

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

FORM 8-K/A
(Amendment No. 1)

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

Date of Report (Date of earliest event reported): June 21, 2018

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

Delaware
(State or other jurisdiction
of incorporation or organization)

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

001-33221
(Commission
File Number)

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

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.

Explanatory Note.

On June 21, 2018, Heron Therapeutics, Inc. (the “Company”) furnished a Current Report on Form 8-K (the “Current Report”). This Amendment No. 1 to Current Report on Form 8-K/A is being filed to reflect the disclosures included in the Current Report under Item 8.01, rather than Item 7.01. For the avoidance of doubt, the information contained in Exhibits 99.1, 99.2 and 99.3 filed herewith is identical to the information furnished in the Current Report.

Item 8.01 Other Events.

On June 21, 2018, the Company issued a press release announcing positive topline results from its Phase 2b study of HTX-011 in patients undergoing total knee arthroplasty and breast augmentation, as described in the press release filed herewith as Exhibit 99.1.

The Company also issued a press release announcing that the U.S. Food and Drug Administration has granted Breakthrough Therapy designation to the Company’s investigational agent, HTX-011, for postoperative pain management, as described in the press release filed 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 filed as Exhibit 99.3 hereto. The attached materials have also been posted on the Company’s website at www.herontx.com. The Company does not undertake any obligation to update this presentation.

The information in Item 8.01 of this Amendment No. 1 to Current Report on Form 8-K/A, including the information contained in Exhibits 99.1, 99.2 and 99.3 filed herewith, shall be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, dated June 21, 2018.
99.2	Press Release, dated June 21, 2018.
99.3	Corporate Presentation, dated June 21, 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.

Date: June 25, 2018

/s/ David L. Szekeres

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



Heron Announces Positive Topline Results from Phase 2b Clinical Studies of HTX-011 in Total Knee Arthroplasty and Breast Augmentation

-HTX-011 Significantly Reduced Both Pain Intensity and Opioid Use in Patients Undergoing Total Knee Arthroplasty-

-HTX-011, Administered via Either Instillation or Nerve Block, Significantly Reduced Both Pain Intensity and Opioid Use in Patients Undergoing Breast Augmentation-

-Conference Call and Webcast Today at 8:30 a.m. ET-

SAN DIEGO, Calif.—(BUSINESS WIRE)—June 21, 2018—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 announced positive topline results from two completed Phase 2b studies of HTX-011: Study 209 (local administration in total knee arthroplasty) and Study 211 (instillation or pectoral pocket nerve block in breast augmentation). HTX-011 achieved the primary endpoints in both studies.

Total Knee Arthroplasty (Study 209) Results

Study 209 was a randomized, placebo- and active-controlled, double-blind, Phase 2b clinical study in patients undergoing primary unilateral total knee arthroplasty to evaluate the analgesic efficacy, safety and pharmacokinetics of HTX-011 locally administered into the surgical site. Following a dose-escalation phase, 222 patients were randomized to receive: (1) HTX-011 400 mg administered via instillation into the surgical site (HTX-011 alone); (2) HTX-011 400 mg administered via instillation into the surgical site with a low dose of ropivacaine injected into the posterior capsule (HTX-011 combination); (3) bupivacaine 125 mg administered via multiple injections into the surgical site; and (4) placebo. Ropivacaine and bupivacaine are generically available standard-of-care local anesthetics used in the management of postoperative pain. This study included a pre-specified hierarchical testing strategy for the primary and key secondary endpoints for the HTX-011 400 mg treatment groups. The primary endpoint was pain intensity as measured by the Area Under the Curve (AUC) from 0 to 48 hours post-surgery (AUC 0-48) for HTX-011 compared to placebo. The key secondary endpoint was pain intensity as measured by the AUC from 0 to 72 hours post-surgery (AUC 0-72) for HTX-011 compared to placebo. The primary and key secondary endpoints were achieved:

- The HTX-011 combination and HTX-011 alone resulted in reductions of 23% and 19%, respectively, in pain intensity measured at rest through 48 hours when compared to placebo ($p < 0.0001$ and $p = 0.0002$, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine ($p = 0.0212$).
- The HTX-011 combination and HTX-011 alone resulted in reductions of 22% and 19%, respectively, in pain intensity measured at rest through 72 hours when compared to placebo ($p < 0.0001$ and $p = 0.0004$, respectively). These pain reductions from HTX-011 were also approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine through 72 hours ($p = 0.0325$).

- With the more conservative assessment of pain with activity, the HTX-011 combination and HTX-011 alone resulted in reductions of 16% and 12%, respectively, in pain intensity measured with activity through 48 hours when compared to placebo ($p < 0.0001$ and $p = 0.0017$, respectively). These pain reductions from HTX-011 were significantly better than that of bupivacaine, which resulted in a reduction of 4% ($p = 0.0012$ and $p = 0.0366$, respectively). Both the HTX-011 combination and HTX-011 alone maintained control of pain with activity through 72 hours with a 15% ($p = 0.0002$) and 11% ($p = 0.0058$) reduction compared to placebo, respectively.
- The HTX-011 combination significantly reduced opioid use through 48 and 72 hours compared to placebo ($p = 0.0091$ and $p = 0.0253$, respectively).

Breast Augmentation (Study 211) Results

Study 211 was a randomized, placebo- and active-controlled, double-blind, Phase 2b dose-finding study in patients undergoing augmentation mammoplasty to evaluate the analgesic efficacy, safety and pharmacokinetics of HTX-011 when administered by instillation into the surgical site or via ultrasound-guided lateral and medial pectoral nerve block before surgery. The study consisted of three cohorts comparing HTX-011 nerve block (60 mg, 120 mg, 240 mg) to the standard dose of bupivacaine 50 mg, administered as a nerve block, and placebo, and a final cohort comparing both HTX-011 400 mg administered by instillation and HTX-011 400 mg administered as a nerve block to the same two control groups. A total of 243 patients were enrolled. The primary endpoint was pain intensity as measured by the AUC from 0 to 24 hours post-surgery (AUC 0-24) compared to placebo. The primary endpoint of the study was achieved:

- HTX-011 400 mg administered by instillation into the surgical site and HTX-011 400 mg administered as a nerve block both resulted in reductions of 22% in pain intensity measured at rest through 24 hours when compared to placebo ($p = 0.0023$ and $p = 0.0055$, respectively). These pain reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 8%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine ($p = 0.0383$).
- With the more conservative assessment of pain with activity, HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions of 24% and 23%, respectively, in pain intensity measured with activity through 24 hours when compared to placebo ($p = 0.0004$ and $p = 0.0015$, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine administered as a nerve block, which resulted in a reduction of 12%.
- HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions in total opioid use of 33% and 26%, respectively, when compared to placebo ($p = 0.0093$ and $p = 0.0435$, respectively). These reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 10%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine ($p = 0.0455$).

There was a strong correlation between pain reduction and the pharmacokinetics of HTX-011 in both studies.

HTX-011 was well tolerated in both studies, with a safety profile comparable to placebo and bupivacaine solution. There were no deaths and no clinically meaningful differences in overall adverse events, serious adverse events, premature discontinuations due to adverse events, potential local anesthetic systemic toxicity related adverse events or wound healing.

“Without appropriate pre-emptive pain management, certain total joint replacement procedures such as a total knee arthroplasty can be very painful for patients,” said Paul F. Lachiewicz, M.D., Consulting Professor, Department of Orthopedic Surgery, Duke University; Chapel Hill Orthopedic Surgery and Sports Medicine. “The superior pain relief provided by HTX-011 compared to the current standard of care may provide a significant clinical benefit for patients and, as part of a multimodal pain management regimen, has the potential to significantly reduce the amount of opioid medication required for patients in the early postoperative recovery period.”

