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

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FORM 8-K

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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 4, 2017

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

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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)

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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))
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**ITEM 7.01 Regulation FD Disclosure.**

On January 4, 2017, Heron Therapeutics, Inc. (the "Company") issued a press release announcing positive topline results from its Phase 2 study of HTX-011 in subjects undergoing abdominoplasty, as described in the press release furnished herewith as Exhibit 99.1.

Also, on January 4, 2017, the Company issued a press release announcing data from its Phase 2 study of HTX-011 in patients undergoing bunionectomy, which establishes the synergy between the local anesthetic bupivacaine and the anti-inflammatory meloxicam, as described in the press release furnished herewith as Exhibit 99.2.

A copy of presentation materials describing a Company update, all or a part of which may be used by the Company in investor or scientific presentations from time to time, is furnished as Exhibit 99.3 hereto. The attached materials have also been posted on the Company's website at [www.heronrx.com](http://www.heronrx.com). The Company does not undertake any obligation to update this presentation.

**ITEM 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, dated January 4, 2017
99.2	Press Release, dated January 4, 2017
99.3	Corporate Presentation, dated January 4, 2017

**SIGNATURE**

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.

Date: January 4, 2017

/s/ David L. Szekeres

David L. Szekeres

Senior Vice President, General Counsel, Business Development and Corporate Secretary

**HERON THERAPEUTICS ANNOUNCES POSITIVE TOPLINE RESULTS FROM PHASE 2 CLINICAL TRIAL OF HTX-011 IN ABDOMINOPLASTY**

*- HTX-011 produced statistically significant reductions in both pain intensity and need for opioids following abdominoplasty (tummy tuck) through 96 hours post-surgery -*

*- Results confirm broad utility of HTX-011 with successful use across wide range of surgeries, from small to very large incisions -*

*- Conference call and webcast at 8:30 a.m. ET on January 5, 2017 -*

SAN DIEGO, Calif.—(BUSINESS WIRE)—January 4, 2017— Heron Therapeutics, Inc. (NASDAQ: HRTX), a commercial-stage biotechnology company focused on developing novel best-in-class treatment solutions to address some of the biggest unmet patient needs, today announced positive topline results from its Phase 2 study of the investigational agent HTX-011 in subjects undergoing abdominoplasty (Study 203). HTX-011 demonstrated statistically significant reductions in both pain intensity and the use of opioid rescue medications through 96 hours following surgery.

Study 203 is a randomized, placebo-controlled, dose-finding, Phase 2 clinical study evaluating the efficacy and safety of locally administered HTX-011 for post-operative anesthesia following abdominoplasty surgery. The Summed Pain Intensity (SPI) score through 96 hours post-surgery (SPI 0-96) was significantly reduced with HTX-011 and produced a statistically significant 36.6 percent reduction in pain through 96 hours following surgery, as measured by SPI 0-96 ( $p=0.0104$ ). Pain was consistently reduced through 96 hours with statistically significant reductions observed between 24 to 48 hours ( $p=0.007$ ), 48 to 72 hours ( $p=0.038$ ), and 72 to 96 hours ( $p=0.016$ ) after a single administration of HTX-011.

Additionally, HTX-011 produced significant reductions ( $p=0.011$ ) in the use of opioid rescue medication through 96 hours following abdominoplasty, as compared to placebo. To date, HTX-011 continues to be generally well-tolerated in Phase 2.

“The most painful period following surgery is the first three to four days. Currently available local anesthetics do not have the duration of action to provide analgesia for these critical first few days. Poorly managed post-operative pain can result in impaired patient function, increased cost of care and potentially lead to chronic pain and long-term opioid use,” commented Harold S. Minkowitz, MD, Diplomate American Board of Anesthesiology, Department of Anesthesiology, Memorial Hermann Memorial City Medical Center. “However, the efficacy of HTX-011 in even one of the largest surgical incisions, like abdominoplasty, demonstrates its potential to provide durable post-operative pain relief in a wide variety of surgical procedures, reducing or eliminating the need for opioids.”

“Today’s abdominoplasty results, combined with previously reported data from our Phase 2 programs in bunionectomy and hernia repair, demonstrate the potential for HTX-011 to provide broad utility and efficacy across multiple surgery types, from the smallest to one of the largest surgical incisions,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. “The robust, long-lasting results seen across multiple surgical settings indicate that HTX-011 has the necessary attributes to be a best-in-class therapeutic for post-operative pain, extending relief following surgery and, in turn, reducing the need for, and risks associated with, opioid intervention.”

HTX-011 is the first long-acting anesthetic that is designed to address both post-operative pain and accompanying inflammation by combining the local anesthetic bupivacaine and the anti-inflammatory meloxicam in a single administration. Targeting both pain and inflammation has allowed HTX-011 to demonstrate an advantage over current standard of care in multiple surgical models in Phase 2 studies.

#### **Conference Call and Webcast**

Heron Therapeutics will host a conference call and webcast on Thursday, January 5, 2017 at 8:30 a.m. ET (5:30 a.m. PT). The conference call can be accessed by dialing 877-311-5906 for domestic callers and 281-241-6150 for international callers. Please provide the operator with the passcode 47808780 to join the conference call. A slide presentation accompanying tomorrow's conference call may also be found on Heron's website at [www.heronrx.com](http://www.heronrx.com) under the investor relations section following the conference call. The conference call will also be available via webcast under the investor relations section of Heron's website. An archive of the teleconference and webcast will be available on Heron's website for 60 days following the call.

#### **About HTX-011 for Post-Operative Pain**

HTX-011, which utilizes Heron's proprietary Biochronomer® drug delivery technology, is an investigational, long-acting formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the prevention of post-operative pain. By delivering sustained levels of both a potent anesthetic and an anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while potentially reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction. HTX-011 is the subject of a broad-based Phase 2 development program designed to target the many patients undergoing a wide range of surgeries who experience significant post-operative pain. Following a planned End of Phase 2 meeting with the Food and Drug Administration, Heron anticipates initiating Phase 3 studies in 2017 and filing a New Drug Application in 2018.

