

Next Generation Product for
Postoperative Pain



HTX-034 Produces Complete Elimination of Pain Through 7 Days in Pig Postoperative Pain Model



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



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

The Commercialization of HTX-011

Advancing Pain Management



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

Established Platform With Experienced Teams in Place

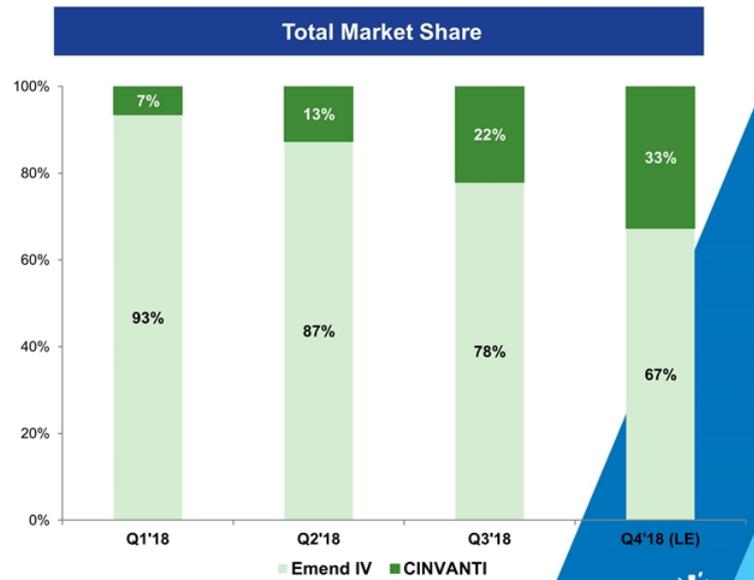
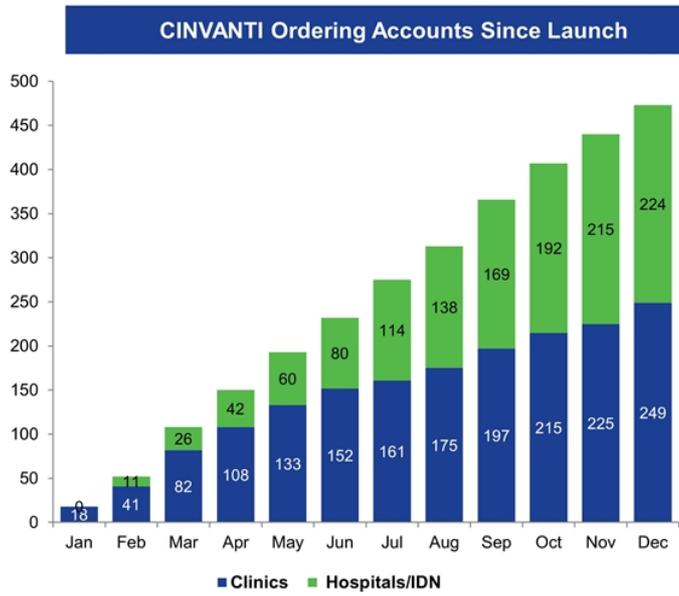
We are prepared for the launch of HTX-011. Our critical teams are already in place, with extensive experience in successful hospital launches.



EXISTING PLATFORM ADVANTAGES

- ✓ Strong KOL relationships
- ✓ Successful hospital and pain management launch experience
- ✓ IND/hospital/ASC expertise and relationships
- ✓ Reimbursement infrastructure in place
- ✓ GPO contracts in place*
- ✓ Full Line Wholesaler agreements and 3PL in place*
- ✓ Safety monitoring structure in place
- ✓ Proven compliant execution
- ✓ Robust systems in place and pressure tested for blockbuster launch

Commercial teams achieved rapid adoption of CINVANTI and captured one-third of the market in the first 12 months of launch

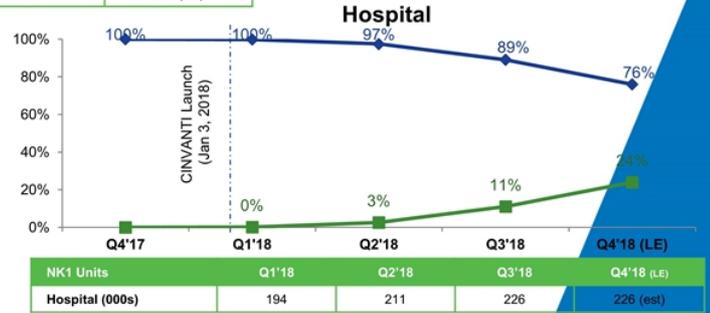
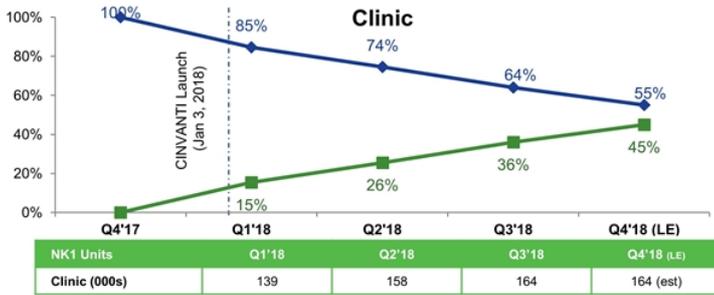


