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Company Update

June 24, 2018

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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.

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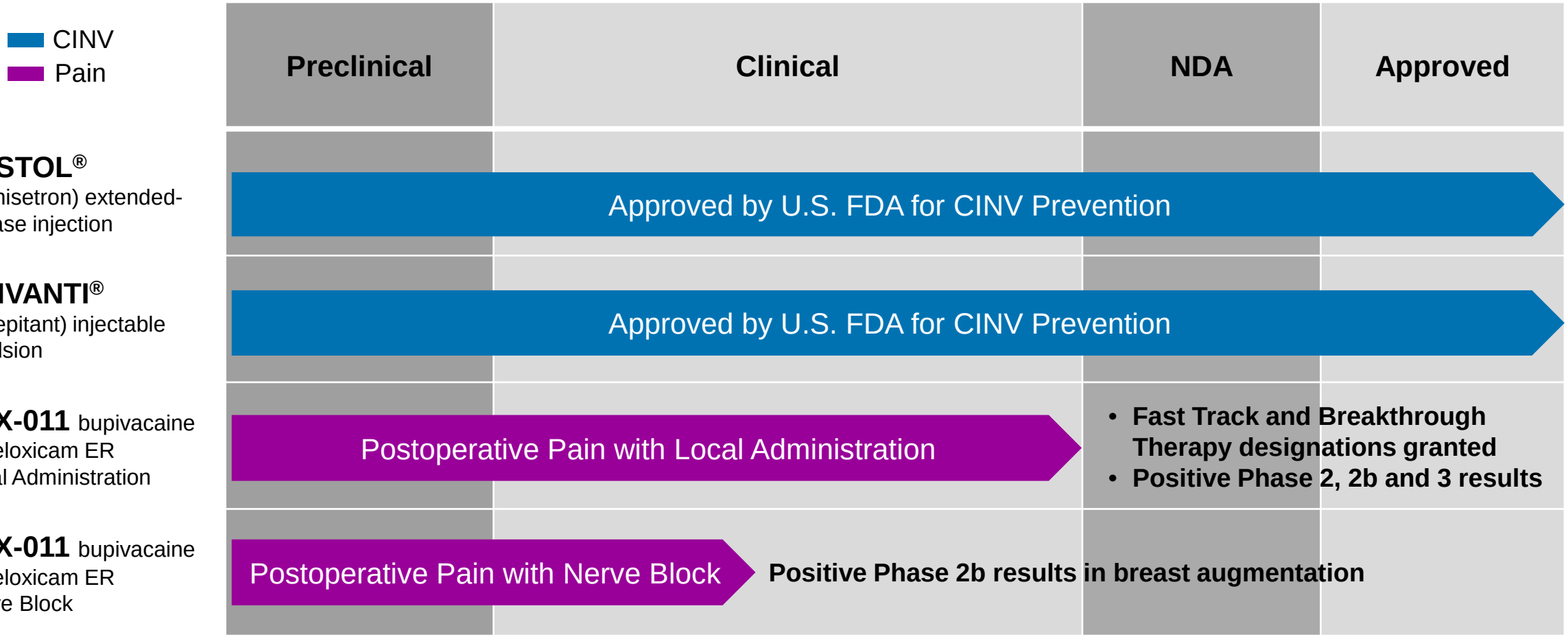
Status of Product Portfolio



HTX-011 for Postoperative Pain Management Has Received FDA 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 by FDA 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

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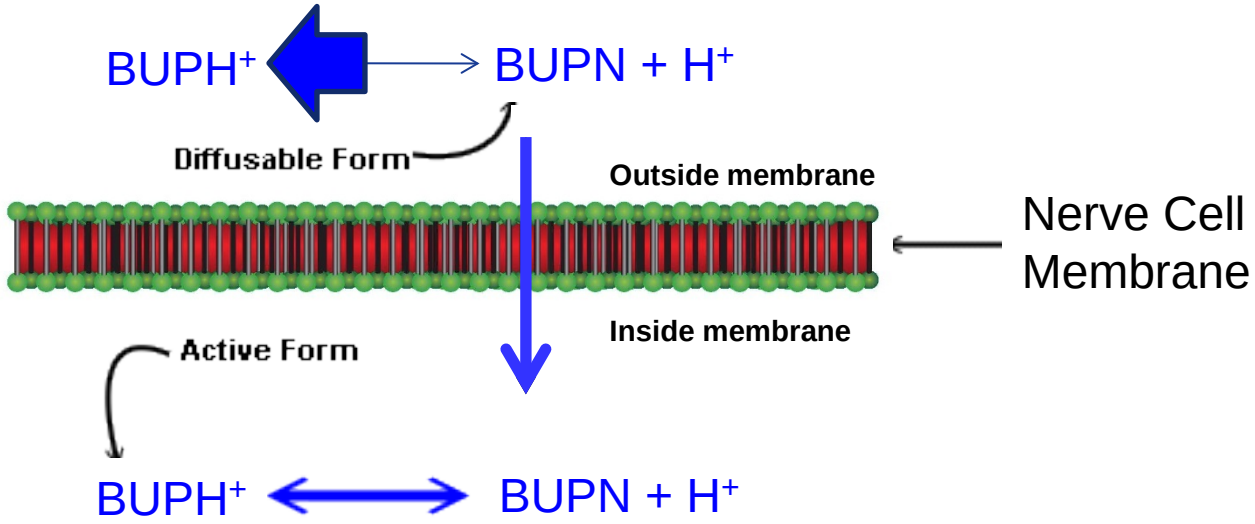
Why HTX-011's Unique Mechanism of Action Resulted in Superior Reduction in Pain and Opioid Use, Qualifying HTX-011 to Receive Breakthrough Therapy Designation

Inflammation Can Reduce the Activity of Local Anesthetics



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

- Acidic environment associated with inflammation results in far less drug penetrating the nerve membrane and reduced anesthetic effects[1,2]
- Bupivacaine is very sensitive to reduced pH
- Addition of meloxicam is designed to help reduce local inflammation and allow bupivacaine to work better in the first several days after surgery

1. Ueno, et al. J of Inflammation Research 1:41-48 2008.
2. Local anesthetic nerve penetration model adapted from Becker and Reed, Anesth Prog 53:98–109 2006

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Postoperative Opioids Are a Gateway to Addiction

MORE THAN 40 MILLION
patients undergoing surgical procedures are prescribed opioids for pain management in the United States each year

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

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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

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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 Relation-ship
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