#### **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 medicines that address major unmet medical 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](http://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: whether the Phase 2 study results are indicative of the results in future studies related to HTX-011, the sufficiency of the Phase 2 data to allow the commencement of Phase 3 registration studies for HTX-011, the potential market opportunity for HTX-011, the timing of initiating Phase 3 studies for HTX-011, the timing of filing a New Drug Application 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 Szekeres  
858-251-4447  
Senior VP, General Counsel, Business Development and Corporate Secretary  
[dszekeres@heronrx.com](mailto:dszekeres@heronrx.com)

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**HERON THERAPEUTICS ESTABLISHES SYNERGY OF BUPIVACAINE AND MELOXICAM WITH HTX-011 FOR PREVENTION OF POST-OPERATIVE PAIN IN PHASE 2 CLINICAL STUDIES**

*- Statistically significant synergy demonstrated with unique proprietary combination of bupivacaine and meloxicam in HTX-011 -*

*- Conference call and webcast at 8:30 a.m. ET on January 5, 2017 -*

SAN DIEGO, Calif.—(BUSINESS WIRE)—January 4, 2017— Heron Therapeutics, Inc. (NASDAQ:HRTX), a commercial-stage biotechnology company focused on developing novel best-in-class treatment solutions to address some of the biggest unmet patient needs, today announced data from its Phase 2 study of HTX-011 in patients undergoing bunionectomy (Study 208) that establishes, for the first time, the synergy between the local anesthetic bupivacaine and the anti-inflammatory meloxicam in HTX-011, an extended-release combination product for the prevention of post-operative pain.

HTX-011 is the first long-acting anesthetic developed to address both post-operative pain and accompanying inflammation by combining bupivacaine and meloxicam in a single administration. Utilizing Heron's Biochronomer® sustained-release drug delivery technology, HTX-011 has demonstrated a statistically significant benefit over each individual component alone, providing evidence for the synergistic activity of bupivacaine and meloxicam in the HTX-011 formulation. Further data from Study 208 demonstrates that a 60 mg dose of HTX-011 produced a statistically significant reduction in both pain and opioid use compared to a 50 mg dose of bupivacaine solution, further supporting the synergy observed with the two components of HTX-011. In addition to these clinical data, Heron also announced preclinical data from a validated animal model demonstrating that the activity of bupivacaine and meloxicam in HTX-011 cannot be replicated by administering bupivacaine locally along with systemic administration of meloxicam.

"We are very excited to have confirmed the synergy between bupivacaine and meloxicam when co-administered in HTX-011, which was previously demonstrated in animal models," said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. "The meloxicam component of HTX-011 allows bupivacaine to work throughout the three to four days of drug release, demonstrating unprecedented concordance between bupivacaine drug levels and reduction in pain. With four positive Phase 2 studies in multiple surgical models spanning small to very large incisions, we believe there is a well-defined rationale for advancing HTX-011 into a broad Phase 3 program this year. We expect to conduct an End of Phase 2 meeting with the Food and Drug Administration in the coming months and are planning for the submission of a New Drug Application in 2018."

Study 208 is a randomized, placebo-and active-controlled, double-blind Phase 2 clinical study in patients undergoing bunionectomy. HTX- 011 demonstrated statistically significant superiority in post-operative pain management when compared to treatment with similar doses of bupivacaine solution, bupivacaine alone in the Biochronomer® polymer and meloxicam alone in the Biochronomer® polymer.

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**Investor Relations and Media Contact:**

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Senior VP, General Counsel, Business Development and Corporate Secretary  
dszekeres@herontx.com

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# Company Update

JANUARY 2017



# Forward-Looking Statements

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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 and net sales for SUSTOL<sup>®</sup>, HTX-019 and HTX-011, whether the HTX-011 Phase 2 study results are indicative of the results in future studies, the sufficiency of the Phase 2 data to allow the commencement of Phase 3 registration studies for HTX-011, the timing of the NDA filing for HTX-011 and HTX-019, the timing of initiating Phase 3 studies for HTX-011, the projected sufficiency of our capital position for future periods, our ability to repay any indebtedness, the progress in the research and development of HTX-011 and our other programs, including the timing of preclinical, clinical, and manufacturing activities, 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

Now Approved by U.S. Food and Drug Administration

**CINVANTI™ (HTX-019)** aprepitant for injection

IV NK<sub>1</sub> for CINV Prevention

NDA submission January 2017

**HTX-011** bupivacaine + meloxicam ER  
 Local Administration

Post-Op Pain in Local Administration

Data from four positive Phase 2 studies in multiple surgical models

**HTX-011** bupivacaine + meloxicam ER  
 Nerve Block

Post-Op Pain in Nerve Block

Phase 2 program in nerve block initiated





**CINV PROGRAMS:  
SUSTOL®  
CINVANTI™ (aprepitant for injection)**

# SUSTOL<sup>®</sup> Performance

## Launch Update



Date of first commercial sale:  
**October 11, 2016**

Q4 performance:  
**~3,200 units sold, \$495 WAC, ~\$1.1M net sales**



**75 practices** have begun trial and evaluation of SUSTOL representing **~20% of the 1.4M targeted Aloxi units**



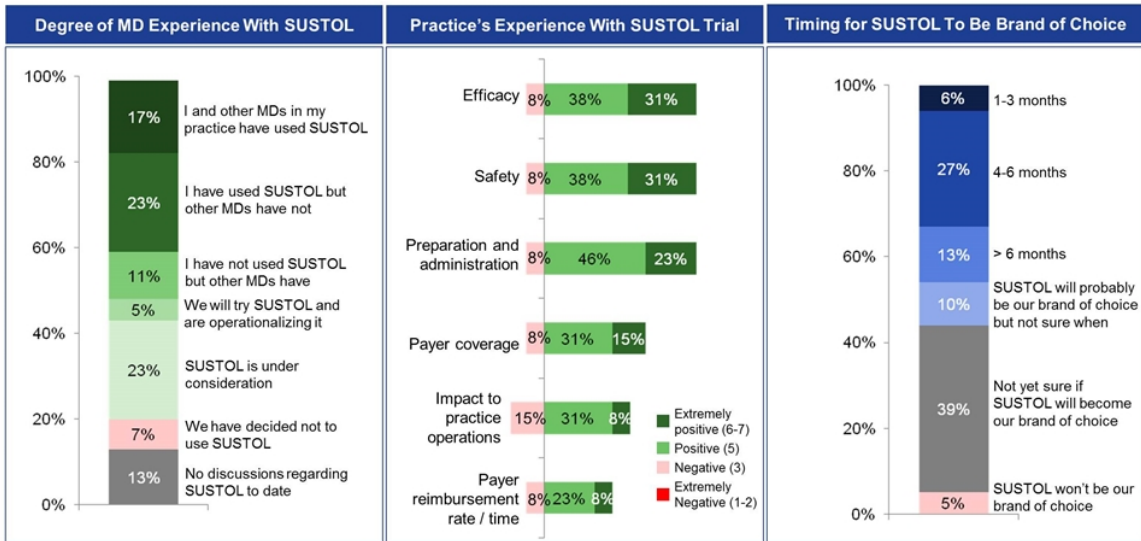
Positive payer coverage: **all 12 Medicare MACs** covering (44M lives) and commercial plans representing **139M**