“With postoperative opioids serving as a gateway to addiction, there is a large unmet need for non-opioid pain alternatives,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. “With the results reported today, we have seen positive results across 7 controlled clinical studies and 5 diverse surgical models, including hernia repair, abdominoplasty, bunionectomy, total knee arthroplasty and breast augmentation. We look forward to submitting an NDA to the FDA for HTX-011 in the second half of 2018.”

Conference Call and Webcast

Heron Therapeutics will host a conference call and webcast today, June 21, 2018, 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 9387615 to join the conference call. A slide presentation accompanying today’s press release and conference call may also be found on Heron’s website at www.herontx.com under the Investor Relations section. The conference call will also be available via webcast under the Investor Relations section of Heron’s website. An archive of today’s teleconference and webcast will be available on Heron’s website for 60 days following the call.

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 alone in five diverse surgical models: hernia repair, abdominoplasty, bunionectomy, total knee arthroplasty and

breast augmentation. HTX-011 was granted Fast Track designation from the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. In the second half of 2018, Heron expects to submit a New Drug Application (NDA) to the FDA for HTX-011.

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 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.herontx.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 timing of the HTX-011 NDA filing and review process 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
Senior VP, General Counsel, Business Development and Corporate Secretary
Heron Therapeutics, Inc.
dszekeres@herontx.com
858-251-4447



**HTX-011 for Postoperative Pain Management Receives
Breakthrough Therapy Designation from FDA**

-Conference Call and Webcast Today at 8:30 a.m. ET-

SAN DIEGO, Calif.—(BUSINESS WIRE)—June 21, 2018—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 announced that HTX-011 for postoperative pain management has received Breakthrough Therapy designation from the U.S. Food and Drug Administration (FDA). HTX-011 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.

Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat serious conditions and for which preliminary clinical evidence indicates substantial improvement over available therapies on clinically significant endpoint(s). Breakthrough Therapy designation was granted for HTX-011 based on the results of Phase 2 studies and two recently completed Phase 3 studies, which showed that HTX-011 produced significant reductions in both pain intensity and the need for opioids through 72 hours post-surgery compared to placebo and bupivacaine solution, the standard of care.

“We are pleased that HTX-011 has received Breakthrough Therapy designation from the FDA,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. “HTX-011 is the only long-acting local anesthetic to demonstrate significantly reduced postoperative pain and opioid use through 72 hours compared to bupivacaine solution, the standard-of-care local anesthetic for postoperative pain management, in Phase 3 studies. We look forward to working towards the submission of an NDA to the FDA for HTX-011 in the second half of 2018.”

Conference Call and Webcast

Heron Therapeutics will host a conference call and webcast today, June 21, 2018, at 8:30 a.m. ET (5:30 a.m. PT) to discuss the receipt of Breakthrough Therapy designation and the positive HTX-011 Phase 2b study results that were also announced today in a separate press release. 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 9387615 to join the conference call. A slide presentation accompanying today’s press release and conference call may also be found on Heron’s website at www.heronrx.com under the Investor Relations section. The conference call will also be available via webcast under the Investor Relations section of Heron’s website. An archive of today’s teleconference and webcast will be available on Heron’s website for 60 days following the call.

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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 alone 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. In the second half of 2018, Heron expects to submit a New Drug Application (NDA) to the FDA for HTX-011.

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HTX-011

Postoperative Pain Program

Topline Results from Phase 2b Studies

June 21, 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 HTX-011; the timing of the NDA filing for HTX-011; the timing of completion and results of clinical studies 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 we take no obligation to update or revise these statements except as may be required by law.

Status of Product Portfolio



- CINV
- Pain

	Preclinical	Clinical	NDA	Approved
SUSTOL® (granisetron) extended-release injection		Approved by U.S. FDA for CINV Prevention		
CINVANTI® (aprepitant) injectable emulsion		Approved by U.S. FDA for CINV Prevention		
HTX-011 bupivacaine + meloxicam ER Local Administration		Postoperative Pain with Local Administration	<ul style="list-style-type: none"> Fast Track and Breakthrough Therapy designations granted Positive Phase 2, 2b and 3 results 	
HTX-011 bupivacaine + meloxicam ER Nerve Block		Postoperative Pain with Nerve Block	Positive Phase 2b results in breast augmentation	



HTX-011 for Postoperative Pain Management Has Received Breakthrough Therapy Designation

- Breakthrough Therapy designation designed to expedite development and review of drugs:
 - Intended to treat serious conditions; and
 - For which preliminary clinical evidence indicates substantial improvement over available therapies on clinically significant endpoint(s)
- Designation granted based on results of Phase 2 studies and two recently completed Phase 3 studies
 - HTX-011 produced significant reductions in both pain intensity and need for opioids through 72 hours post-surgery compared to placebo and bupivacaine solution, the standard of care
- HTX-011 was also granted Fast Track designation in November 2017



Postoperative Opioids Are a Gateway to Addiction



AS MANY AS 2.6 MILLION patients that take opioids to manage pain after surgery may become persistent opioid users each year



UP TO 440,000 patients will become addicted to opioids each year



In addition
>1 BILLION OPIOID PILLS are taken home from the hospital after surgery each year

70% of all these opioid pills 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

>\$15 BILLION of the annual healthcare costs associated with addiction can be attributed to postoperative pain management





**HTX-011 ACHIEVED STATISTICALLY SIGNIFICANT
REDUCTIONS IN PAIN AND THE NEED FOR
OPIOIDS VS. BUPIVACAINE IN EVERY PHASE 2
STUDY AND BOTH PHASE 3 STUDIES**

Seven Positive Controlled Studies to Be Included in HTX-011 New Drug Application (NDA)



NDA, planned in 2H 2018, will request broad label for reduction of postoperative pain and opioid analgesics for 72 hours after surgery

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

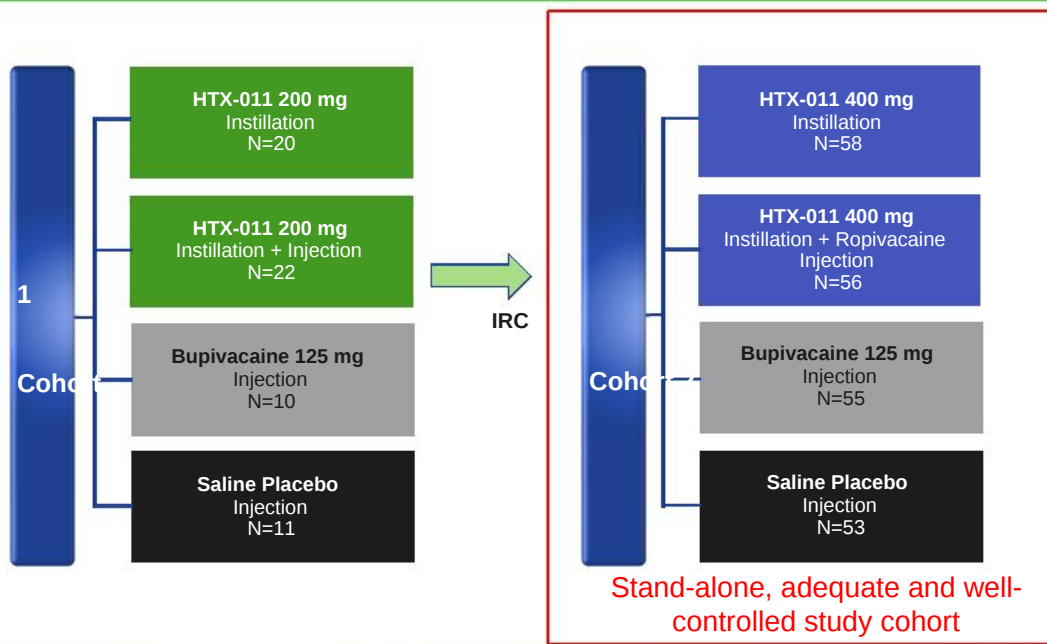
PBO = placebo; BPV = bupivacaine solution; PK = pharmacokinetic; PD = pharmacodynamics; TKA = total knee arthroplasty