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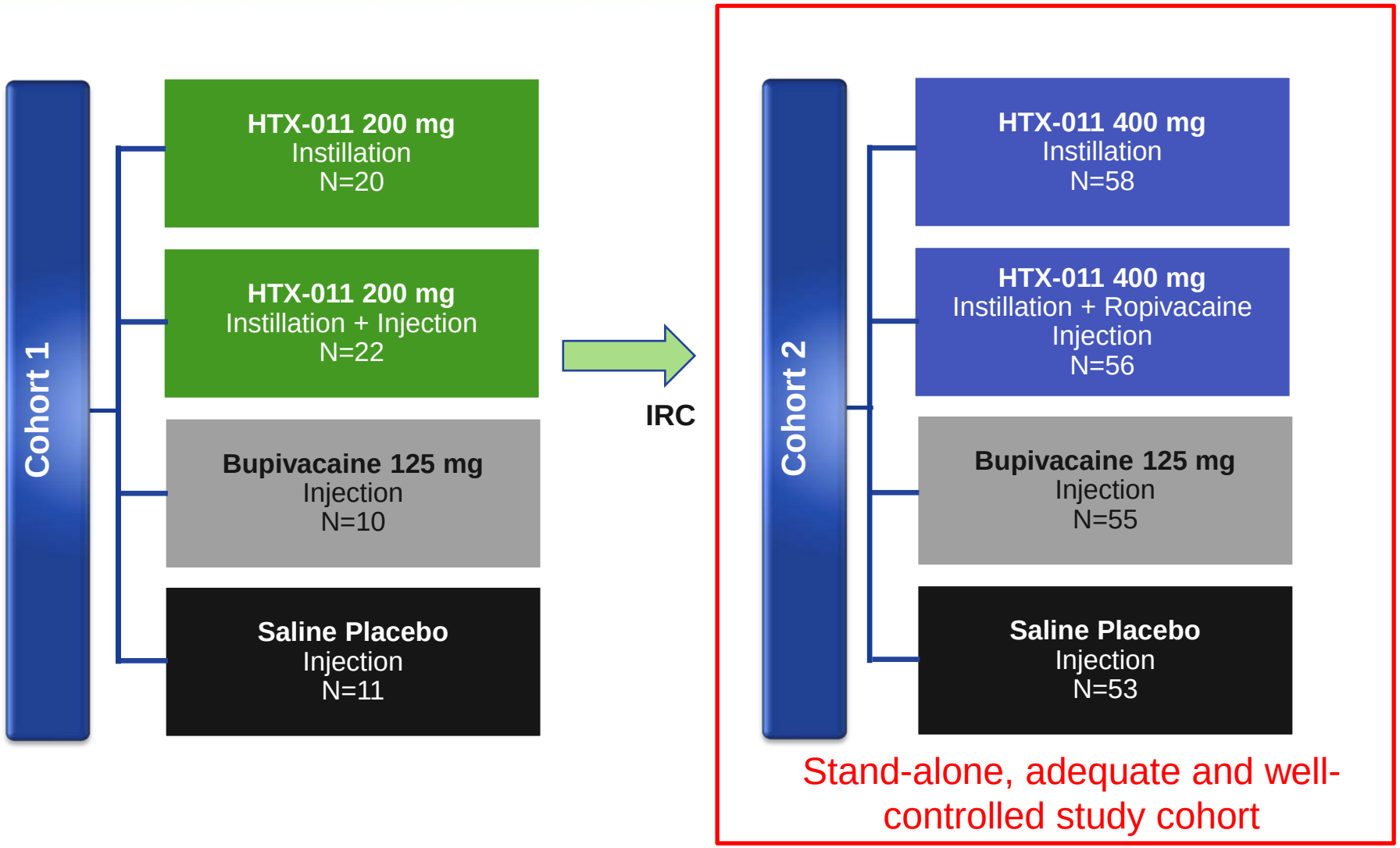
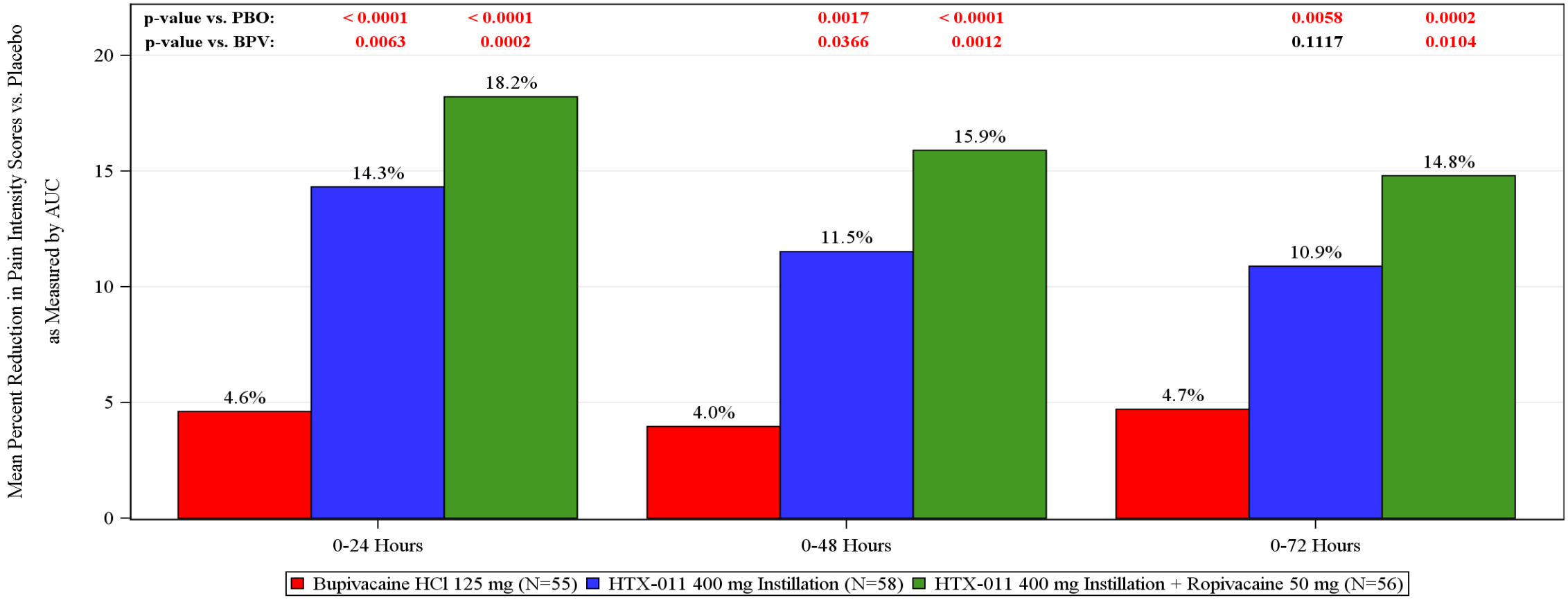
RECENTLY COMPLETED PHASE 2B STUDIES

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



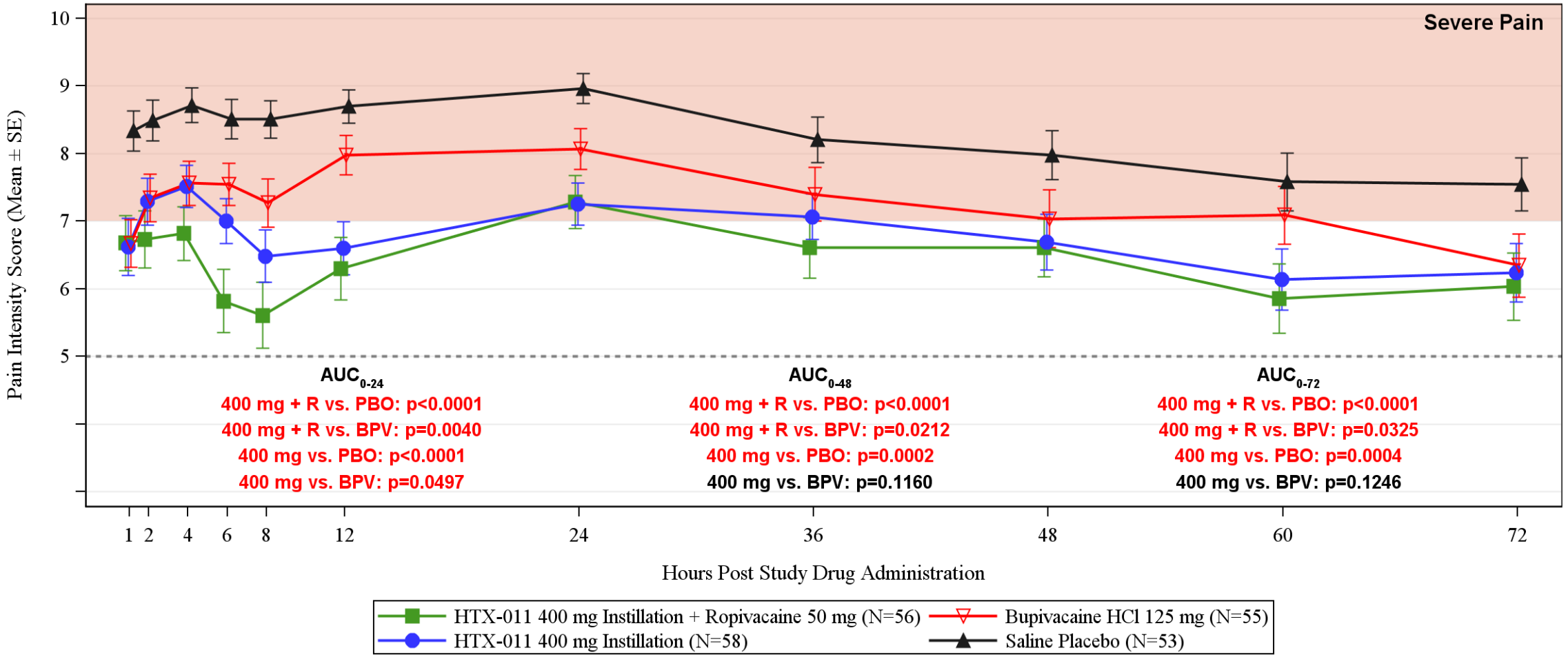
Study 209: Both HTX-011 Arms Reduce Pain with Activity Significantly Better than Placebo and Bupivacaine through 48 Hours

HTX-011 achieved primary endpoint for AUC_{0-48} at rest, and with activity



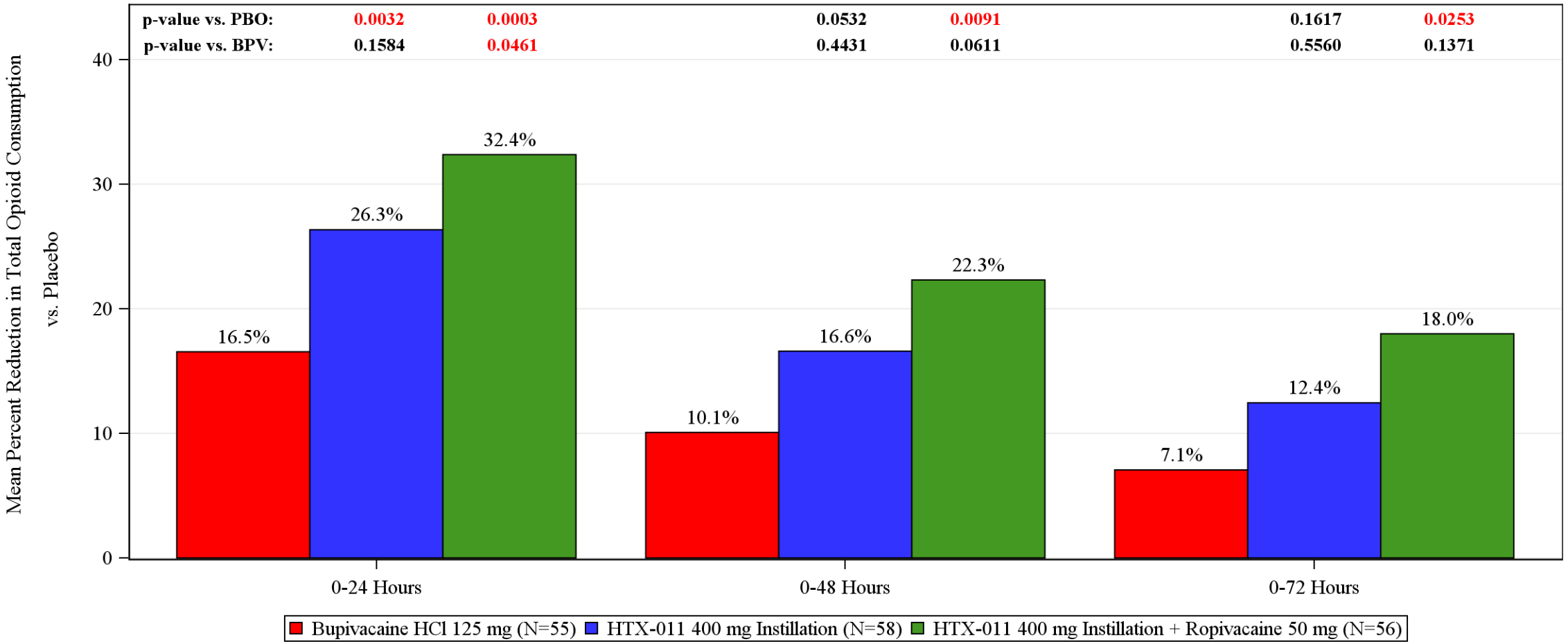
wWOCF for use of opioid rescue medication and LOCF for missing pain data