## Market Research Insights

(Conducted eight weeks post-launch)

- Practices go through a **“buying process” to evaluate adoption** of new drugs which may last several quarters
  - Practices assess coverage, time to payment, reimbursement rate in addition to clinical experience and impact to practice operations
- HCPs who have begun SUSTOL trial, report **positive experiences both clinically and operationally**
- Most RNs with SUSTOL experience are **satisfied** and have been able to **administer it successfully**

# 46 Percent of MDs Evaluating SUSTOL® as Potential Branded Agent of Choice (~6-9 Month Timeline)



Which of the following best describes you / your practice? Please select one.  
 - Putnam Physician Survey Nov 2016 (N=85)

What has been the experience with SUSTOL use in your practice? Please rate 1-7.  
 - Putnam Practice Manager Survey Nov 2016 (N=40)

In what timeframe do you expect SUSTOL to become the practice's branded 5-HT3 of choice?  
 - Putnam Physician Survey Nov 2016 (N=85)



# 2017 CINV Franchise Outlook

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Heron expects steady but measured growth in SUSTOL® trial and adoption

- **Anticipate \$15M - \$25M in SUSTOL net sales in 2017**



CINVANTI™ (HTX-019) program advancing

- File NDA in January 2017
- Anticipate approval Q4 2017, launch Q1 2018
- If approved, Heron would be the first company to address both mechanisms of action for the prophylaxis of CINV with injectable products
- Offers strong strategic and operational fit with existing commercial organization



# **Post-Operative Pain Program**

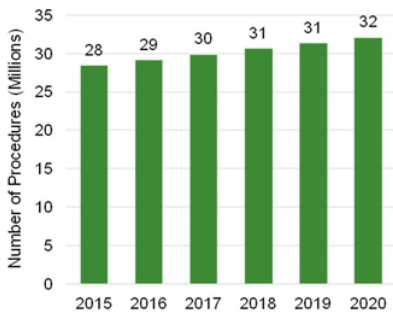
## **HTX-011: Proprietary Extended-Release Combination of Bupivacaine + Meloxicam**



# Market Is Large and Local Anesthetic Use Is Common, but Long-Acting Anesthetics Have Not Fulfilled the Promise

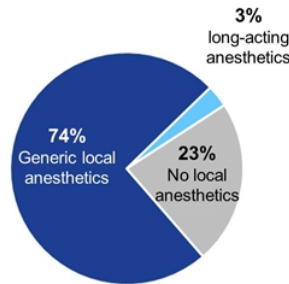


## Procedures Requiring Post-Operative Pain Relief, 2015-2020<sup>1</sup>



Procedure growth driven by aging population and more active seniors

## Local Anesthetic Usage Across Key Surgeries, 2015<sup>1\*</sup>



## Key Limiters of Current Long-Acting Anesthetics Penetration

- Perceived inability to achieve marketed duration of efficacy<sup>2</sup>
- No large scale studies have shown superiority versus bupivacaine solution
- HCPs not persuaded that incremental efficacy is worth the cost
- Formulary access restrictions<sup>2</sup>
  - Many institutions restrict usage to certain departments, procedures, or do not have a long-acting local anesthetic on formulary
  - Very low penetration in ASC and office settings<sup>1</sup>

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



# HTX-011 Has the Potential to Transform Post-Operative Pain Management



Product Attribute	Generic Local Anesthetics	Long-Acting Local Anesthetics	HTX-011
Extended-release formulation	No	Yes	Yes
Synergistic MOA potentiates local anesthetic efficacy by reducing inflammation	No	No	Yes
Consistent 72 hour efficacy	No	No	Yes
Head-to-head superiority vs. bupivacaine	N/A	No	Yes
Applicable in large and small procedures without admixture with bupivacaine solution	N/A	No	Yes
Flexible administration with potential safety advantages	No	No	Yes

"I would love a product that is superior to Exparel® in that it actually provided 72 hours of pain relief; this would reduce rates of nausea, vomiting, and constipation and help us discharge patients sooner."

– General Surgeon<sup>1</sup>

"We're looking for an injectable lasting 72 hours; this would address the critical, most painful window of time following surgery and could potentially eliminate the need for additional pain treatments."

– Plastic Surgeon<sup>1</sup>

"If a local anesthetic could provide significant pain relief for 48-72 hours, patients could be up and moving more quickly and have significant reduction in length of stay as well as opioid use post-operatively."

– Orthopedic Surgeon<sup>1</sup>

"If we could numb the surgical area for three days, we would have a lot of patient satisfaction and if a patient is satisfied, they're not going to be calling us for the next three days."