Source: Heron 867 data December 31, 2018



Commercial teams demonstrated the ability to execute across both clinic and hospital

EMEND IV
CINVANTI



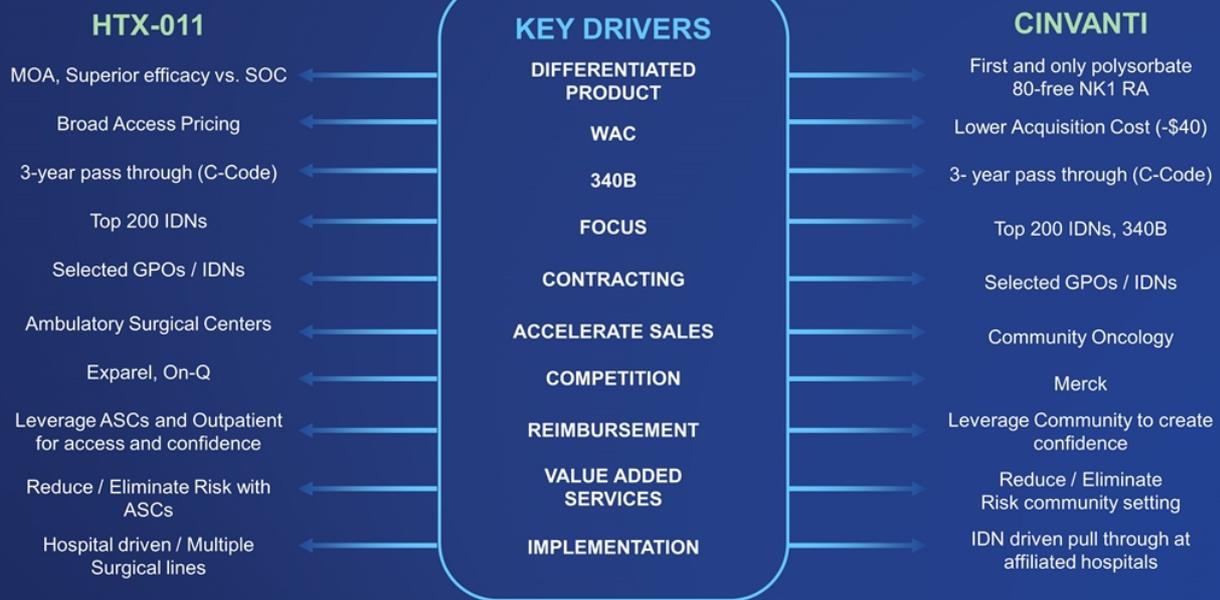
Source(s): Heron 867 data, Heron DDD 5HT3, NK1 Data

* Share calculation Q1'18 – Q3'18 = Cinvanti Q Units/Cinvanti + Emend IV Q Units. Q4'18 Cinvanti share calculated by keeping total NK1 market flat to Q3'18

** Total includes units classified as "Other" Class of Trade in data



Key CINVANTI Learnings to Support HTX-011 Launch



The Market is Large and Waiting for an Effective Non-opioid Solution

Theoretical and Target Market

~29M Annual US Surgical Procedures Requiring Postoperative Pain Management

~13.5M procedures

Initial Targets
Higher volume procedures across 4 major specialties

- ~5.9M Orthopedic
- ~4.2M General Surgery
- ~2.6M OB/GYN
- ~0.8M Plastic Surgery

~15.5M procedures

Secondary Targets
Other procedures requiring postoperative pain management but not amongst initial targets for one or more of these reasons:

- Non-core specialties
- Relatively lower pain scores
- Lower volume per procedure