RECENTLY COMPLETED PHASE 2B STUDIES

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





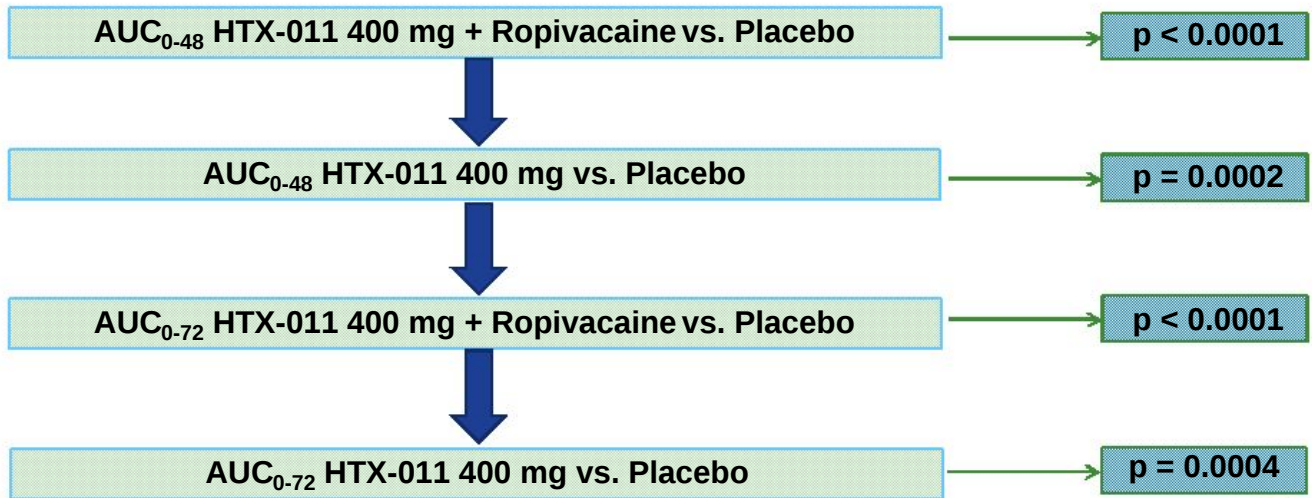
Study 209: Subject Demographics (ITT)

	Saline Placebo (N=53)	Bupivacaine Solution 125 mg (N=55)	HTX-011 400 mg (N=114)	Total (N=222)
Age (years) – mean (SD)	61.5 (8.3)	61.4 (9.4)	62.8 (9.0)	62.1 (8.9)
Sex – n (%)				
Female	25 (47.2%)	35 (63.6%)	53 (46.5%)	113 (50.9%)
Male	28 (52.8%)	20 (36.4%)	61 (53.5%)	109 (49.1%)
Race – n (%)				
Asian	0	1 (1.8%)	1 (0.9%)	2 (0.9%)
American Indian or Alaska Native	0	0	2 (1.8%)	2 (0.9%)
Black or African Descent	8 (15.1%)	7 (12.7%)	11 (9.6%)	26 (11.7%)
White	45 (84.9%)	47 (85.5%)	100 (87.7%)	192 (86.5%)
Ethnicity – n (%)				
Hispanic or Latino	12 (22.6%)	16 (29.1%)	25 (21.9%)	53 (23.9%)
Not Hispanic or Latino	41 (77.4%)	39 (70.9%)	89 (78.1%)	169 (76.1%)



Study 209: Phase 2b TKA Results Hierarchy

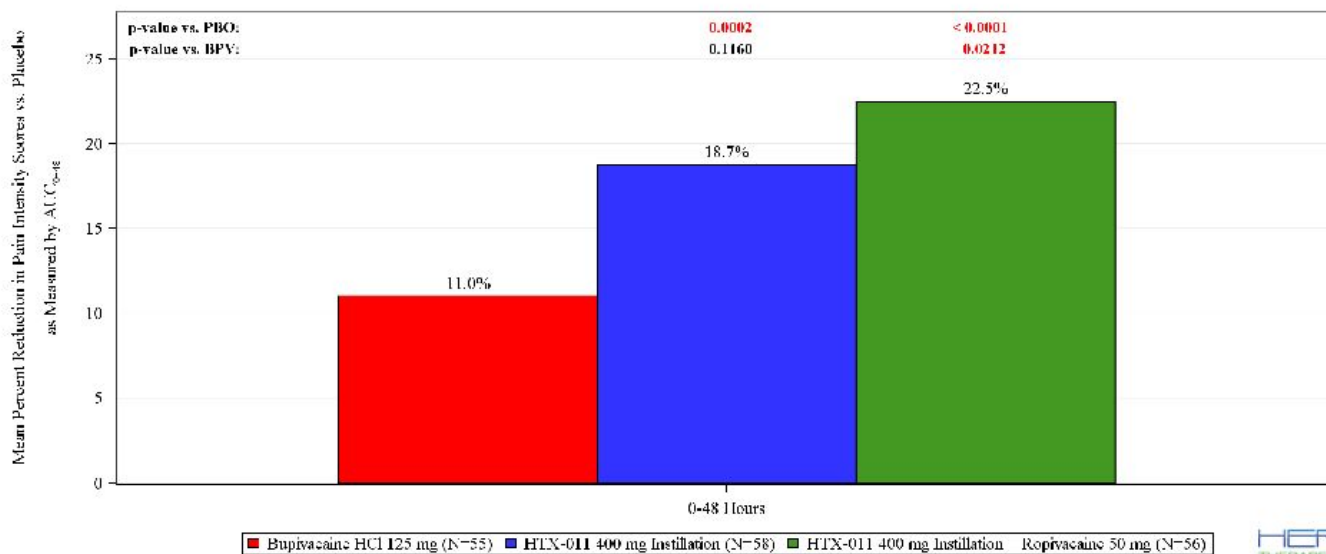
HTX-011 via instillation achieved primary and key secondary endpoints for pain