– Anesthesiologist<sup>1</sup>

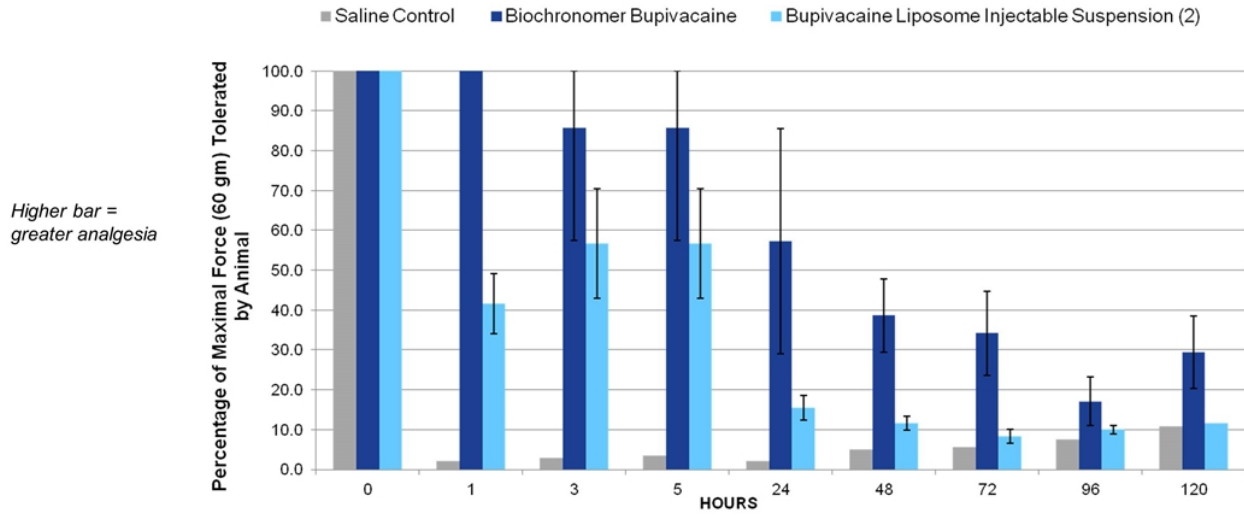


Source: 1 – DRG physician and P&T member interviews (2016; n=106)

# Biochronomer® Bupivacaine Produced Significant Reductions in Pain in Preclinical Models<sup>1</sup>



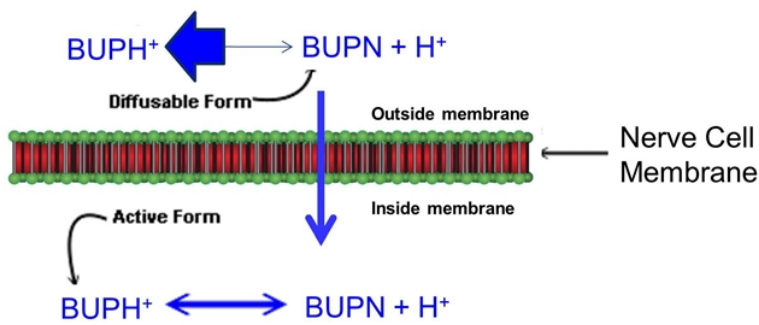
## Pig Post-Operative Pain Model



1. Post-operative pain model in pigs from Castle et al, 2013 EPJ
2. Human dose of bupivacaine liposome with 40% smaller incision (n=4 pigs)

# Inflammation Plays a Key Role in Pain Management

(Current local anesthetics do not address this)



- Inflammation produces an acidic environment
- Shifts the balance to ionized form, which is unable to penetrate nerve cell membrane

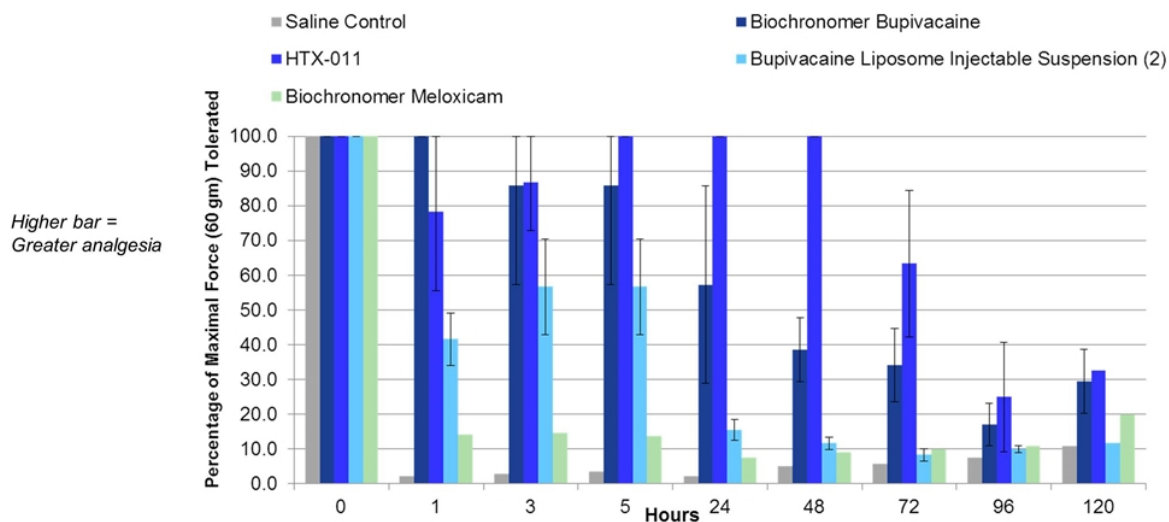
- Acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects<sup>1,2</sup>
- Bupivacaine is very sensitive to reduced pH
- Addition of meloxicam is designed to help reduce local inflammation and allow bupivacaine to work better 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's Unique Combination of Bupivacaine & Meloxicam Produced Marked Analgesia Through 72 Hours<sup>1</sup>