Study 209: Significant Separation between HTX-011 Arms and Placebo through 72 Hours for Pain at Rest



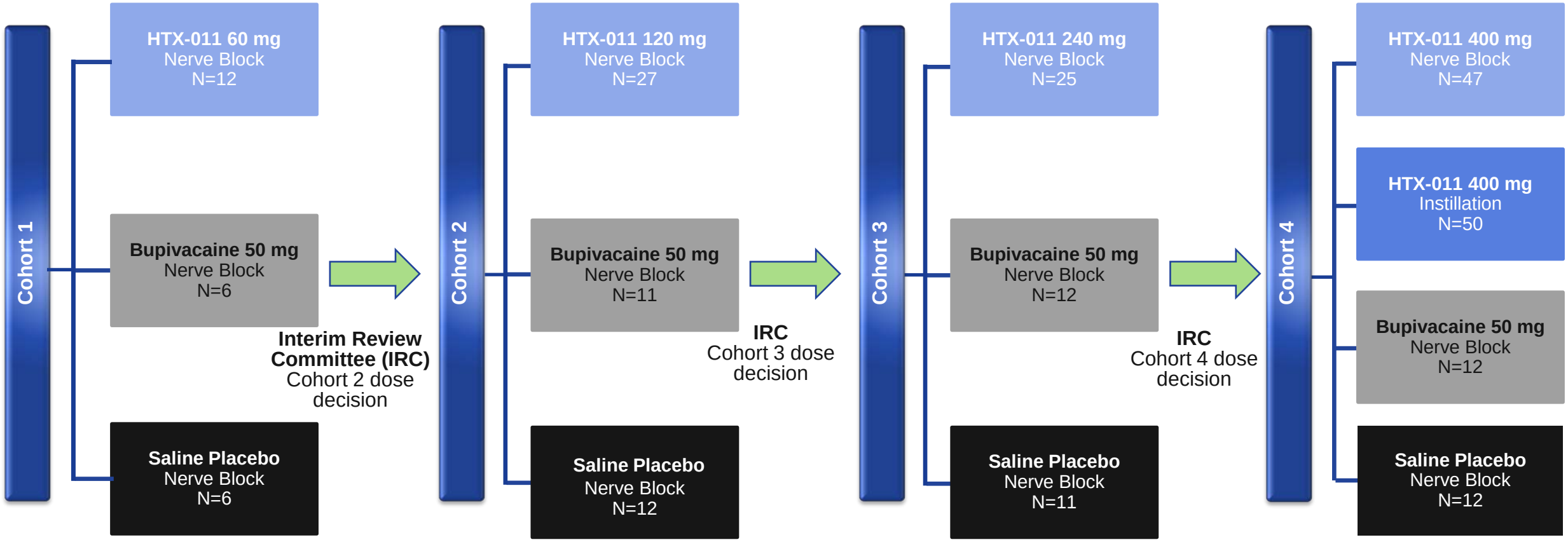
Notes:
Pain intensity collected at rest
wWOCF for use of opioid rescue medication and LOCF for missing pain data

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

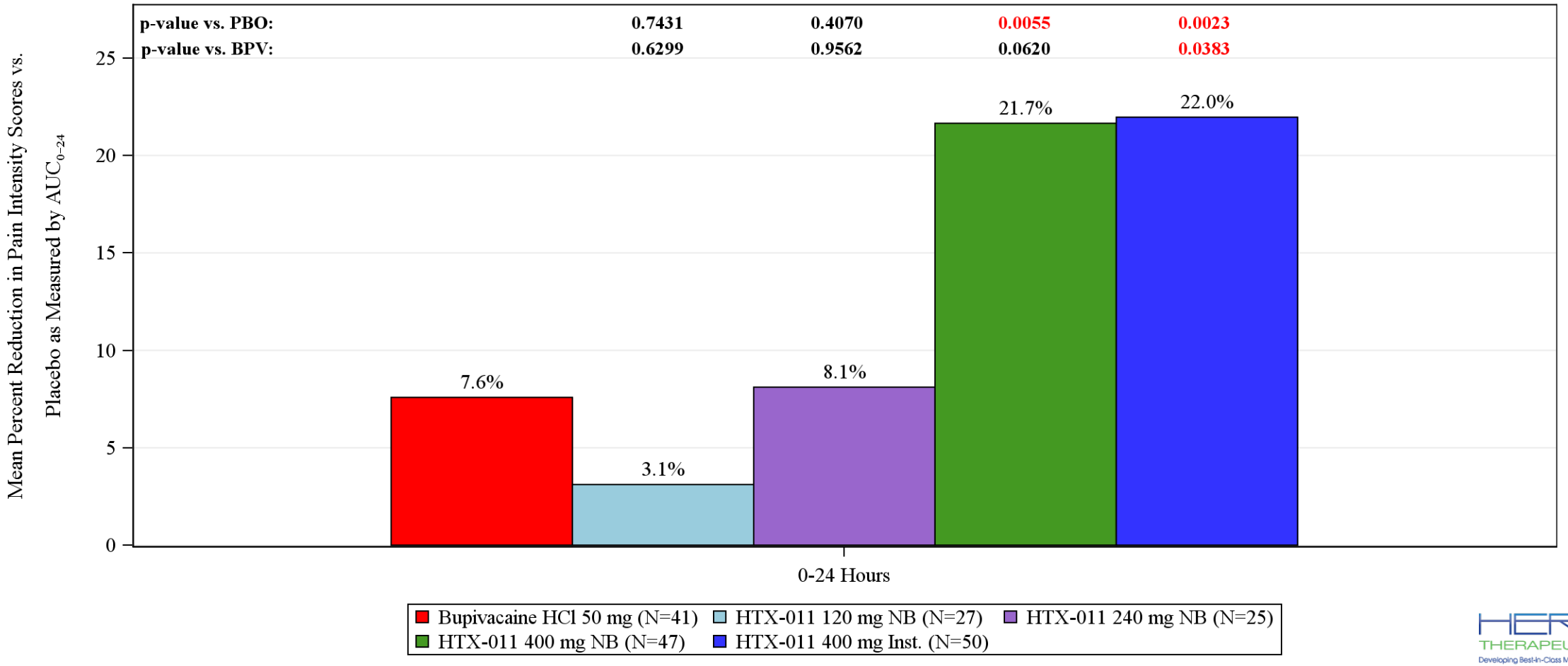
Study 211: Phase 2b Breast Augmentation Study Design



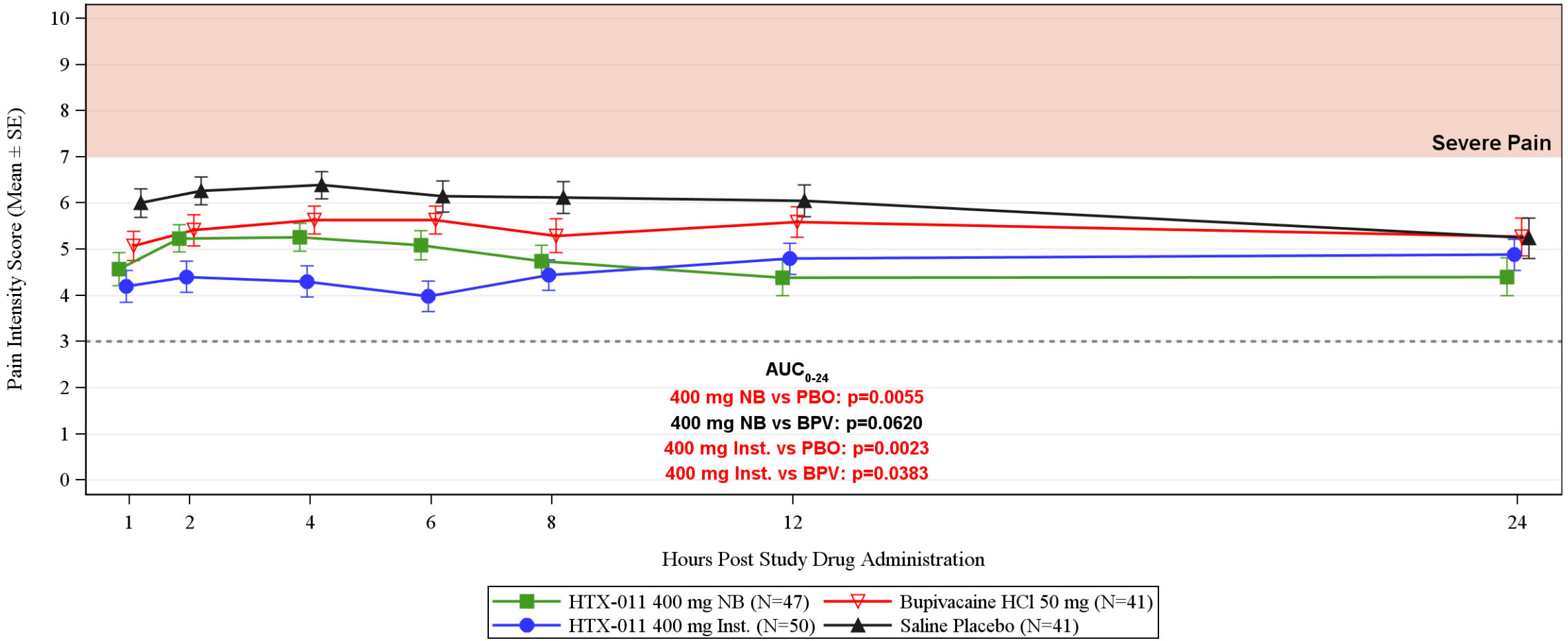
Protocol includes additional optional cohorts to evaluate other doses and administration techniques