Local Anesthetic Route of Delivery *



THE LARGEST OPPORTUNITY TO DRIVE VALUE AND CREATE CHANGE

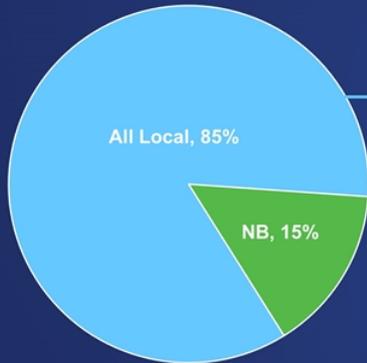
NB: Nerve Block



* Local Anesthetics are used in ~70% of procedures

HTX-011 is focused on the largest market opportunity

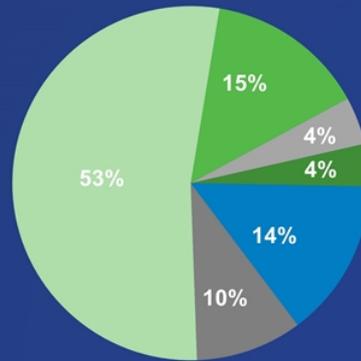
Local Anesthetic Route of Delivery



NB: Nerve Block

THE LARGEST OPPORTUNITY TO DRIVE VALUE AND CREATE CHANGE

Local Anesthetic Volume Share

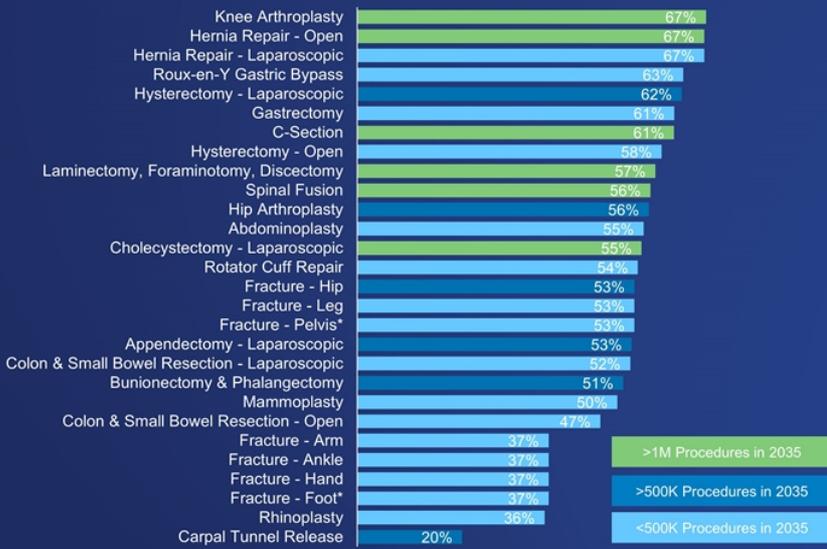


N = 22M Procedures

- Bupivacaine
- Lidocaine
- Exparel
- Others
- Ropivacaine NB
- Bupivacaine NB

Physicians indicated a raw preference share of 56% for HTX-011 across the covered procedures

Preference Share (% , Raw)



Overall Wt. Average Preference Share

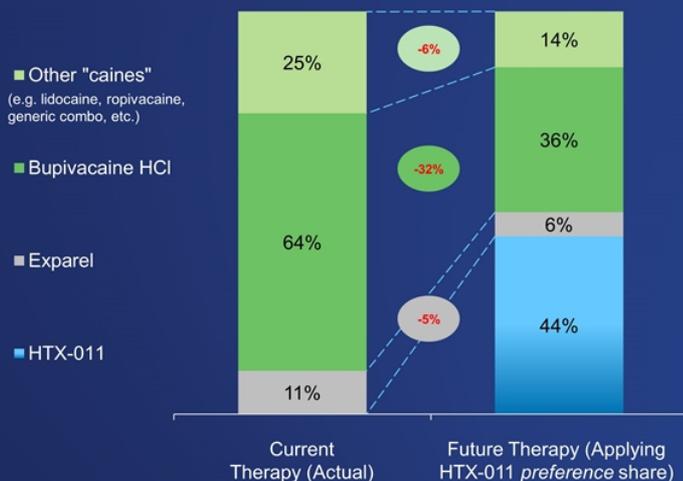


- Raw preference share for HTX-011 from physicians: 56%
- The top procedures where physicians expected to use HTX-011 were knee arthroplasty and hernia repair
- Several procedures saw higher raw preference shares than prior market research, notably knee & hip arthroplasty, C-section, laparoscopic hysterectomy and spine procedures

Reference: DRG Postoperative Pain Quantitative Research (Nov 2018) - n = 290 physicians; *Less than 100K procedures at peak

HTX-011 Enjoyed a Physician Preference Share of 44%

Adjusted Physician Preference Share Distribution



- HTX-011 is likely to initially convert share from Exparel, as well as the rest of the local anesthetics (bupivacaine & other "caines")
- There is an additional opportunity to convert physicians not using local anesthetics; physicians indicated a willingness to use HTX-011 in ~30% of procedures where they are currently not using local anesthetics

Current therapy based on Claims data from 2017 for Exparel, other agents are based on 2018 Physician Survey