## Pig Post-Operative Pain Model

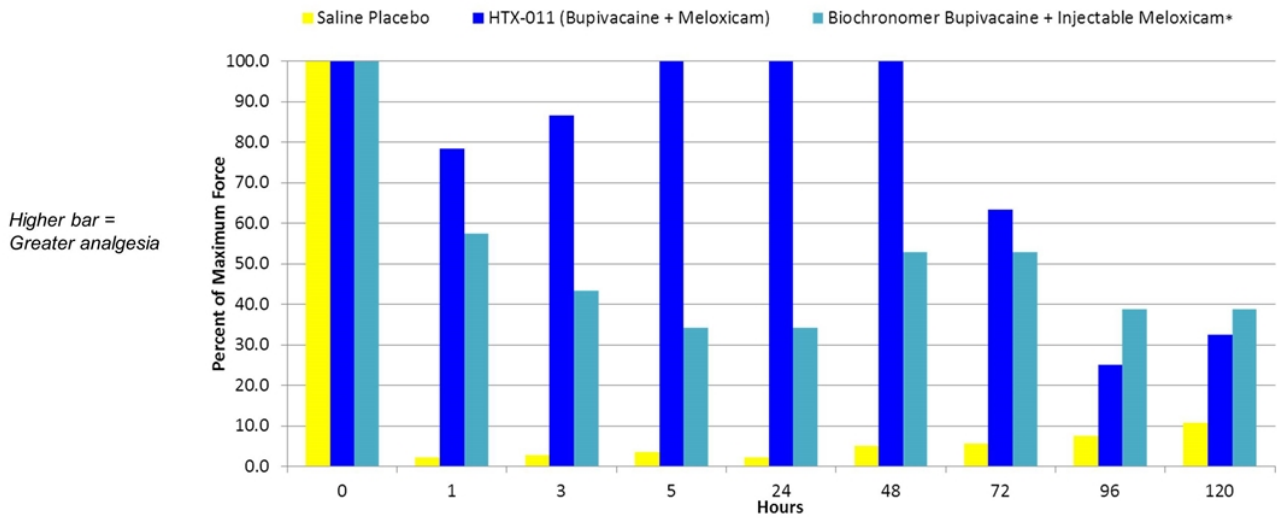


1. Post-operative pain model in pigs from Castle et al, 2013 EPJ
2. Human dose of bupivacaine liposome with 40% smaller incision (n=4 pigs in each arm)

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



## Pig Post-Operative Pain Model



\*Same dose of meloxicam as in HTX-011 administered SQ  
Post-operative pain model in pigs from Castle et al, 2013 EPJ

(n=4 pigs in each arm)

# HTX-011 Clinical Experience Shows It Has the Potential to Transform Post-Operative Pain Control



- Previously released HTX-011 clinical data has demonstrated:
  - Unprecedented statistically significant reductions in both pain and opioid use lasting up to 96 hours after surgery
  - Utility in both small procedures (bunion) and medium size procedures (hernia)
  - Ease of use: instillation, which is a faster, easier and potentially safer route of administration was demonstrated to be equally effective to standard injections
    - Future studies will utilize the instillation route of administration, as appropriate
  - Formulation work now complete; only data from the optimized formulation will be presented in the future
- Data included in this presentation will further confirm the above and provide evidence of even broader utility, including one of the largest incisions, abdominoplasty



## **HTX-011 STUDY 203: Phase 2 Abdominoplasty**



# Study 203: Abdominoplasty Study Design & Demographics



- HTX-011 200mg Inj
- HTX-011 400mg Inj
- HTX-011 600mg Inj
- Saline Placebo Injection

HTX-011 400 mg significantly reduced pain (SPI<sub>0-24</sub> p=0.012); no additional benefit seen with 600mg

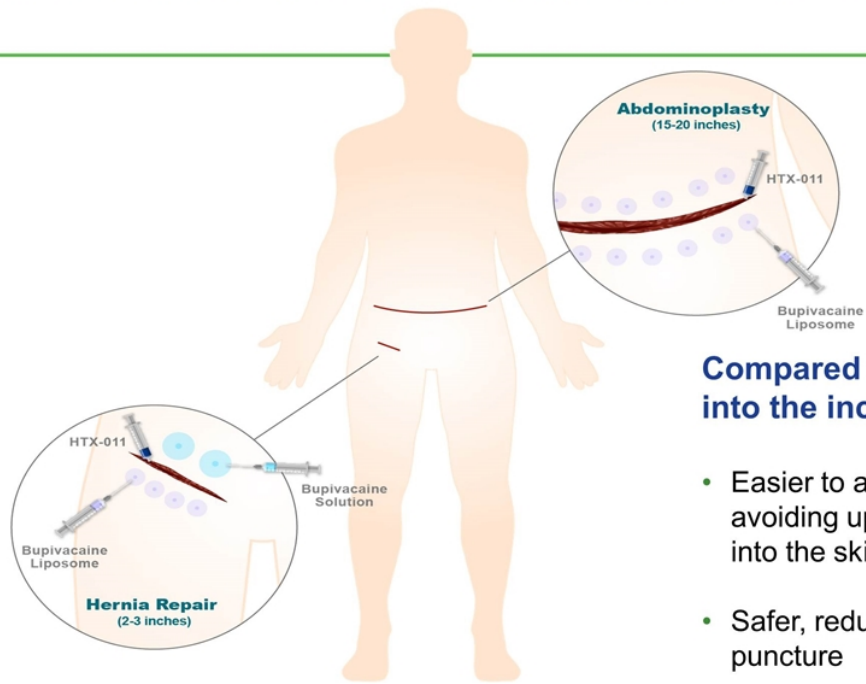
- HTX-011 400mg Instillation\*
- Saline Placebo Instillation\*

Data from instillation, the optimal route of administration, presented

Characteristic	Parameter	Saline Placebo	HTX-011 400mg
<b>Age (Years)</b>	n	21	20
	Mean	43.0	41.4
	Minimum	29	27
	Maximum	58	60
<b>Gender n (%)</b>	Male	0 (0)	0 (0)
	Female	21 (100)	20 (100)
<b>Race n (%)</b>	Caucasian	16 (76.2)	15 (75.0)
	African American	5 (23.8)	5 (25.0)
	Asian	0 (0)	0 (0)
	Other	0 (0)	0 (0)
<b>Ethnicity n (%)</b>	Hispanic	5 (23.8)	7 (35.0)
	Not Hispanic	16 (76.2)	13 (65.0)

\*Drug products predominately instilled with a small number of injections around the plication