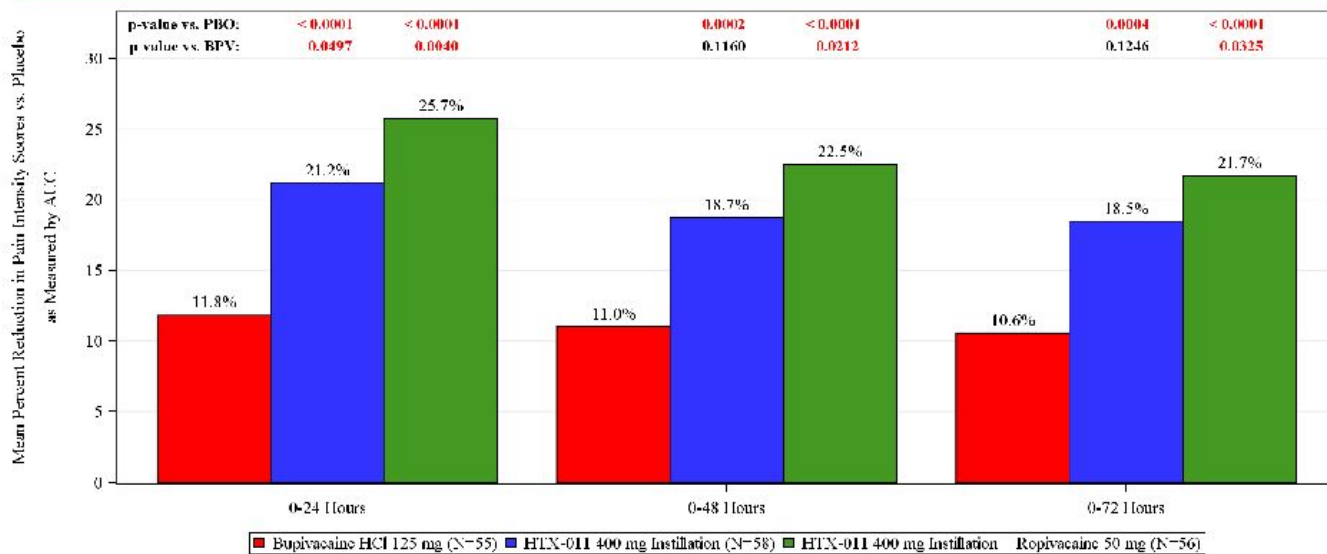
Study 209: Pain Reduction from HTX-011 at Rest Approximately Double that of Bupivacaine



HTX-011 achieved primary endpoint for AUC₀₋₄₈



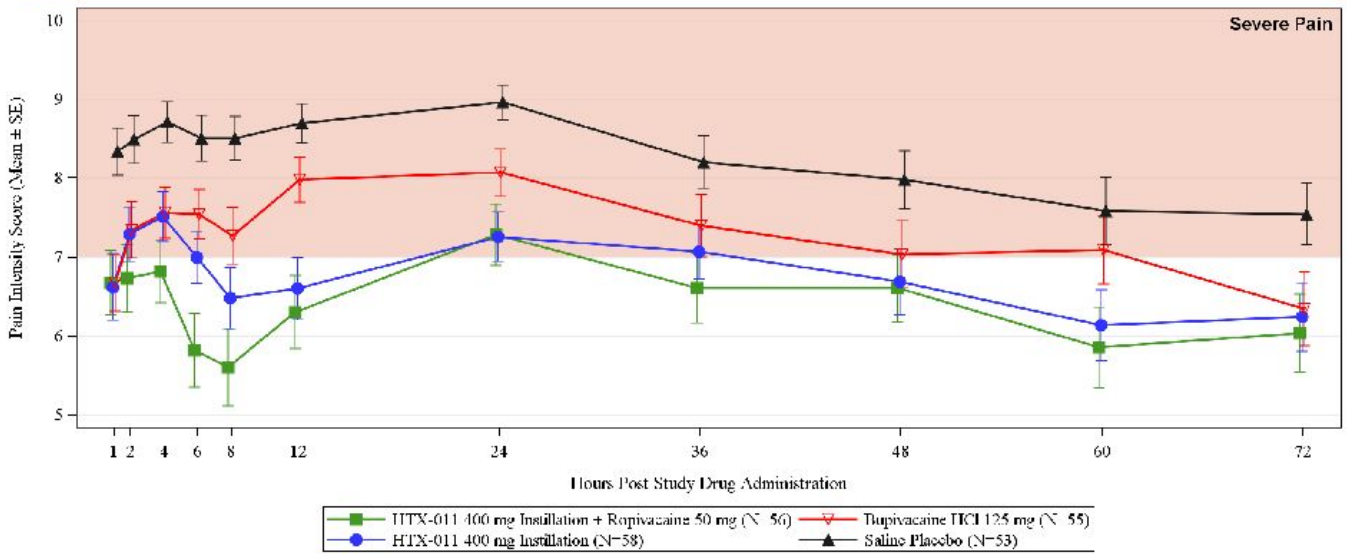
Study 209: Both HTX-011 Arms Significantly Reduce Pain at Rest Compared to Placebo through 72 Hours



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



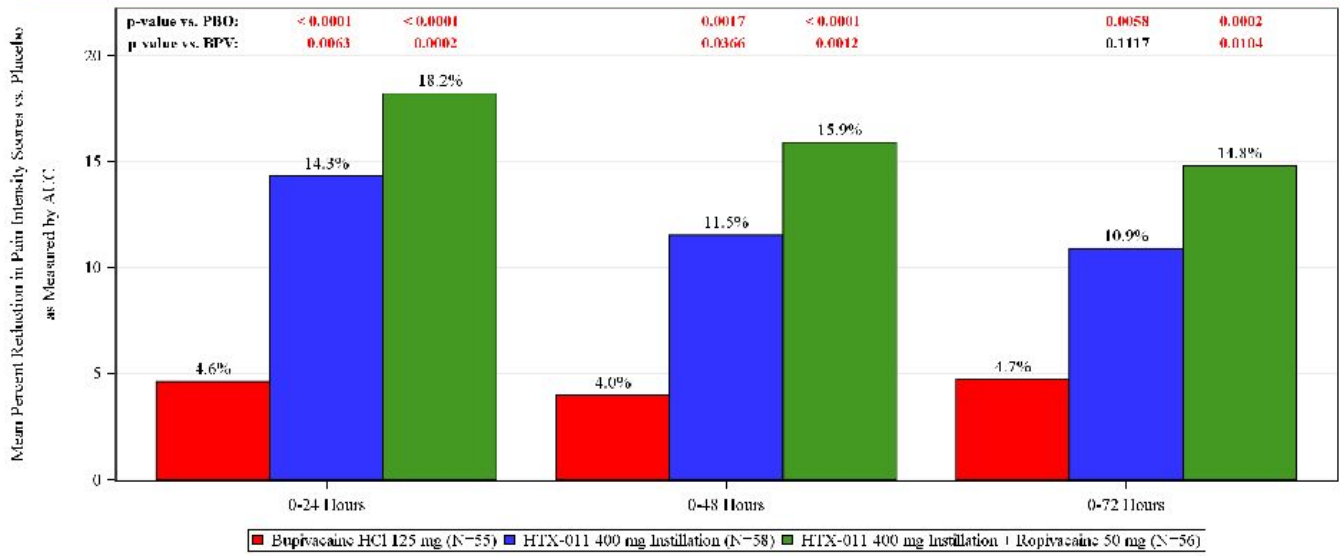
Study 209: Significant Separation between HTX-011 Arms and Placebo through 72 Hours