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

HTX-011 achieved primary endpoint for AUC_{0-24} with activity and at rest

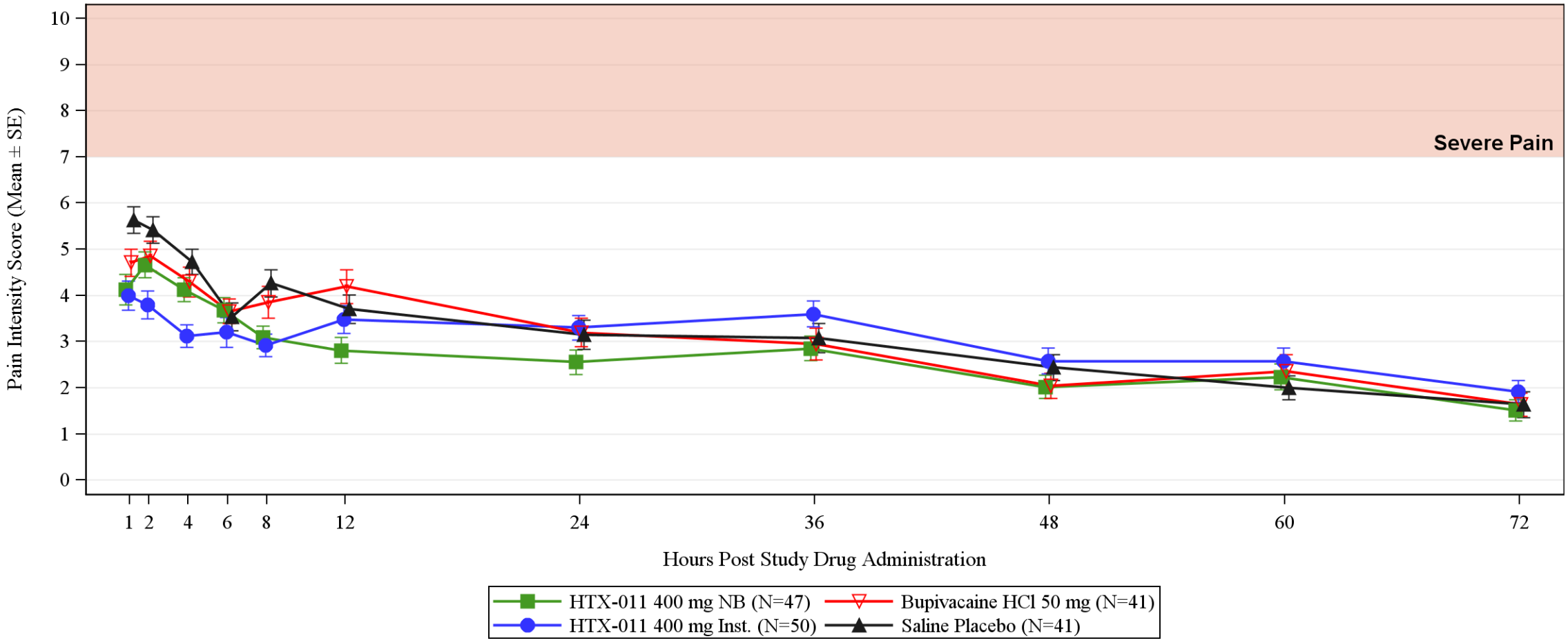


Study 211: HTX-011 Instillation Shows Superior Reduction in Pain at Rest Intensity Early and HTX-011 Nerve Block Shows Durable Response



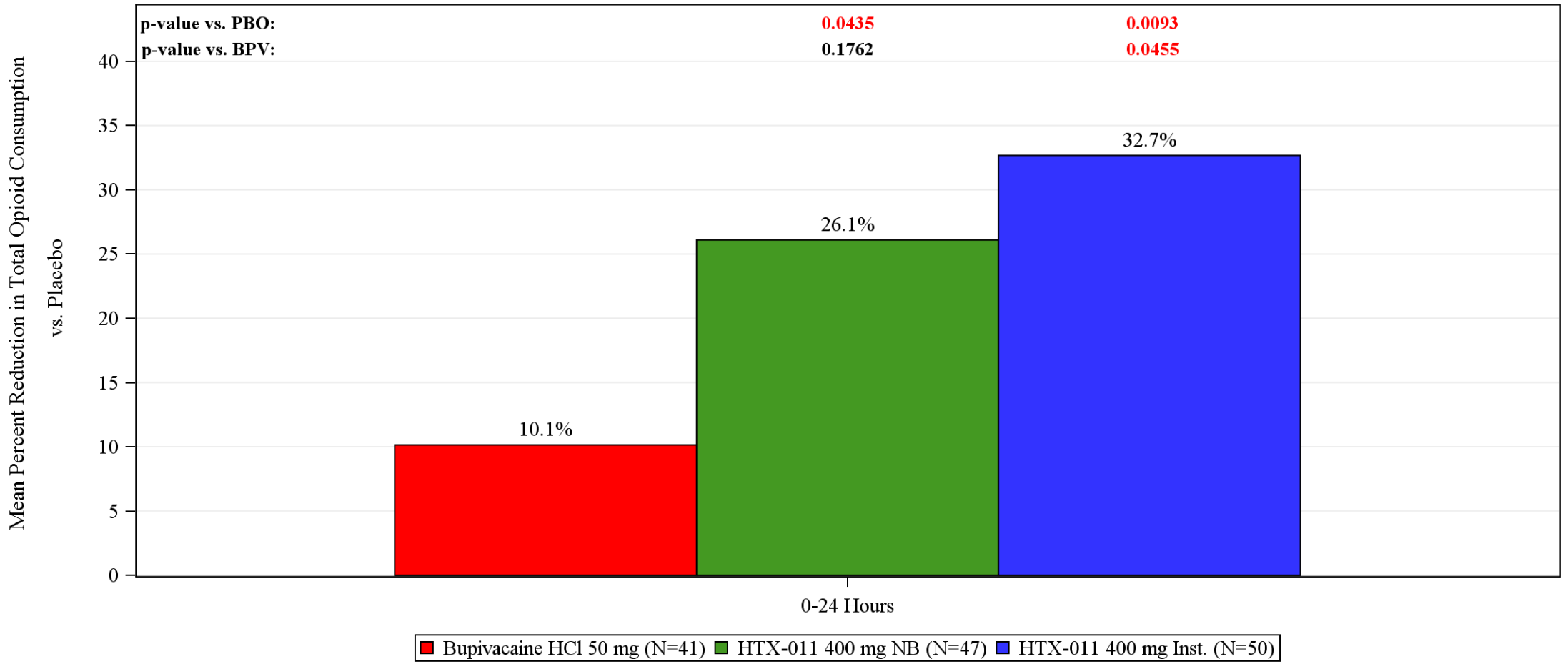
Notes:
Pain intensity collected at rest
wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing pain data

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

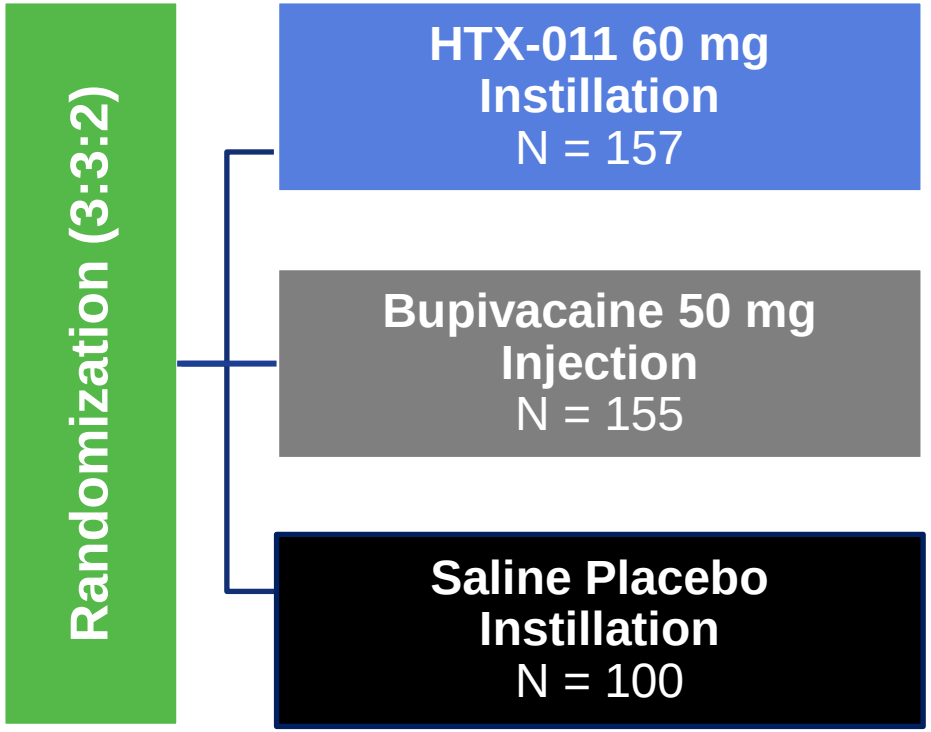
Study 211: Both HTX-011 Arms Significantly Reduce Opioid Use vs. Placebo through 24 Hours