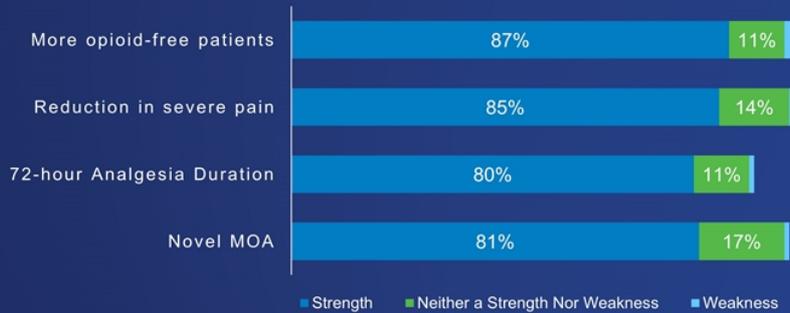
Data from analysis of physician static survey & conjoint - Sample includes n = 330 physicians

Customers Value HTX-011's Superior Product Profile

71%

71% of physicians would advocate for HTX-011 to be on formulary

- Highly favorable feedback from both physicians and pharmacy directors, driven by key differentiators versus bupivacaine, including a novel MOA supported by superior pain reduction, opioid reduction, and opioid-free endpoints



- High preference shares across initial target procedures
- Based on phase 3 and 2b procedures (bunion, hernia, TKA), 64% would use in all procedures they deemed appropriate
- 95% preferred bupivacaine (versus placebo) as the Phase 3 comparator

Reference: DRG Postoperative Pain Quantitative Research (Nov 2018) - n = 290 physicians;

60%

Aggregated preference share across specialties and key surgeries was 60%

68%

68% of Pharmacy Directors found HTX-011's profile more valuable than Exparel and 88% would grant access at an equivalent price

Being Second to Market is NOT a Significant Obstacle to Commercial Success

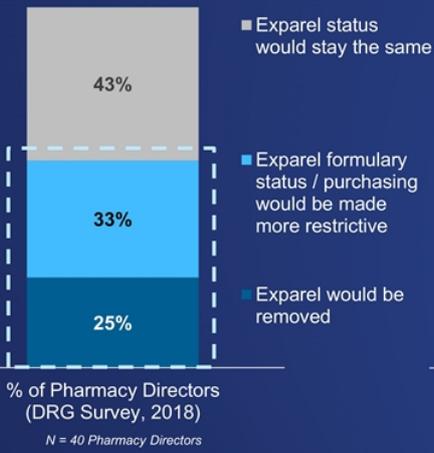
Exparel® is a small obstacle to HTX-011 uptake as its penetration is less than 6%

- Across product attributes, surgeons and pharmacy directors surveyed consistently prefer HTX-011 over Exparel for the following reasons:
 - Significant reduction in severe pain resulting in significant increase in opioid-free patients
 - Superior efficacy profile of HTX-011 through 72 hours, with significant benefit over bupivacaine HCl
 - Unique mechanism of action
 - Simple route of administration eliminating the need for up to 120 injections, with no need for extensive training
- Surveyed pharmacy directors state that they would provide better access to HTX-011 than to Exparel

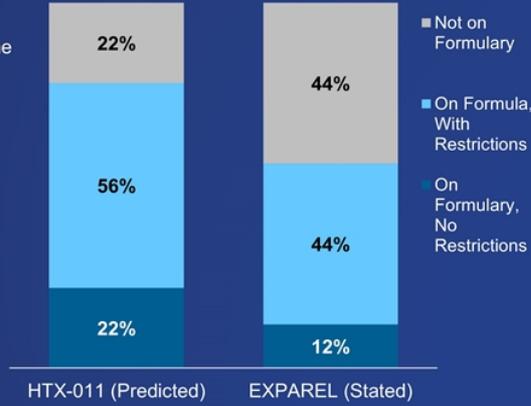
Reference: DRG Pharmacy Director Surveys

Pharmacy Directors Prefer HTX-011 to Exparel®

Impact of HTX-011 Launch on Exparel Formulary Status



Formulary Status of Exparel vs. Expected HTX-011 Status



Most pharmacy directors indicate HTX-011 would displace Exparel on formulary

- Over 50% of pharmacy directors report that if HTX-011 became available on their institution's formulary, Exparel would be subject to greater restrictions or would be entirely removed from formulary
- For institution's with less formulary consolidation, Exparel may continue to be stocked to accommodate a small segment of patients not using HTX-011

*"We can encourage use of [HTX-011] by making use of standing order sets and our EMR system, so if we continued to carry Exparel, we would make it restricted to only patients contraindicated to Product X."
- Pharmacy Director*

Reference: DRG Pharmacy Director Survey (2018); Q27. What would happen to EXPAREL if Product X was approved on formulary at your institution?