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



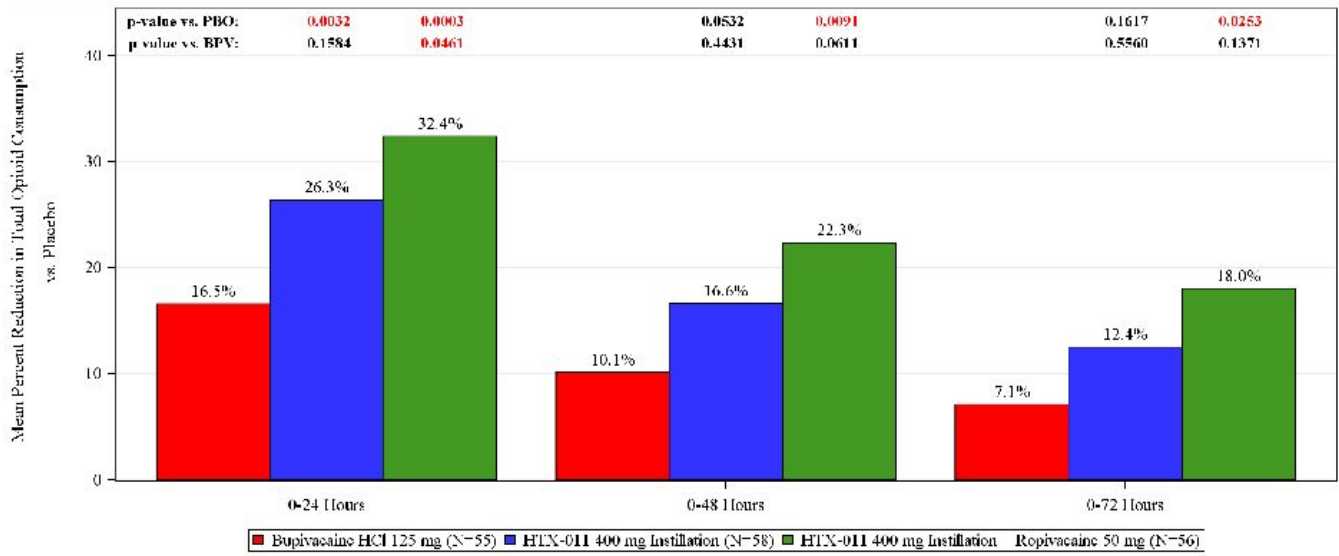
Study 209: Both HTX-011 Arms Reduce Pain with Activity Significantly Better than Placebo and Bupivacaine through 48 Hours



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



Study 209: HTX-011 plus Ropivacaine Significantly Reduces Opioid Use vs. Placebo through 72 Hours

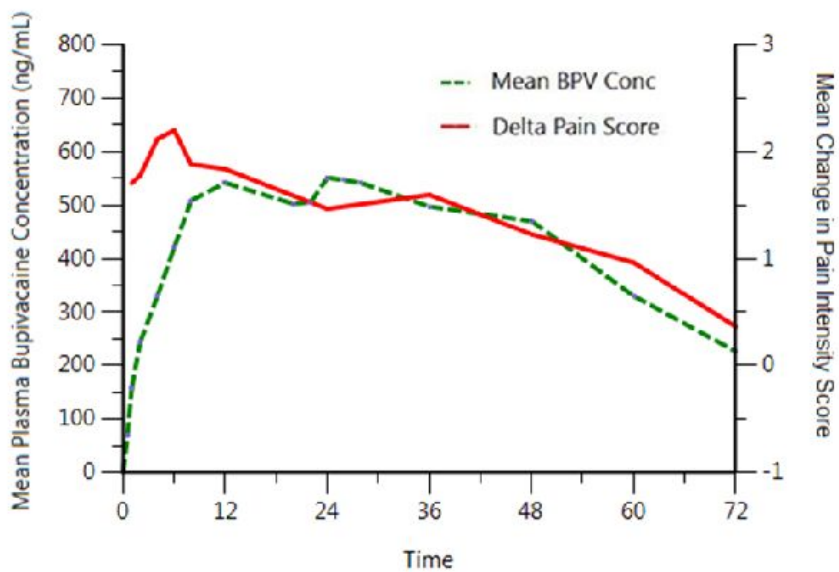


Opioid consumption is presented in mean milligrams of morphine equivalents



Study 209: Strong Correlation between Pain Reduction and Pharmacokinetics of HTX-011 in TKA

HTX-011 400 mg Via Instillation





Study 209: HTX-011 Well Tolerated in TKA

HTX-011 was well tolerated, with a safety profile comparable to placebo and bupivacaine solution:

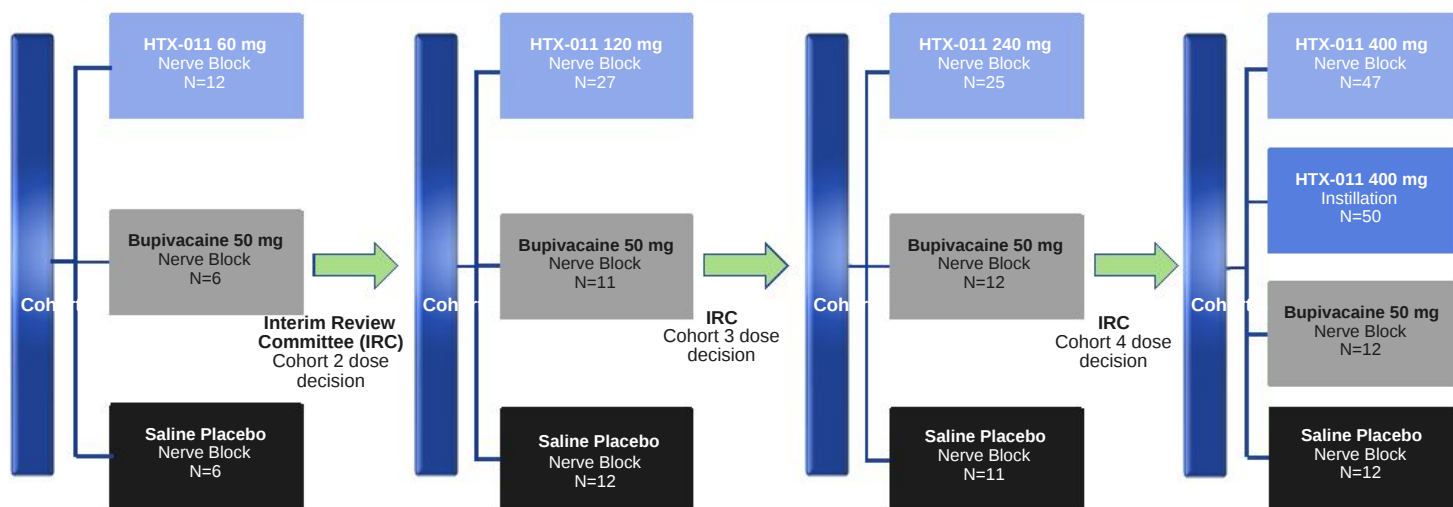
- No clinically meaningful differences in overall adverse events
- No difference in the incidence of serious adverse events
- No difference in premature discontinuations due to adverse events
- No deaths
- No clinically meaningful differences in potential local anesthetic systemic toxicity (LAST) adverse events in this highly vascular model
- No increase in potential LAST when given with another local anesthetic, ropivacaine
- No difference in wound healing

Study 209: TKA Summary



- HTX-011 achieved primary and key secondary endpoints
- Both HTX-011 arms achieved significant reductions in pain at rest vs. placebo through 48 hours
 - Also significantly reduced pain at rest through 72 hours vs. placebo
- Both HTX-011 arms achieved significant reductions in pain with activity (the most conservative assessment) vs. placebo and bupivacaine through 48 hours
 - HTX-011 plus ropivacaine maintained superiority to both placebo and bupivacaine through 72 hours
- There was significant separation of the HTX-011 mean pain curves vs. placebo through 72 hours
- Strong correlation between PK and PD in TKA
- HTX-011 with or without ropivacaine was generally well tolerated in TKA