# HTX-011: Instillation Faster, Easier and Potentially Safer

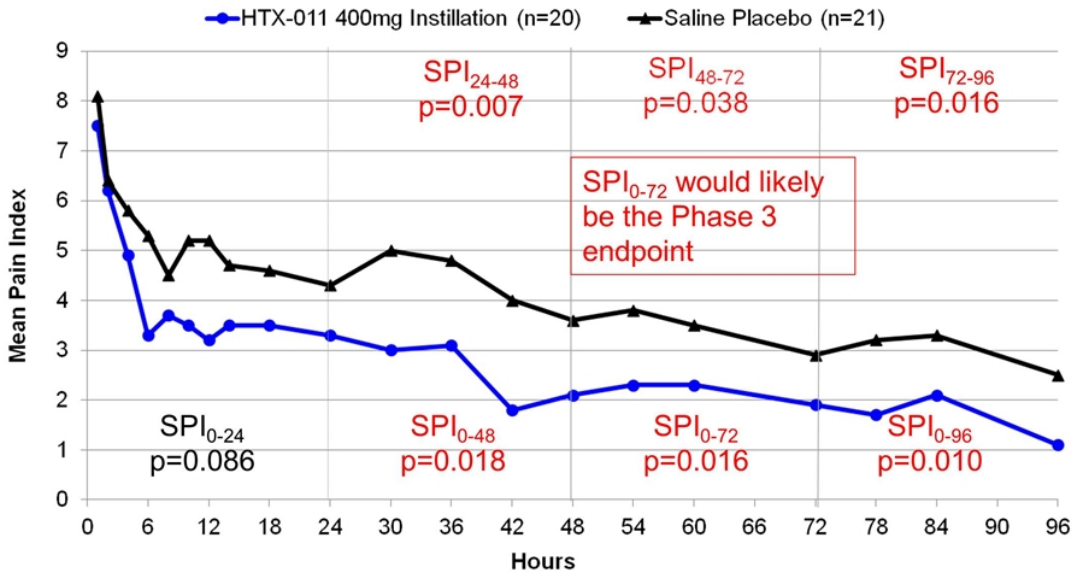


## Compared to injection, instillation into the incision site is:

- Easier to administer and less invasive, avoiding up to 50 or more injections into the skin with large operations
- Safer, reducing the risk of venous puncture

# Study 203: Mean Pain Intensity Scores\*

HTX-011 Is Significantly Better Than Placebo Through 96 Hours After Abdominoplasty



\*LOCF method used to account for missing data, no adjustment for use of rescue medications

- Results confirm that HTX-011 can be successfully used in even the largest incisions
- 53 patients an arm should be sufficient to achieve  $p < 0.05$  for  $SPI_{0-24}$



## Study 203: HTX-011 Significantly Reduces Opioid Use

Mean Opioid Rescue Over Time	Placebo (P) (n=21)	HTX-011 400 mg (n=20)
0 – 24 hours	25.9mg	16.1mg p=0.014
0 – 48 hours	40.8mg	27.2mg p=0.021
0 – 72 hours	51.3mg	32.7mg p=0.011
0 – 96 hours	52.9mg	33.2mg p=0.011

HTX-011 produced significant reductions in opioid rescue medication through 96 hours after abdominoplasty

# Study 203: Treatment-Emergent Related Adverse Reactions for All Cohorts\*



Preferred Term	Saline Placebo (n=84)	HTX-011 (n=68)
Any Adverse Event	25.0%	25.0%
Nausea	7.1%	7.4%
Vomiting	1.2%	2.9%
Headache	3.6%	7.4%
Dizziness	3.6%	0
Hypoesthesia	1.2%	2.9%
Wound dehiscence	2.4%	1.5%
Pruritus	8.3%	2.9%
Hypotension	2.4%	4.4%
Decreased appetite	0	2.9%

\*Adverse events considered at least possibly related with an incidence of >2%



## **HTX-011 STUDY 208: Phase 2 Bunionectomy**

# Study 208: Bunionectomy Study Design & Demographics



- HTX-011 200mg
- HTX-011 120mg
- HTX-011 60mg
- Bupivacaine 50mg
- Saline Placebo
- HTX-002 120mg
- HTX-009 120mg
- HTX-011 30mg on-going

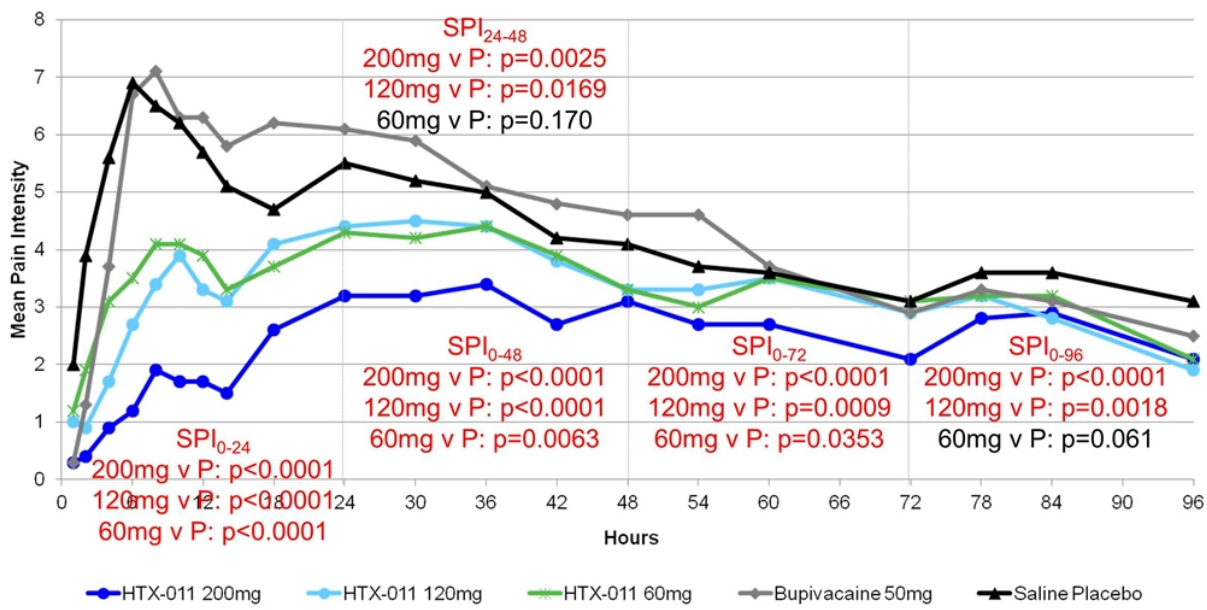
Open wound and closed wound injections combined

Characteristic	Parameter	Saline	Bupivacaine	HTX-011 200mg	HTX-011 120mg	HTX-011 60mg
Age (Years)	n	86	15	30	56	35
	Mean	49.9	52.7	52	49.6	54.2
	Minimum	21	36	20	24	24
	Maximum	76	84	71	75	76
Gender n (%)	Male	12 (14.0)	2 (13.3)	5 (16.7)	11 (19.6)	4 (11.4)
	Female	74 (86.0)	13 (86.7)	25 (83.3)	45 (80.4)	31 (88.6)
Race n (%)	Caucasian	50 (58.1)	8 (53.3)	24 (80.0)	38 (67.9)	21(60.0)
	African American	30 (34.9)	6 (40.0)	4 (13.3)	17 (30.4)	13 (37.1)
	Other	6 (7.0)	1 (6.7)	2 (6.7)	1 (1.8)	1 (2.9)
Ethnicity n (%)	Hispanic	21 (24.4)	2 (13.3)	5 (16.7)	18 (32.1)	7 (20.0)
	Not Hispanic	65 (75.6)	13 (86.7)	25 (83.3)	38 (67.9)	28 (80.0)