HTX-011 has Strategic Advantages Across Each Setting of Care

Clearly differentiated strategy supported by building advocacy with pharmacy, surgeons, and anesthesiologists

**13.5
MILLION
INITIAL TARGET
PROCEDURES**

Hospitals account for 91%, including top 200 IDNs (12.3M procedures)

52%
Hospital Inpatient
(7M procedures)

- Part of DRG payment
- 3 SKUs/lower average cost
- ~50% connected 340B hospitals

39%
Hospital Outpatient
(5.3M procedures)

- 3-year pass through (C-Code)
- 340B opportunity
- High value IDN and procedure focus

Ambulatory surgical centers account for 8% (1.1M procedures)

8%
Ambulatory Surgical Centers (ASCs)
(1.1M procedures)

- ASP +6%
- Lower access barriers
- Targeted facilities
- Connected to top IDNs
- Targeted high value procedures

47% of the opportunity lends itself to favorable reimbursement and access

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

340B Hospital Summary

- ~2258 hospitals (excluding children's & psych)
 - Perform 8.4M outpatient surgeries
 - 4.4M inpatient surgeries/year
- Manufacturers required to provide 23.1% discount off ASP/WAC
- Discount does not impact ASP or best price calculations
- Effective January 1, 2018, CMS reimbursement to hospitals for 340B drugs changed significantly from ASP+6% to ASP-22.5%
- Change enables CMS to capture most of the discounts manufacturers provide eligible hospitals
- **Products with pass-through status are exempt from this reimbursement change**

340B Drug Reimbursement

With C-Code	Without C-Code
ASP + 6%	ASP - 22.5%

High-Value Procedures in Initial Target Market

	Procedure	Annual Volume ('000s, US, 2015)						Overall % Local Anesthetic Use
		Total Procedures	Inpatient	Outpatient (C-code)	ASC (C-Code)	Medicare	Non-Medicare	Survey
Ortho Surgery	Knee arthroplasty	815	721	65	28	41%	59%*	87%
	Hip arthroplasty	337	325	7	5	43%	57%*	81%
	Shoulder arthroplasty	107	96	8	2	47%	52%*	89%
	Rotator cuff repair	550	11	343	192	27%	73%*	86%
	Spine procedures	750	463	249	36	35%	65%*	95%
General Surgery	Hernia repair	1,096	200	777	106	25%	74%	77%
	Hemorrhoidectomy	504	10	147	73	9%	37%*	88%
	Colon and small bowel resection	483	461	18	0.7	33%	66%*	82%
Plastic Surgery	Abdominoplasty	160	29	118	11	16%	83%	72%
	Mammoplasty	>300	10	92	19	6%	34%	85%
OB/GYN	C-Section	1,285	1273	6.1	0	2%	98%*	32%

*Note: For settings in which procedure-specific breakdown of Medicare vs. non-Medicare was not available, the overall Medicare vs. non-Medicare breakdown was applied to the total volume of procedures occurring in the given setting

Completed studies

Heron is Well Positioned to Execute a Blockbuster Launch for HTX-011

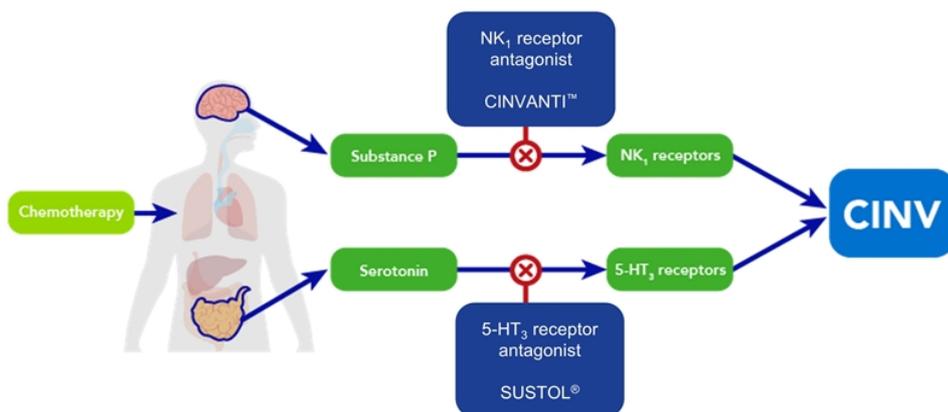
- ✓ Proven track record with hospital launch success
- ✓ Existing robust platform and structure to support launch
- ✓ Significant unmet need and market opportunity
- ✓ Highly focused launch strategy to accelerate sales
- ✓ Unprecedented value proposition

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

CINV Commercial Products



CINV Prophylaxis Typically Requires Two Complimentary Mechanisms of Action



NK₁ receptor antagonists

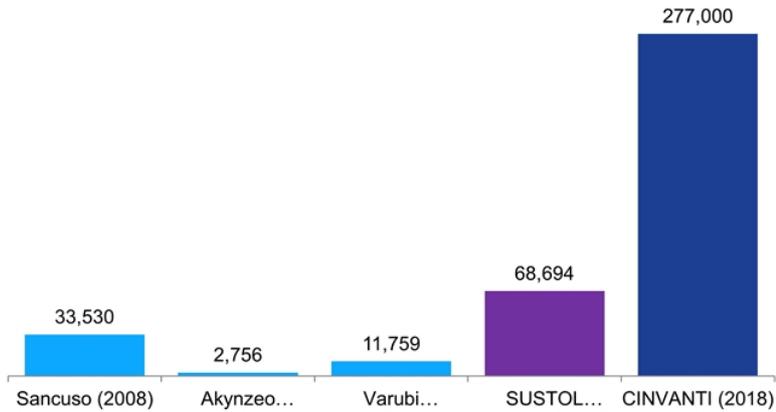
- Substance P is primary driver of delayed CINV, but related to ~15% of acute failures
- EMEND® IV (fosaprepitant), which has 90% share of the US NK₁ market, contains the synthetic surfactant polysorbate 80 that has been associated with **serious** hypersensitivity and infusion site reactions