Opioid consumption is presented in mean milligrams of morphine equivalents

PHASE 3

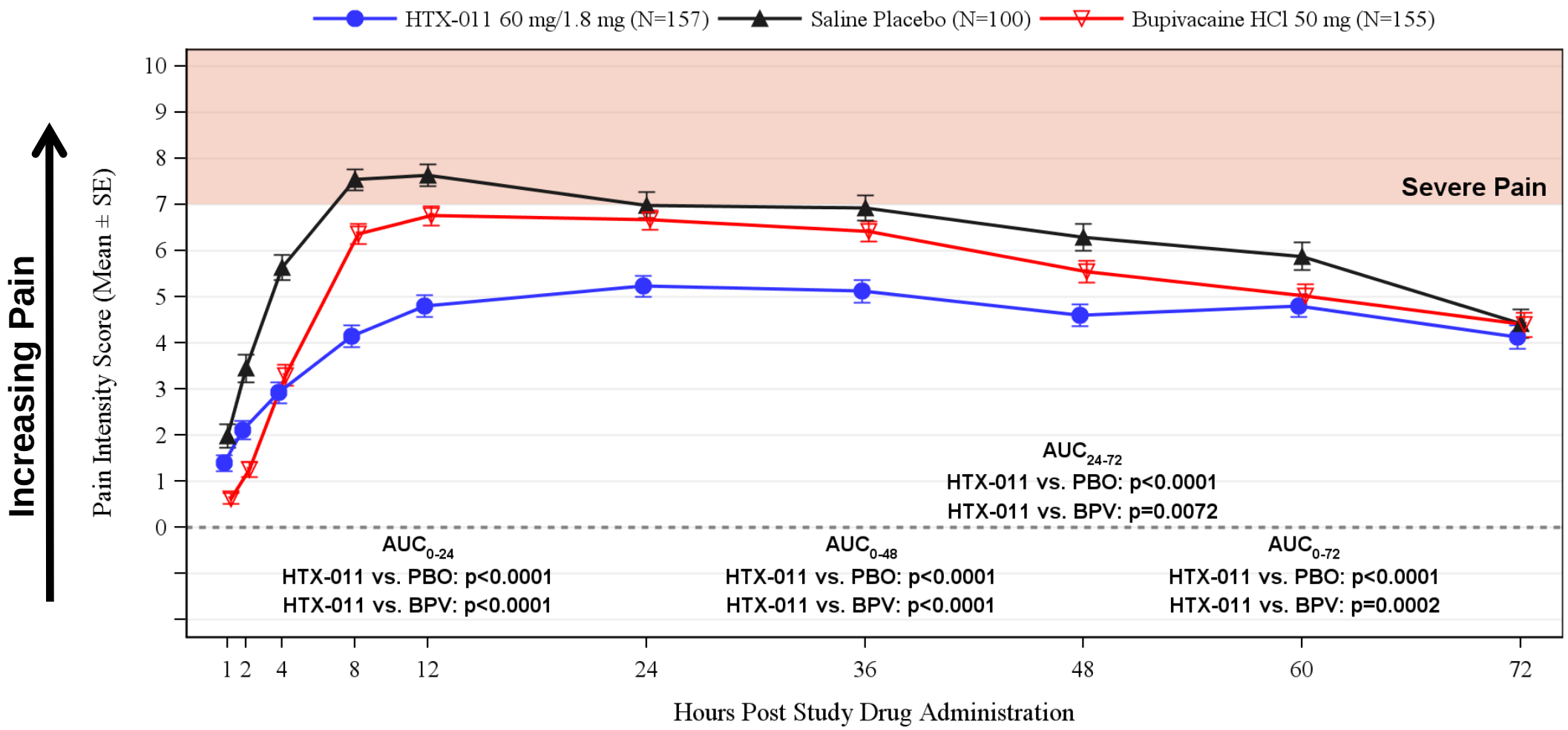
Study 301/EPOCH1: Phase 3 Bunionectomy
Study Design



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

EPOCH
Evaluation of Pain Relief and Opioid Control

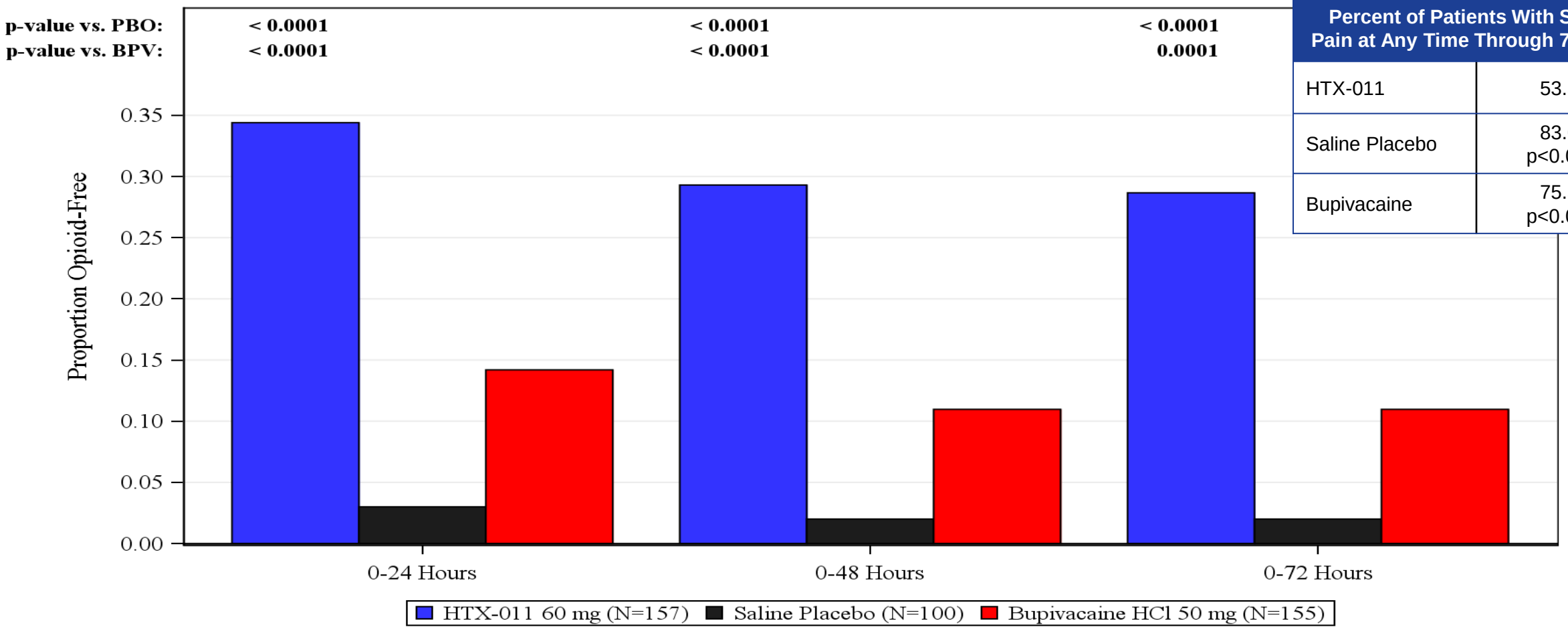
Study 301: HTX-011 Reduces Pain After Bunionectomy Significantly Better Than Placebo or Bupivacaine (Standard-of-Care)



wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data

Source: Figure 14.2.7

Study 301: HTX-011 Significantly Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo



Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011	53.5%
Saline Placebo	83.0% p<0.0001
Bupivacaine	75.5% p<0.0001

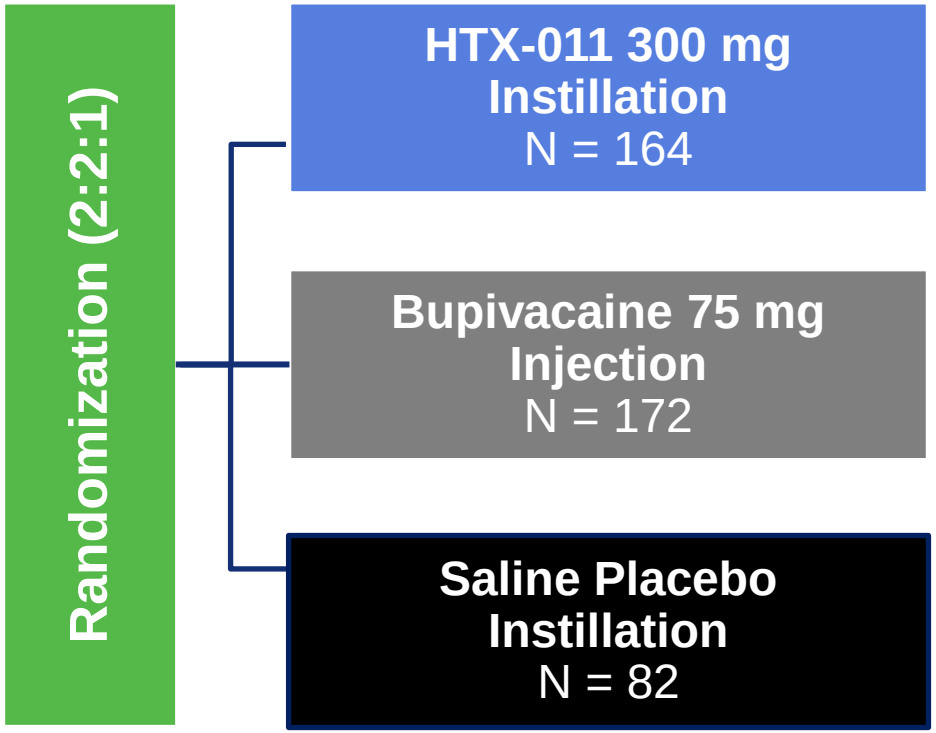
Source: Figure 14.2.3

Study 301: Incidence of Treatment Emergent Adverse Events Occurring in ≥ 5% in the HTX-011 Group