# Study 208: Mean Pain Intensity Scores\*

HTX-011 Is Significantly Better Than Placebo For All Doses Tested



SPI<sub>0-72</sub> would likely be the Phase 3 endpoint

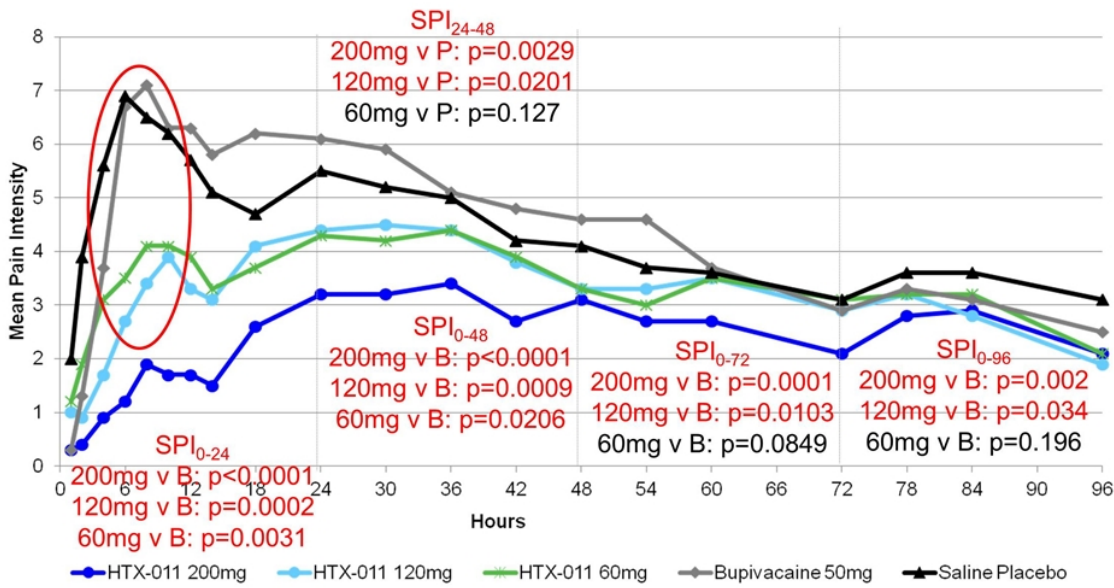


\*LOCF method used to account for missing data, no adjustment for use of rescue medications



# Study 208: Mean Pain Intensity Scores\*

HTX-011 Is Significantly Better Than Bupivacaine For All Doses Tested



60mg of bupivacaine combined with meloxicam in HTX-011 is significantly better than 50mg of bupivacaine solution through 48 hours

\*LOCF method used to account for missing data, no adjustment for use of rescue medications

# Study 208: HTX-011 Significantly Reduces Opioid Use



Mean Opioid Rescue Over Time	Placebo (P) (n=86)	Bupivacaine Solution (B) (n=15)	HTX-011 120 mg (n=56)	HTX-011 60 mg (n=35)
<b>0 – 24 hours</b>	16.5mg	16.3mg	8.0mg p<0.0001 v P p=0.0008 v B	8.2mg p<0.0001 v P p=0.002 v B
<b>0 – 48 hours</b>	26.6mg	28.6mg	17.8mg p=0.0008 v P p=0.0117 v B	15.2mg p=0.0009 v P p=0.0103 v B
<b>0 – 72 hours</b>	33.2mg	35.8mg	23.8mg p=0.0122 v P p=0.0457 v B	20.5mg p=0.0053 v P p=0.0226 v B
<b>0 – 96 hours</b>	33.8mg	35.8mg	24.6mg p=0.0181 v P p=0.0727 v B	20.7mg p=0.005 v P p=0.0255 v B

Doses down to 60mg HTX-011 produced significant reductions in opioid rescue medication and significant increases in median time to first opioid (increased by 300%) and the percent of opioid-free patients through 96 hours (increased by 240%)



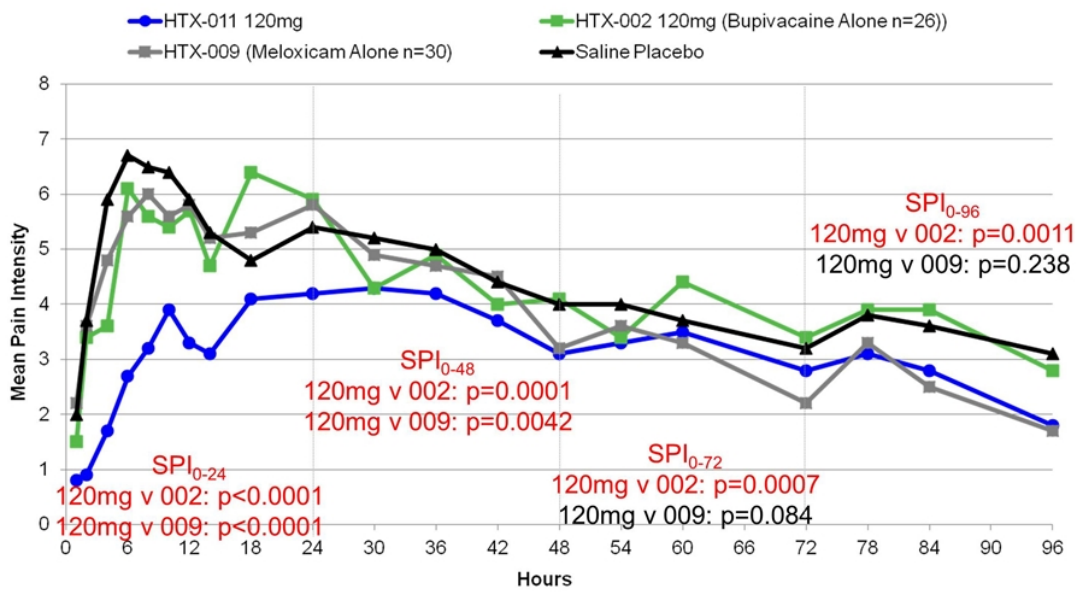
# Study 208: Treatment-Emergent Related Adverse Reactions for All Cohorts\*