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

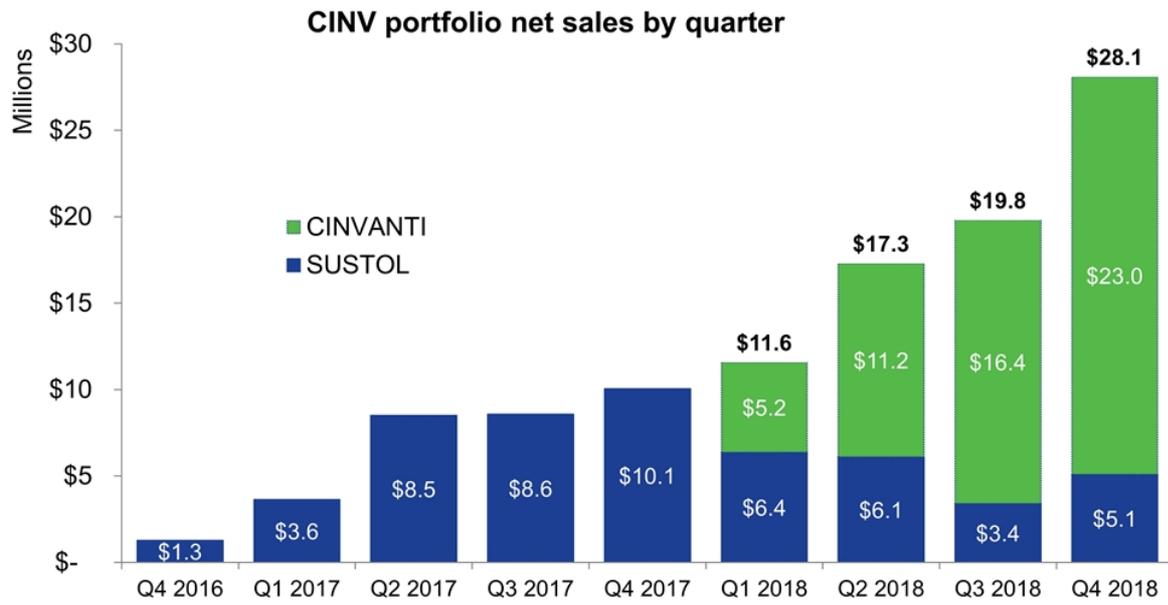
Heron's CINV Portfolio Continues to Outperform All CINV Branded Launches in Past 10 Years

First 12 Months of Sales for All CINV Brand Launches in Last 10 Years

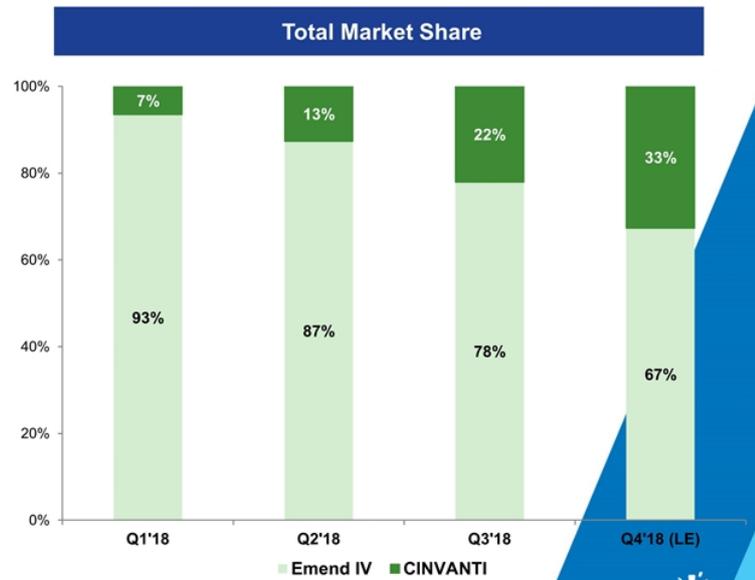
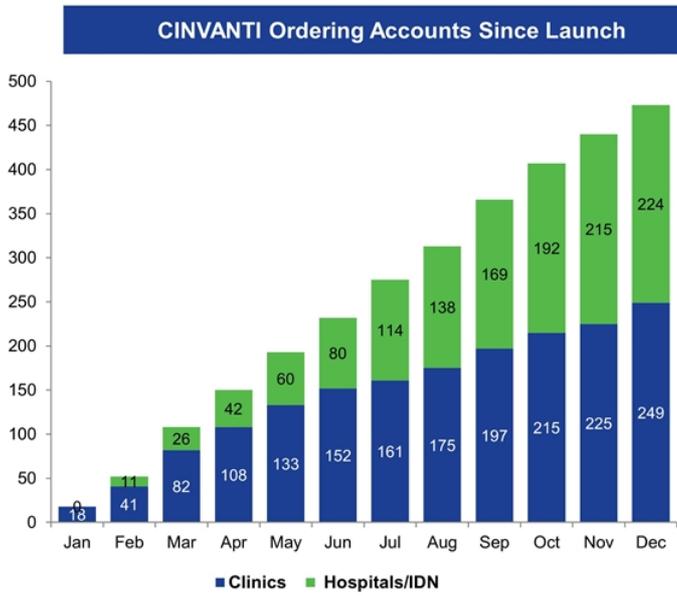