Preferred Term	HTX-011 60 mg (N=157)	Saline Placebo (N=101)	Bupivacaine HCl 50 mg (N=154)
Any TEAE	83.4%	78.2%	85.1%
Nausea	37.6%	43.6%	45.5%
Dizziness	21.7%	17.8%	23.4%
Incision site oedema	17.2%	12.9%	14.3%
Vomiting	14.6%	18.8%	21.4%
Headache	14.0%	9.9%	13.0%
Incision site erythema	12.7%	7.9%	11.7%
Post procedural contusion	12.1%	12.9%	11.7%
Bradycardia	7.6%	5.9%	7.8%
Impaired healing	6.4%	1.0%	3.9%
Constipation	5.7%	6.9%	11.7%
Muscle twitching	5.7%	5.0%	5.2%
Pruritus	5.1%	5.9%	0.6%

Source: Table14.3.1.3

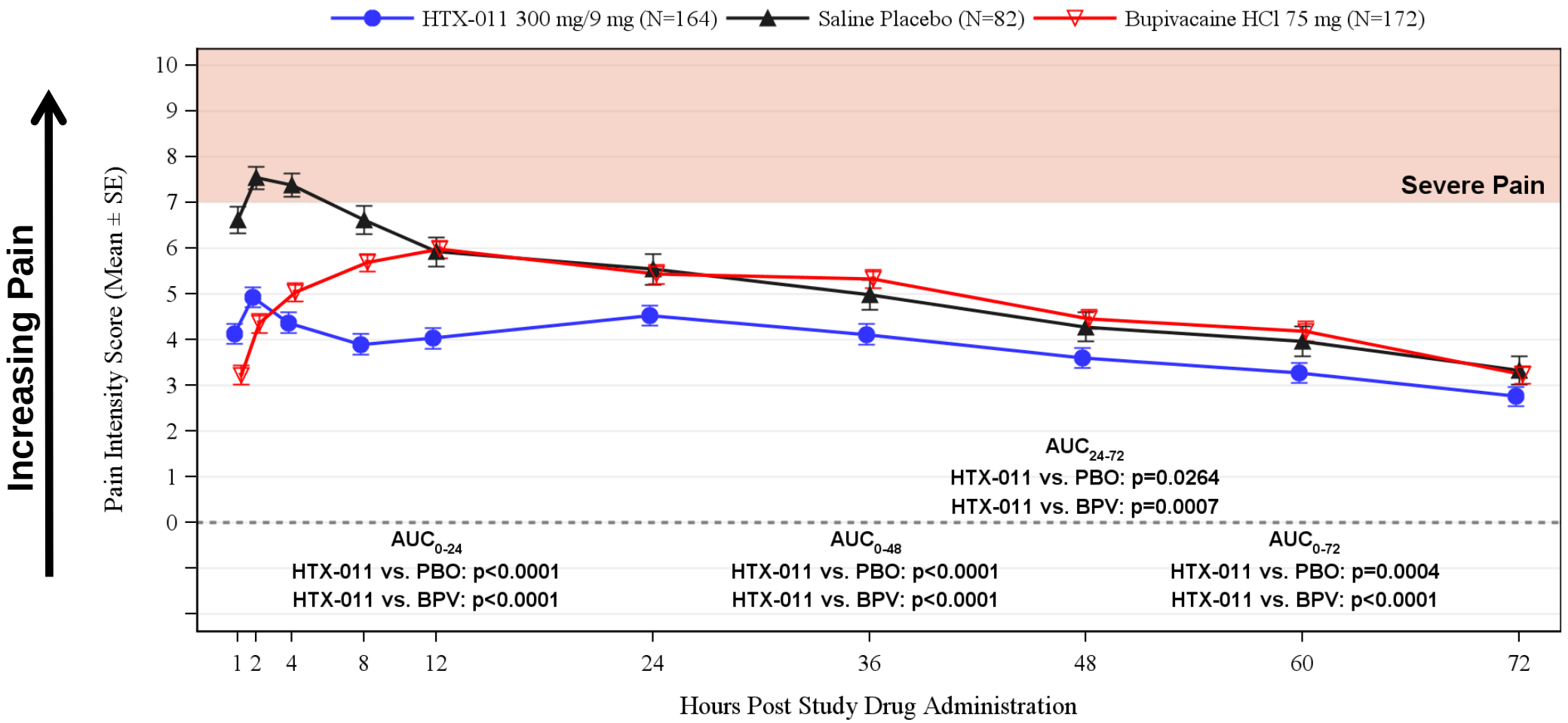
Study 302/EPOCH2: Phase 3 Herniorrhaphy
Study Design



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

EPOCH
Evaluation of Pain Relief and Opioid Control

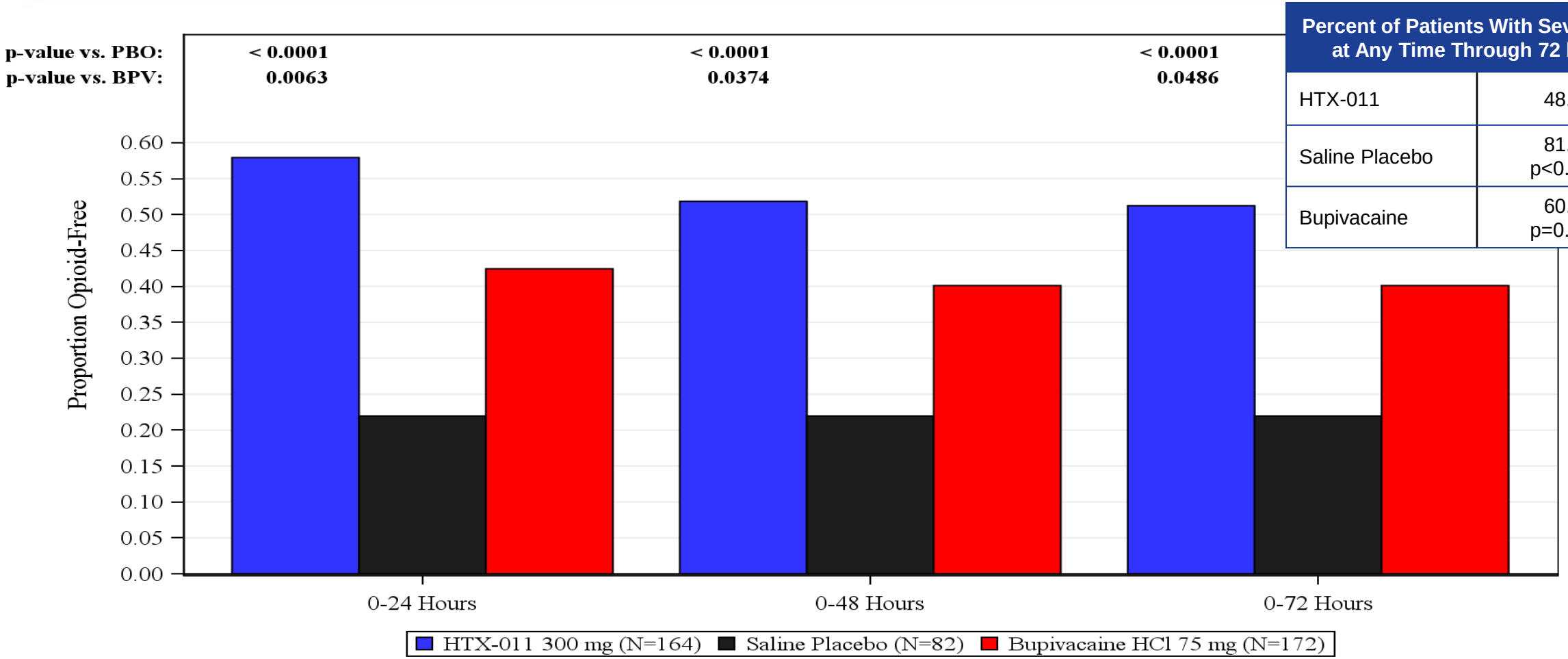
Study 302: HTX-011 Reduces Pain After Herniorrhaphy Significantly Better Than Placebo or Bupivacaine (Standard-of-Care)



wWOCF, windowed-worst observation carried-forward for use of opioid rescue medication and LOCF for missing data

Source: Figure 14.2.7

Study 302: HTX-011 Significantly Increases Proportion of Opioid-Free Subjects vs Bupivacaine and Placebo



Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011	48.8%
Saline Placebo	81.7% p<0.0001
Bupivacaine	60.5% p=0.0372