Study 211: Phase 2b Breast Augmentation Study Design



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



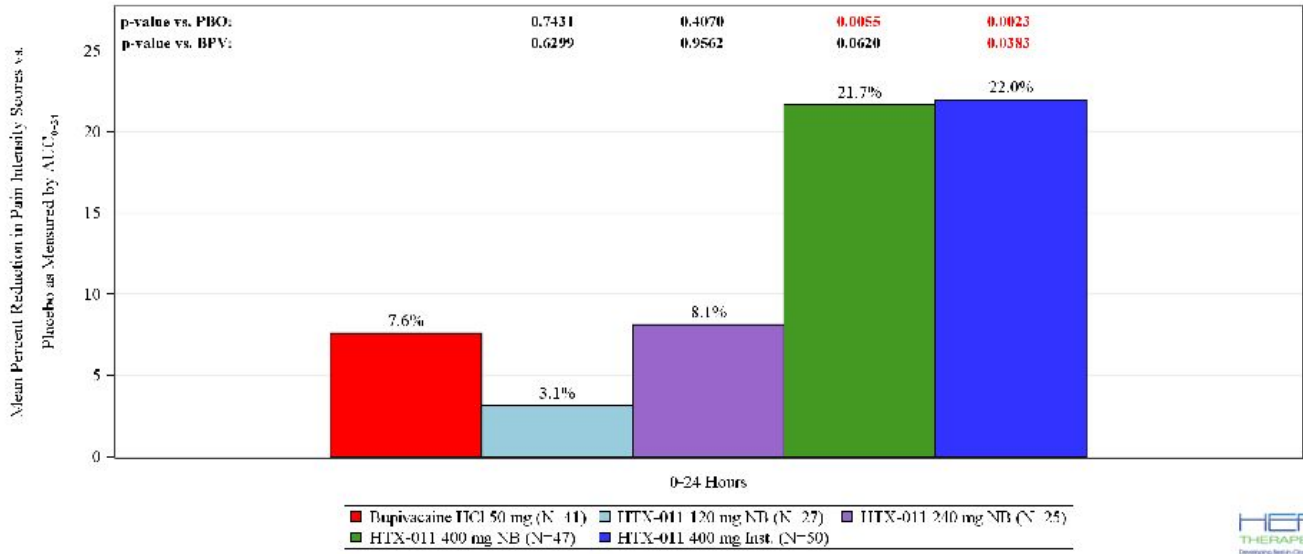
Study 211: Subject Demographics (ITT)

	Saline Placebo (N=41)	Bupivacaine HCL 50 mg (N=41)	HTX-011 (N=161)	Total (N=243)
Age (years) – mean (SD)	31.3 (9.0)	30.4 (7.8)	31.4 (7.8)	31.2 (8.0)
Sex – n (%)				
Female	41 (100%)	41 (100%)	161 (100%)	243 (100%)
Race – n (%)				
Asian	2 (4.9%)	2 (4.9%)	7 (4.3%)	11 (4.5%)
Black or African Descent	7 (17.1%)	3 (7.3%)	26 (16.1%)	36 (14.8%)
White	32 (78.0%)	35 (85.4%)	127 (78.9%)	194 (79.8%)
Multiple	0	1 (2.4%)	1 (0.6%)	2 (0.8%)
Ethnicity – n (%)				
Hispanic or Latino	16 (39.0%)	17 (41.5%)	61 (37.9%)	94 (38.7%)
Not Hispanic or Latino	25 (61.0%)	24 (58.5%)	100 (62.1%)	149 (61.3%)

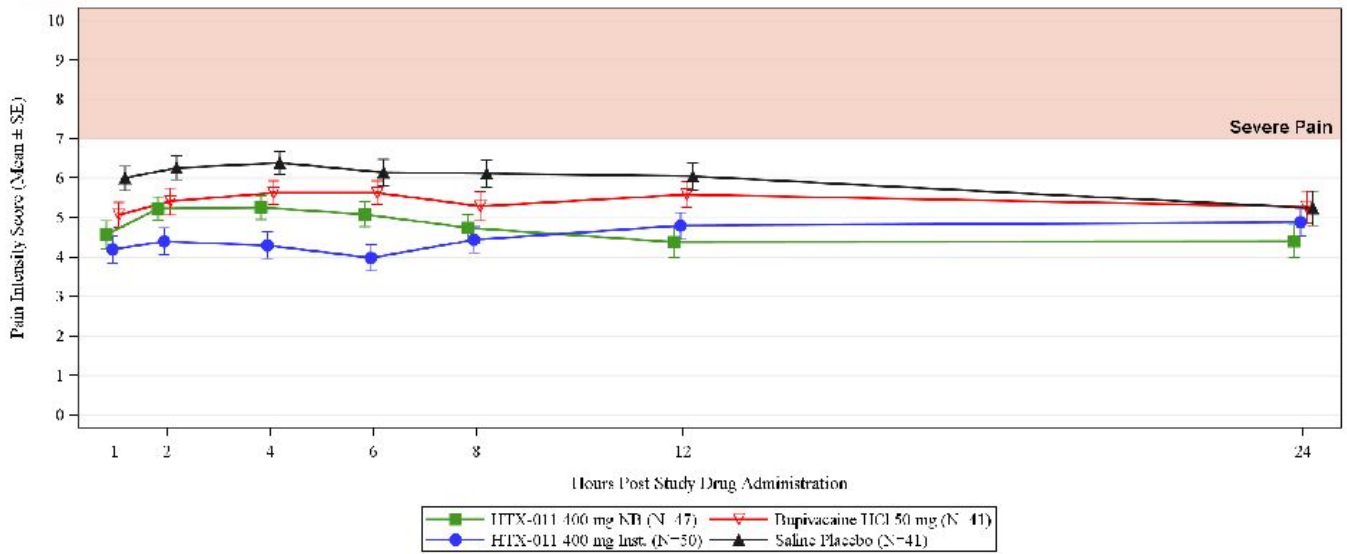
Study 211: Pain Reduction from HTX-011 at Rest Approximately Triple that of Bupivacaine



HTX-011 achieved primary endpoint for AUC₀₋₂₄



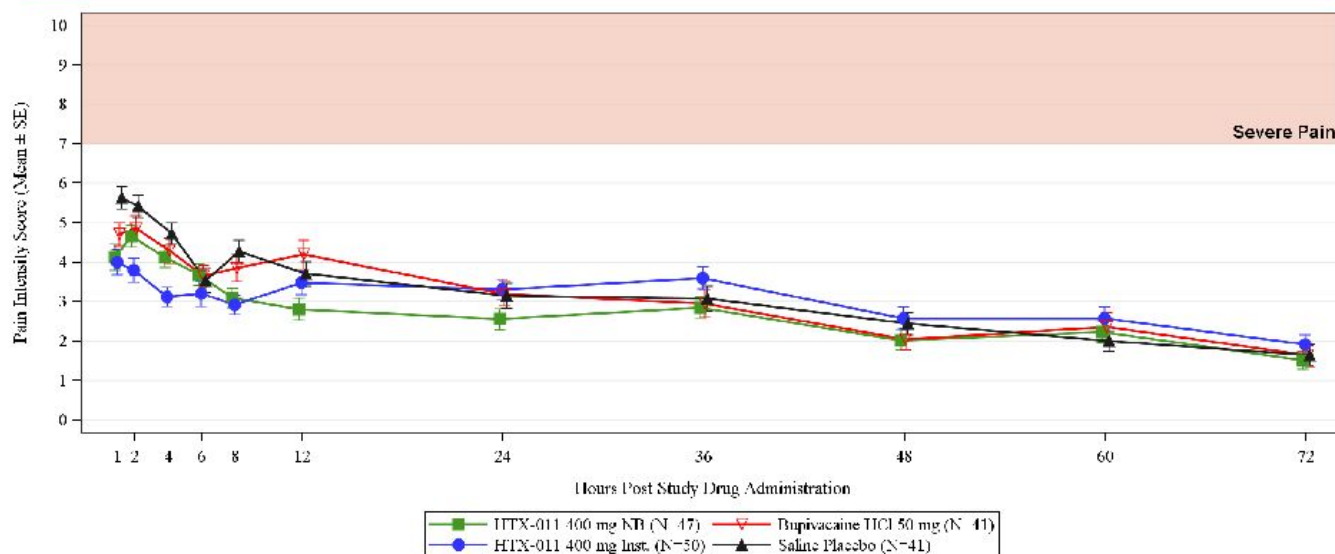
Study 211: HTX-011 Instillation Shows Superior Reduction in Pain Intensity Early and HTX-011 Nerve Block Shows Durable Response