Sources: IMS DDD; Heron actuals (distributor 867 reports); due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2; Varubi includes actuals for months 1-12

CINV Portfolio Achieved \$76.7M in Net Product Sales in 2018 and Over \$100M Since Inception



CINVANTI Accounts and Market Share Continue to Grow

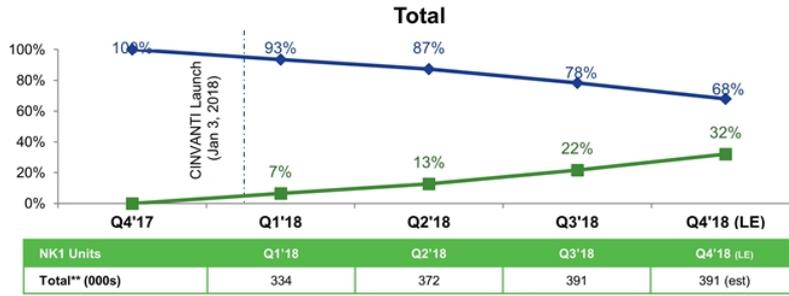


Source: Heron 867 data December 31, 2018



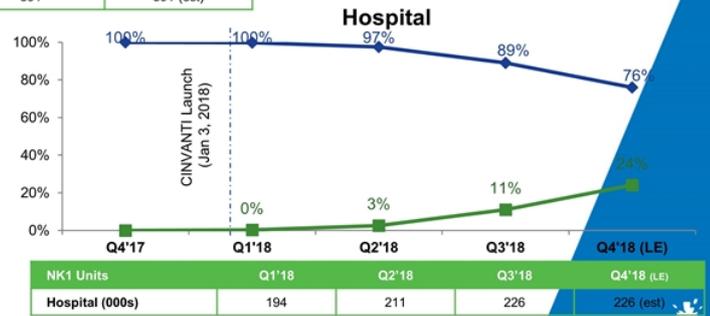
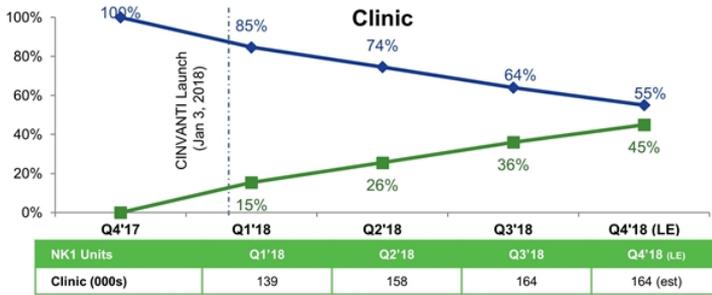
CINVANTI Market Share is Climbing Steadily Across All Segments

EMEND IV
CINVANTI



Factors influencing further share growth:

- Unique J code Jan 2019
- Long tail of use (30-40% of use is in hundreds of smaller practices) is challenging to reach, with minimal contract advantages



Source(s): Heron 867 data, Heron DDD 5HT3, NK1 Data

65 Share calculation Q1'18 – Q3'18 = Cinvanti Q Units/Cinvanti + Emend IV Q Units. Q4'18 Cinvanti share calculated by keeping total NK1 market flat to Q3'18