Preferred Term	Saline Placebo (n=86)	Bupivacaine (n=15)	HTX-011 (n=121)
Any Adverse Event	20.9%	20.0%	27.3%
Nausea	9.3%	13.3%	14.0%
Vomiting	11.6%	6.7%	3.3%
Erythema	1.2%	0	5.0%
Headache	1.2%	0	5.8%
Swelling	0	0	2.5%

\*Adverse events considered at least possibly related with an incidence of >2%

# HTX-011 Is Significantly Better Than Individual Components Providing Evidence of Synergy



\*LOCF method used to account for missing data, no adjustment for use of rescue medications

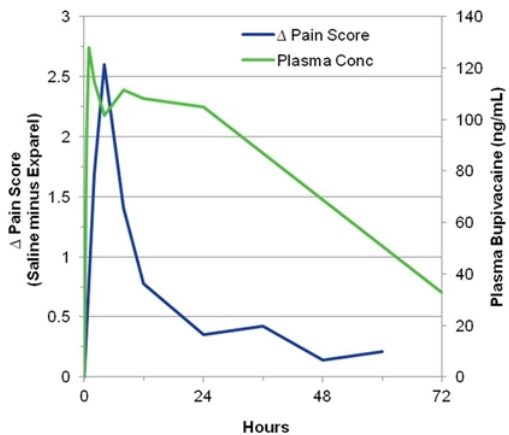


# CONFIRMATION OF THE MELOXICAM HYPOTHESIS

# No Extended Release Bupivacaine Has Demonstrated a PK-PD Relationship

## EXPAREL® (ER Bupivacaine)

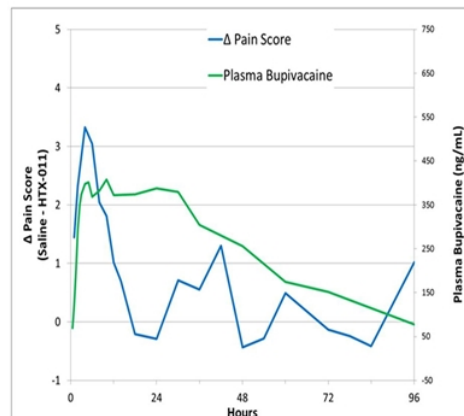
- No PK-PD Relationship



PK – PD data from Exparel® Bunionectomy Study; Golf, et. al.

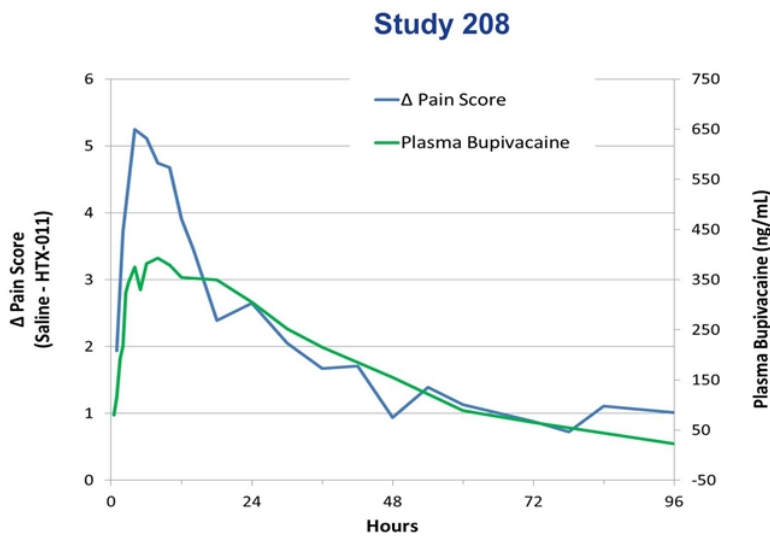
## HTX-002 (ER Bupivacaine)

- No PK-PD Relationship



# Unique Combination of Bupivacaine & Meloxicam Demonstrates Clear PK-PD Relationship

- For the first time an extended release local anesthetic has shown a clinical PK – PD relationship



**Similar PK – PD relationship observed with HTX-011 in Study 202 Hernia Repair**

# Heron Established Synergy of Bupivacaine & Meloxicam



1

Statistically significant superiority of HTX-011 directly compared to bupivacaine alone or meloxicam alone in the Biochronomer polymer in Study 208

2

Statistically significantly superiority of similar doses of HTX-011 versus bupivacaine solution in Study 208 for pain and opiate use

3

HTX-011 is the first extended release local anesthetic to show a clear PK – PD relationship

4

Synergy of HTX-011 co-formulation established versus local bupivacaine plus systemically administered meloxicam

**9 patents filed on the combination**

**Robust market protection through 2035**







## Post-Operative Pain Program Summary

# Summary: HTX-011 Is Poised to Fulfill the Promise of Long-Acting Local Anesthetics in Post-Op Pain



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 supports value story	✓
Consistent 72-hour efficacy <ul style="list-style-type: none"><li>- Pain reduction</li><li>- Opioid reduction</li></ul>	✓
Applicable in large and small procedures without admixture with bupivacaine solution – reducing chance of dosing errors and systemic toxicity	✓
Flexible administration with potential safety advantages	✓
Potential to address most pressing unmet needs cited by key stakeholders – patients, surgeons, anesthesiologists & formulary decision makers	✓
De-risked Phase 3 development program and extensive patent protection through 2035	✓

# Key Catalysts in Pain & CINV Franchises



HTX-011 for Post-Operative Pain	CINVANTI™ (HTX-019) for CINV	SUSTOL® for CINV
✓ Early Q1 Top-line abdominoplasty data	Q1 (Jan.) – NDA submission	2017 net sales guidance: \$15M - \$25M
✓ Early Q1 Phase 2 program in nerve block initiated	Q4 – NDA Approval	
End-of-Phase 2		
Initiation of Phase 3 studies		
NDA filing 2018		