Source: Figure 14.2.3

Study 302: Incidence of Treatment Emergent Adverse Events Occurring in ≥ 5% in the HTX-011 Group

Preferred Term	HTX-011 300 mg (N=163)	Saline Placebo (N=82)	Bupivacaine HCl 75 mg (N=173)
Any TEAE	73.0%	74.4%	73.4%
Nausea	18.4%	34.1%	21.4%
Constipation	17.2%	18.3%	23.7%
Dizziness	14.7%	15.9%	24.3%
Headache	12.9%	12.2%	13.9%
Bradycardia	9.2%	7.3%	9.2%
Dysgeusia	9.2%	3.7%	12.1%
Skin odor abnormal	8.0%	1.2%	0.6%

Source: Table14.3.1.3

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 in 4 of 5 surgical models
  - Small imbalance in wound healing events in bunionectomy likely due to the vasodilatory effects of bupivacaine with superficial surgery; incidence higher for bupivacaine HCl and HTX-011 compared with the saline placebo. No wound healing imbalances in the other 4 surgical models
- No deaths on HTX-011 (one on bupivacaine)

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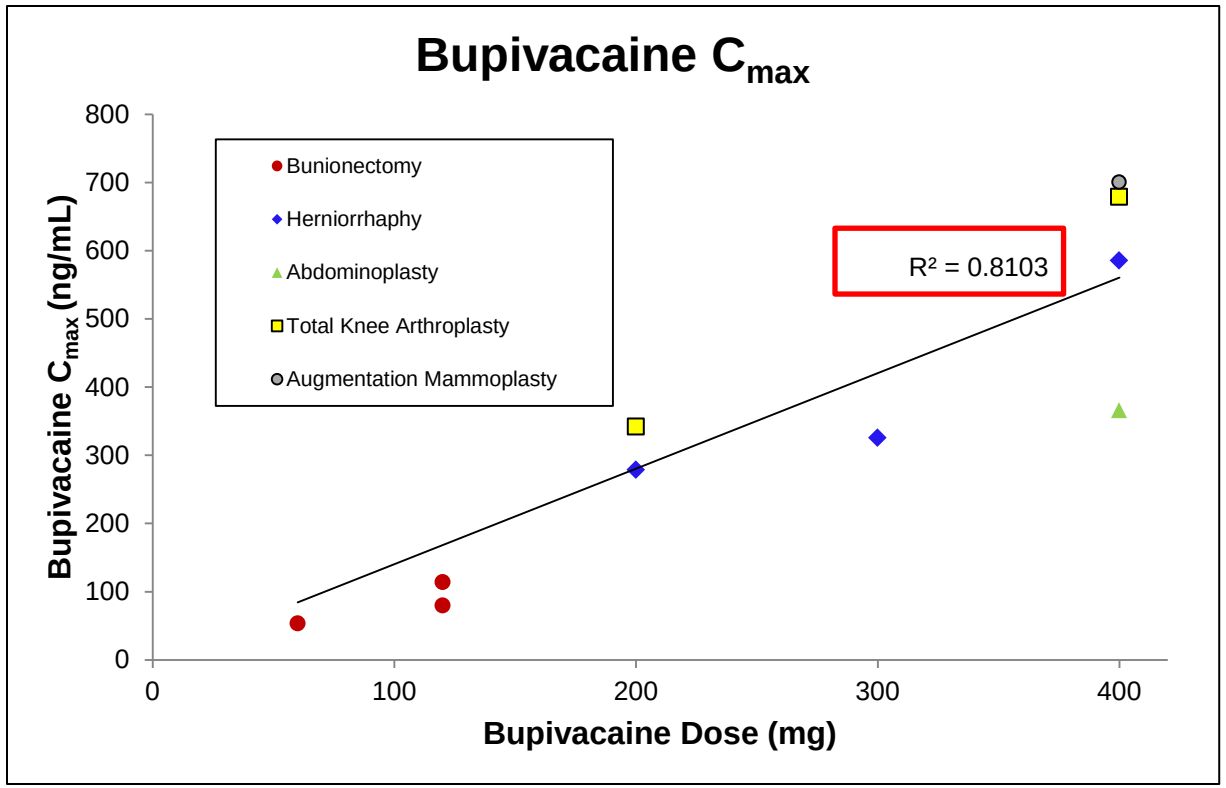
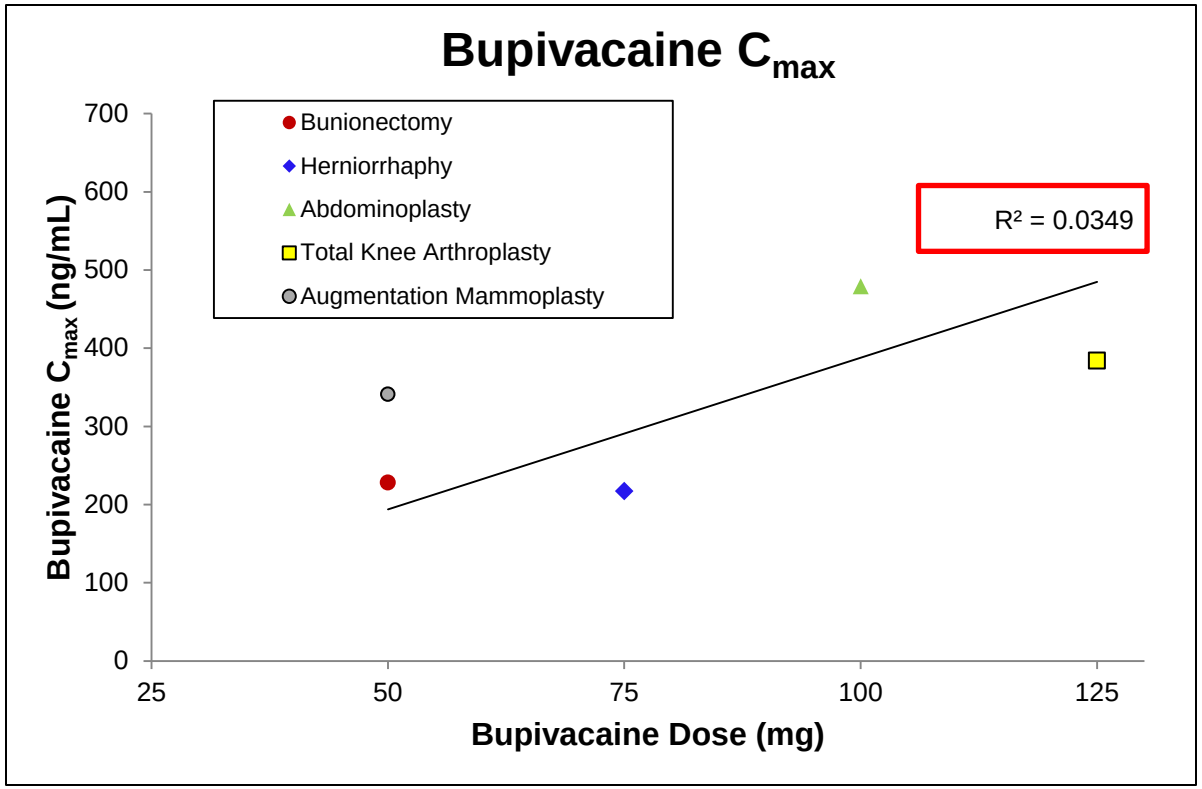
CONSISTENT PHARMACOKINETICS AND STRONG CORRELATION BETWEEN PK – PD ACROSS SURGICAL MODELS

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

HTX-011

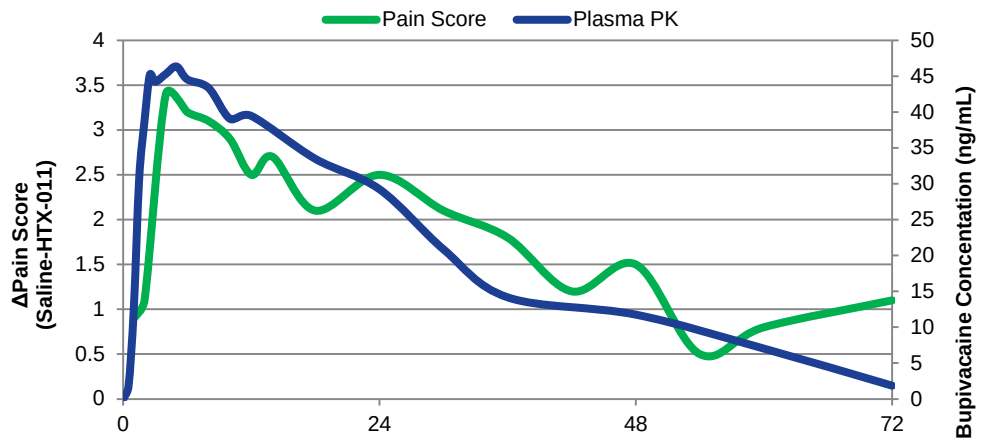


Bupivacaine HCl

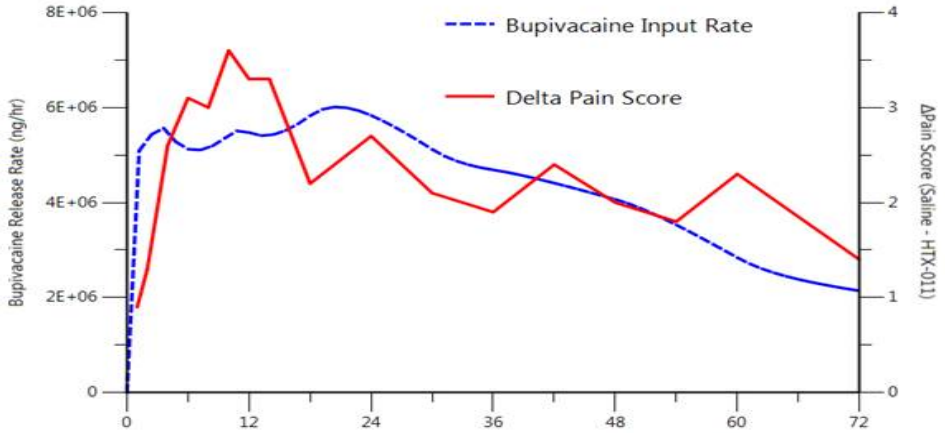


Excellent Correlation Between Pain Reduction and Pharmacokinetics of HTX-011 Across Surgical Models