** Total includes units classified as "Other" Class of Trade in data



Strategy to preserve CINVANTI through generic arbitrage

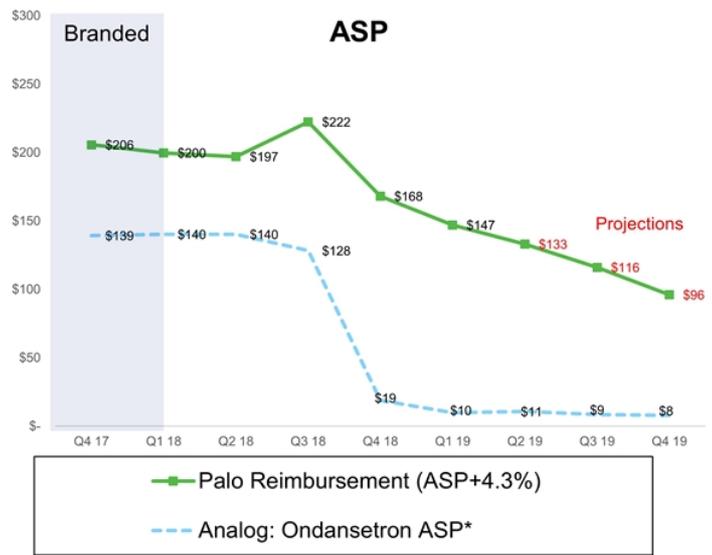
- Leverage favorable 340B pass through status, ASP+ 6% through 2020
- Potential Q1 2019 label expansion to include IVP further differentiating CINVANTI from Emend and generics
- Long term contracts extending beyond September of 2019
- CINVANTI has become an established brand across both clinics and hospital capturing one-third of the market in Q4 2018

ALOXI/Palonosetron Arbitrage is Lasting Much Longer Than the Zofran/Ondansetron Arbitrage



- Generic manufacturers have evolved and become more disciplined on pricing to maximize revenue
- Even with multiple generics on the market, the price of palonosetron has not dropped as quickly as in the past
- Slower decline in prices leads to a slower drop in ASP and a longer arbitrage
- Although the DoJ is investigating the lack of competition between generic manufacturers, we do not expect substantive changes in the slope of the palonosetron ASP decline

Therefore, the arbitrage will continue to impact SUSTOL sales through most of 2019



* Ondansetron launch aligned



2019 CINV Franchise Outlook



SUSTOL®: While we expect to see sales of SUSTOL slowly improve, the core business will continue to be weak during the protracted palonosetron arbitrage



CINVANTI®

- We expect to see steady growth in the marketplace through mid-year due to what we believe is the best overall profile compared to the other available NK₁ antagonists
- CINVANTI (aprepitant) injectable emulsion received unique J-Code J0185 effective January 1, 2019
- Generic aprepitant IV is expected in September 2019
 - Due to significant sales in 340b hospitals and other factors, we do not expect this arbitrage to have the same magnitude as the Aloxi arbitrage



CINV Franchise

- **2018 net product sales: \$76.7M**
 - 2018 guidance: \$60M - 70M raised to \$70M - \$72M
- **2019 guidance: \$115M - \$120M**

Financial Summary

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share data)	Three Months Ended September 30, 2018	Nine Months Ended September 30, 2018
Net product sales	\$ 19,786	\$ 48,630
Operating expenses ¹	61,566	181,253
Other income, net	3,434	3,342
Net loss ¹	\$ (38,346)	\$ (129,281)
Net loss per share ²	\$ (0.49)	\$ (1.81)
Net cash used in operations	\$ (35,876)	\$ (158,318)

Condensed Balance Sheet Data (In thousands)	September 30, 2018
Cash, cash equivalents and short-term investments	\$ 364,800
Accounts receivable, net	\$ 53,633
Total assets	\$ 470,896
Total stockholders' equity	\$ 406,808

Common shares outstanding at September 30, 2018 totaled 78.0 million.

¹ Includes \$8.1 million and \$23.6 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2018, respectively.

² Based on 77.8 million and 71.5 million weighted-average common shares outstanding for the three and nine months ended September 30, 2018, respectively.

Key Catalysts in Pain Management & CINV Franchises

HTX-011 & HTX-034 for Postoperative Pain	CINVANTI [®] and SUSTOL [®] for CINV
<ul style="list-style-type: none"> ✓ FDA accepted NDA <ul style="list-style-type: none"> ➢ Priority Review Designation ➢ PDUFA date April 30, 2019 ➢ No Advisory Committee planned 	<ul style="list-style-type: none"> ✓ 2018 net sales: \$76.7M <ul style="list-style-type: none"> • 2018 net sales guidance for CINV: \$60M - \$70M raised to \$70M - \$72M
<ul style="list-style-type: none"> ✓ Additional Phase 2 clinical studies using HTX-011 as the cornerstone of an opioid-free multimodal pain regimen 	<ul style="list-style-type: none"> • 2019 net sales guidance for CINV franchise: \$115M - \$120M
<ul style="list-style-type: none"> • Publication of Phase 3 and Phase 2b studies 	
<ul style="list-style-type: none"> • Anticipated launch in 3Q2019 (if approved) 	
<ul style="list-style-type: none"> • Phase 2 with HTX-034 in 2H2019 	

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





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