Notes:
 Pain intensity collected at rest
 wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing pain data

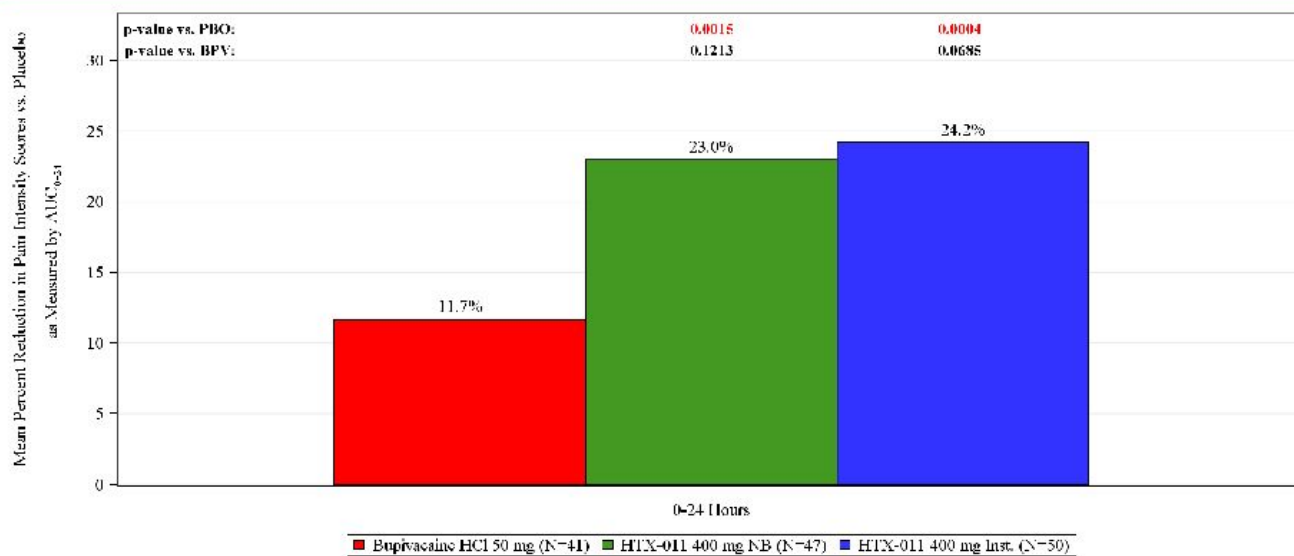


Study 211: Raw Pain Scores in All Arms Drop Quickly; Difficult to Discriminate between Arms after 24 Hours

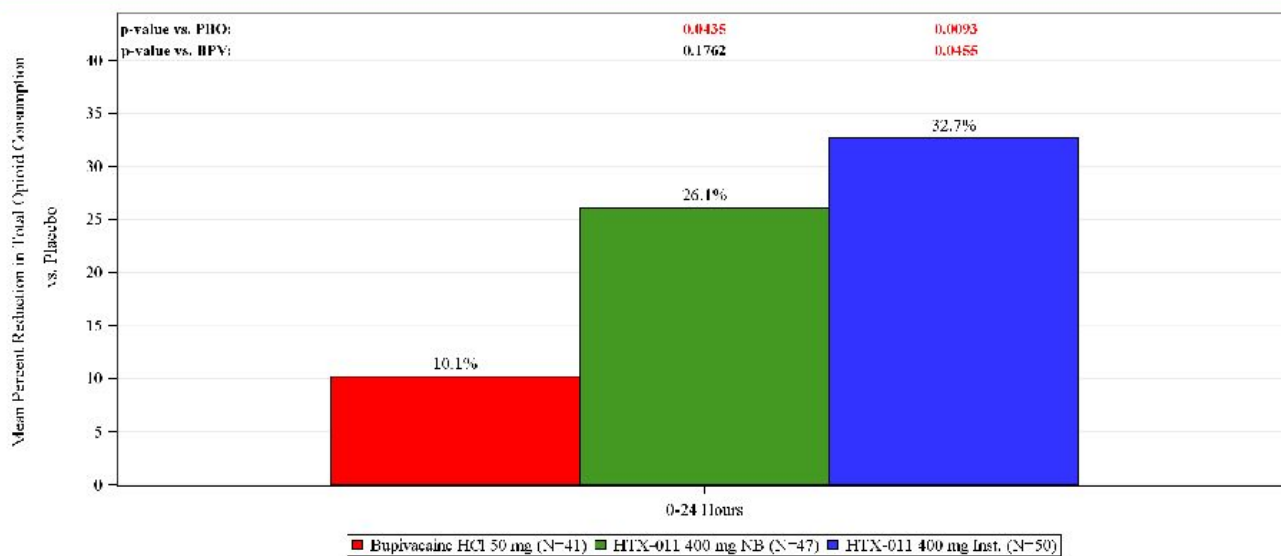


Notes:
 Raw pain intensity collected at rest
 Scores not adjusted for opioid use

Study 211: Both HTX-011 Arms Reduce Pain with Activity Significantly Better than Placebo through 24 Hours

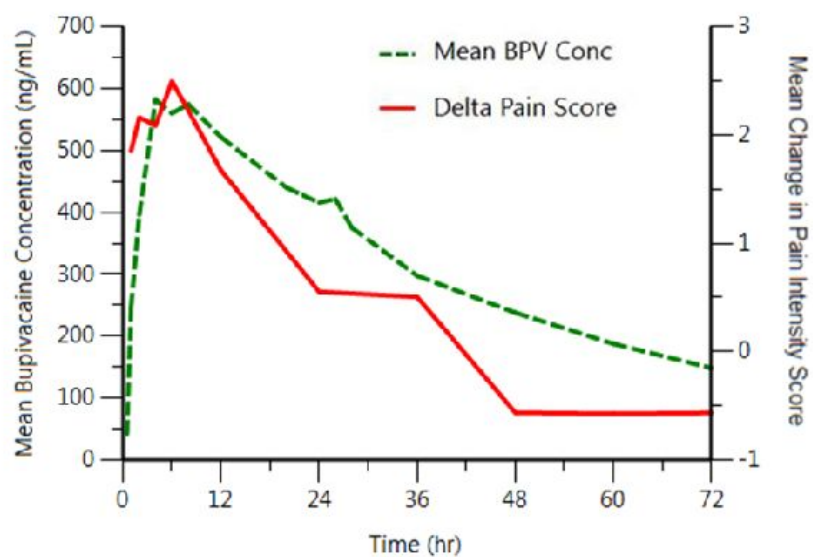


Study 211: Both HTX-011 Arms Significantly Reduce Opioid Use vs. Placebo through 24 Hours



Opioid consumption is presented in mean milligrams of morphine equivalents

Study 211: Strong Correlation between Pain Reduction and Pharmacokinetics of HTX-011 Instillation in Breast Augmentation





HTX-011 Well Tolerated in Breast Augmentation

HTX-011 was well tolerated, with a safety profile comparable to placebo and bupivacaine solution:

- No clinically meaningful differences in overall adverse events
- No difference in the incidence of serious adverse events
- No premature discontinuations due to adverse events
- No deaths
- No clinically meaningful differences in potential LAST adverse events
- No evidence of wound healing issues with local administration into the breast pocket



Study 211: Breast Augmentation Summary

- HTX-011 achieved the primary endpoint
- Both HTX-011 arms achieved significant reductions in pain at rest vs. placebo through 24 hours
- Both HTX-011 arms achieved significant reductions in pain with activity (the most conservative assessment) vs. placebo through 24 hours
- HTX-011 instillation (the most commercially relevant route for cosmetic surgery) produced the greatest reduction in pain and opioid use, beating both placebo and bupivacaine nerve block
- Strong correlation between PK and PD in breast augmentation with instillation
- HTX-011 administered via instillation or as a nerve block was generally well tolerated in breast augmentation with no wound healing issues

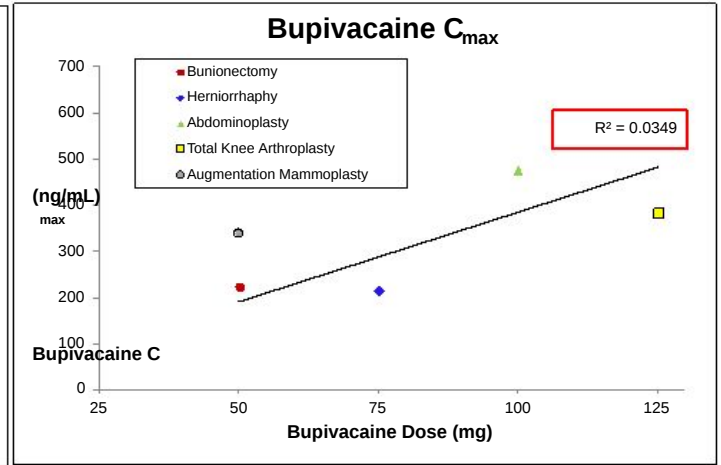
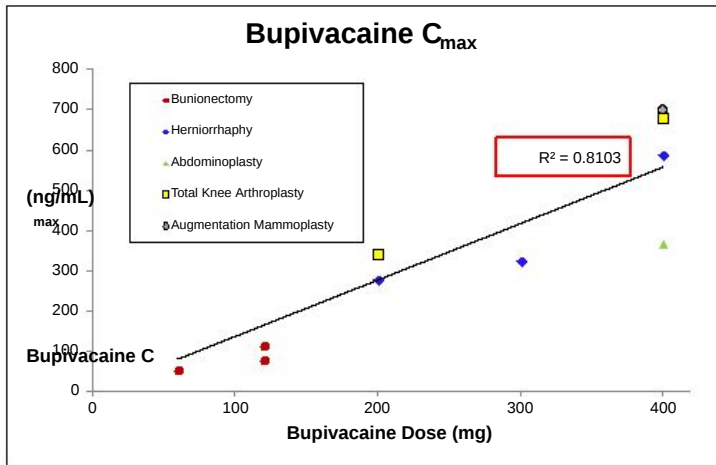


CONSISTENT PHARMACOKINETICS

HTX-011 Pharmacokinetics Across 5 Diverse Surgical Models Are More Dose-Linear than Bupivacaine Solution

Bupivacaine C_{max} With HTX-011

Bupivacaine C_{max} With Bupivacaine HCl



Phase 2b Conclusions

- HTX-011 plus ropivacaine was significantly superior to both placebo and bupivacaine in TKA
- HTX-011 demonstrated significant activity via both instillation and nerve block in breast augmentation
- Pharmacokinetics of HTX-011 remained consistent across 5 diverse surgical models with consistent correlation between PK and PD
- HTX-011 has been generally well tolerated up to 400 mg by instillation and as a nerve block
- Results from 7 positive Phase 2/3 studies across 5 surgical models are intended to support broad use of HTX-011 across a full range of surgical procedures

Large US Market Opportunity

Target Market Opportunity

~28M Annual US Surgical Procedures Requiring Postoperative Pain Management That Were Considered Potentially Suited for HTX-011



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

\$4.9B

Secondary Targets

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

\$1.9B

Tertiary Targets

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

\$2.3B

*Based on the current WAC of Exparel

HTX-011 Has Demonstrated Significant Clinical Benefit in Several of the High-Value Procedures in Initial Target Market



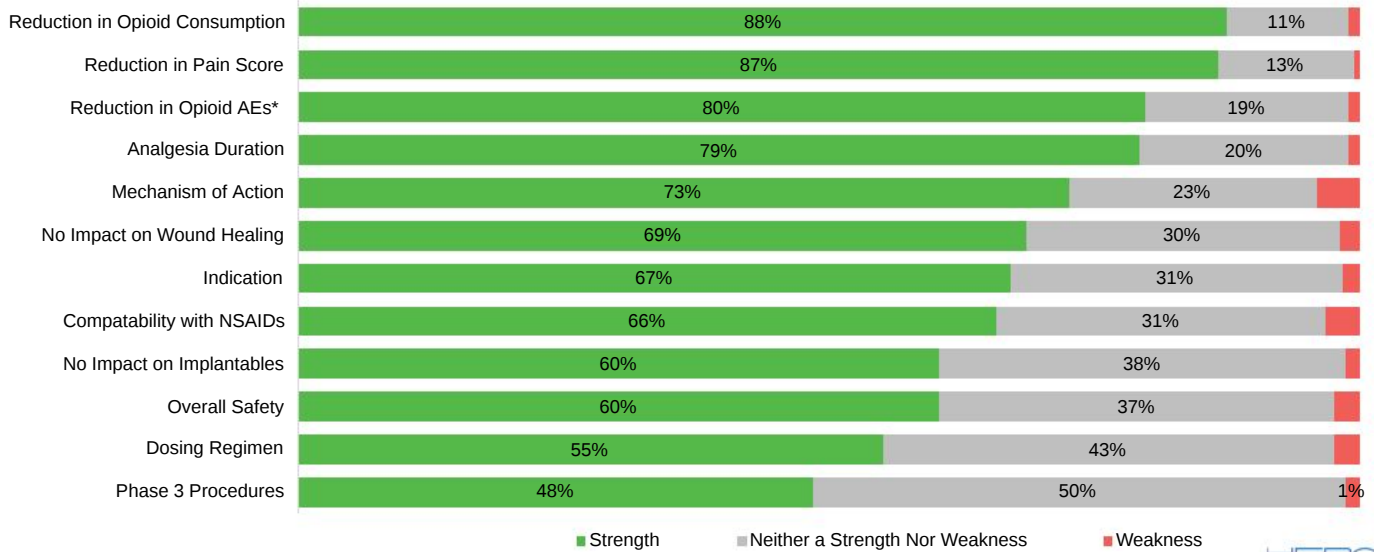
	Procedure	Annual Volume ('000s, US, 2015)	Overall % Local Anesthetic Use	HTX-011 Significantly Superior to Bupivacaine
		<i>Claims</i>	<i>Survey</i>	
Ortho Surgery	Knee arthroplasty	815	85%	YES
	Hip arthroplasty	337	78%	
	Shoulder arthroplasty	107	98%	
	Rotator cuff repair	550	90%	
	Spine procedures	750	100%	
General Surgery	Hernia repair	1,096	67%	YES
	Hemorrhoidectomy	504	86%	
	Colon and small bowel resection	483	69%	
Plastic Surgery	Abdominoplasty	160	73%	YES
	Mammoplasty	>300	86%	YES
OB/GYN	C-Section	1,285	TBD	

Completed studies



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