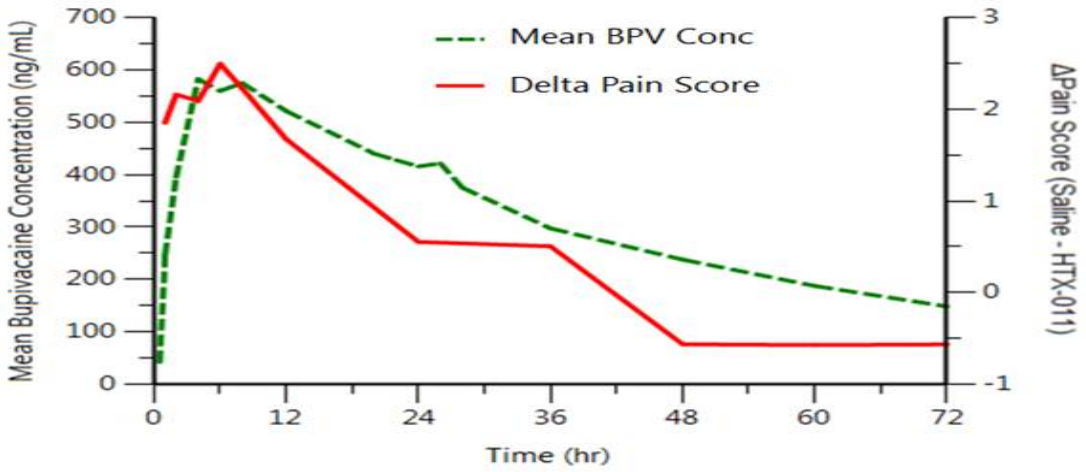
Bunionectomy



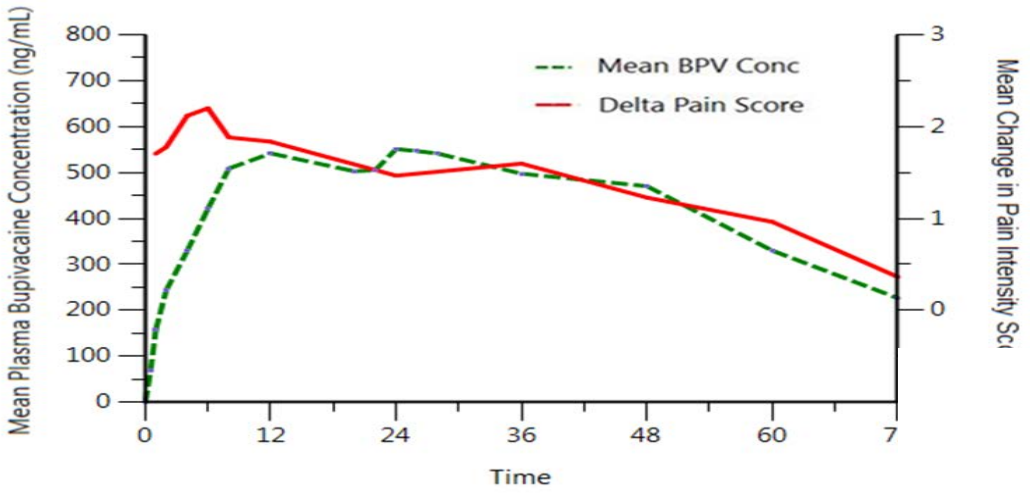
Hernia Repair



Breast Augmentation



Total Knee Arthroplasty



HTX-011 NDA Filing Plans

- Goal is to file an NDA in 2H2018 requesting a broad label for reduction of postoperative pain and opioid analgesics for 72 hours after surgery
- 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, in both Phase 3 studies
- NDA will contain PK, efficacy and safety data from 5 surgical models with HTX-011 doses from 60 mg to 400 mg to support a broad label:
  - Bunionectomy (Phase 2 & 3 data)
  - Herniorrhaphy (Phase 2 & 3 data)
  - Abdominoplasty (Phase 2 data)
  - Total Knee Arthroplasty (Phase 2b data)
  - Breast augmentation (Phase 2b data)

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9.7 Million Out of the 15 Million Initial Target Procedures (65%) Will Occur in Outpatient Setting

Hospitals account for 76%
[11.4 M procedures]

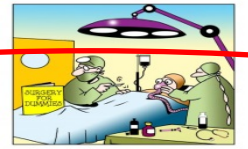
35% Inpatient
[5.3M procedures]

- **MS-DRG / Bundled Payment**
- **X-Code Opportunity**

41% Hospital Outpatient
[6.1M procedures]

- **C-Code / J-Code**
- **Surgical Supply Package / APCs**

Remaining outpatient facilities account for 24%
[3.6 M procedures]



10% Ambulatory Surgical Centers (ASCs)
[1.5M procedures]

- **C-Code / J-Code**
- **Surgical Supply Package / APCs**

14% Other (Physician Practices)
[2.1M procedures]

- **C-Code / J-Code**
- **Surgical Supply Package / APCs**

Hospital Sales Force will cover approximately 76%+ of total opportunity (Inpatient, HOPD and Hospital owned ASCs)

Large US Market Opportunity

Theoretical and Target Market

~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

Theoretical Market Size*

*Based on the current WAC of Exparel

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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
		Claims	*Survey*	
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

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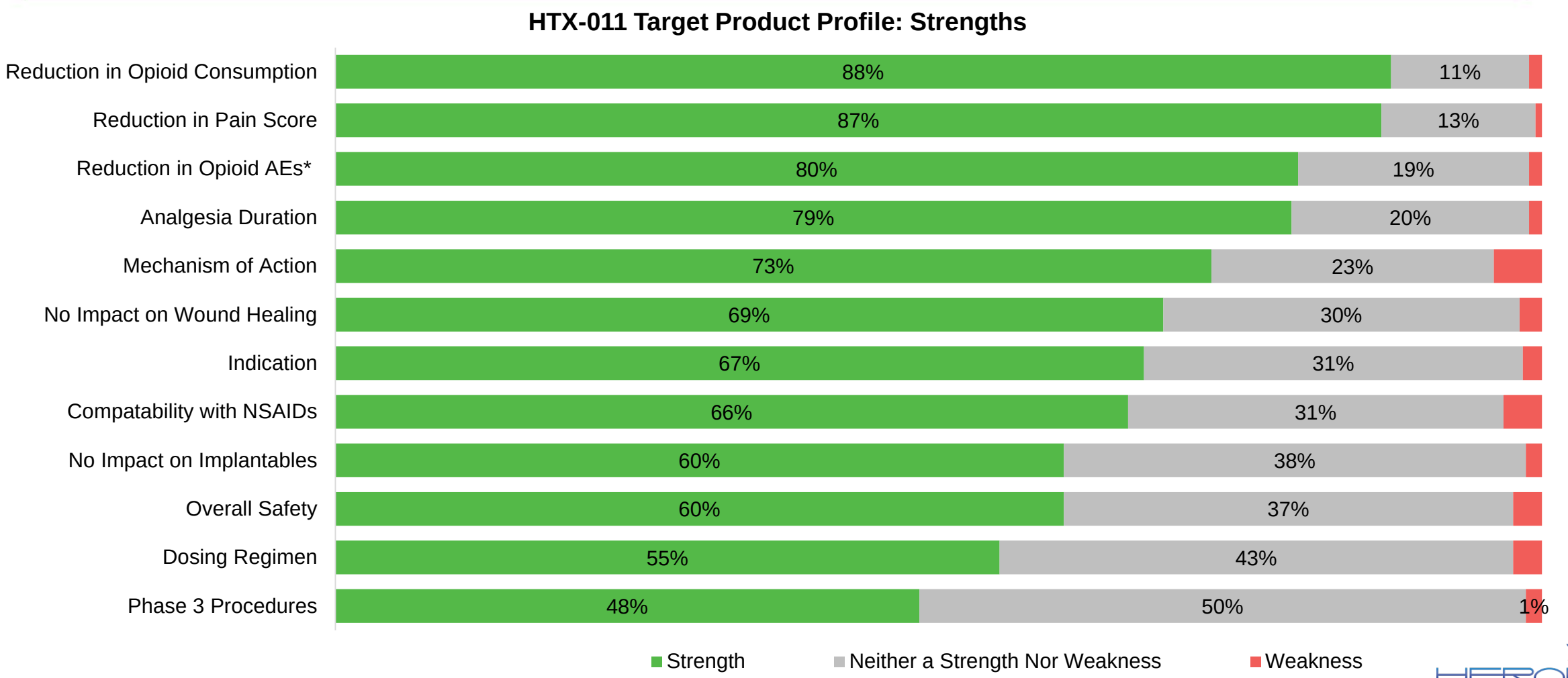
Overwhelmingly Positive Response by Physicians and Pharmacists to HTX-011's Target Product Profile



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

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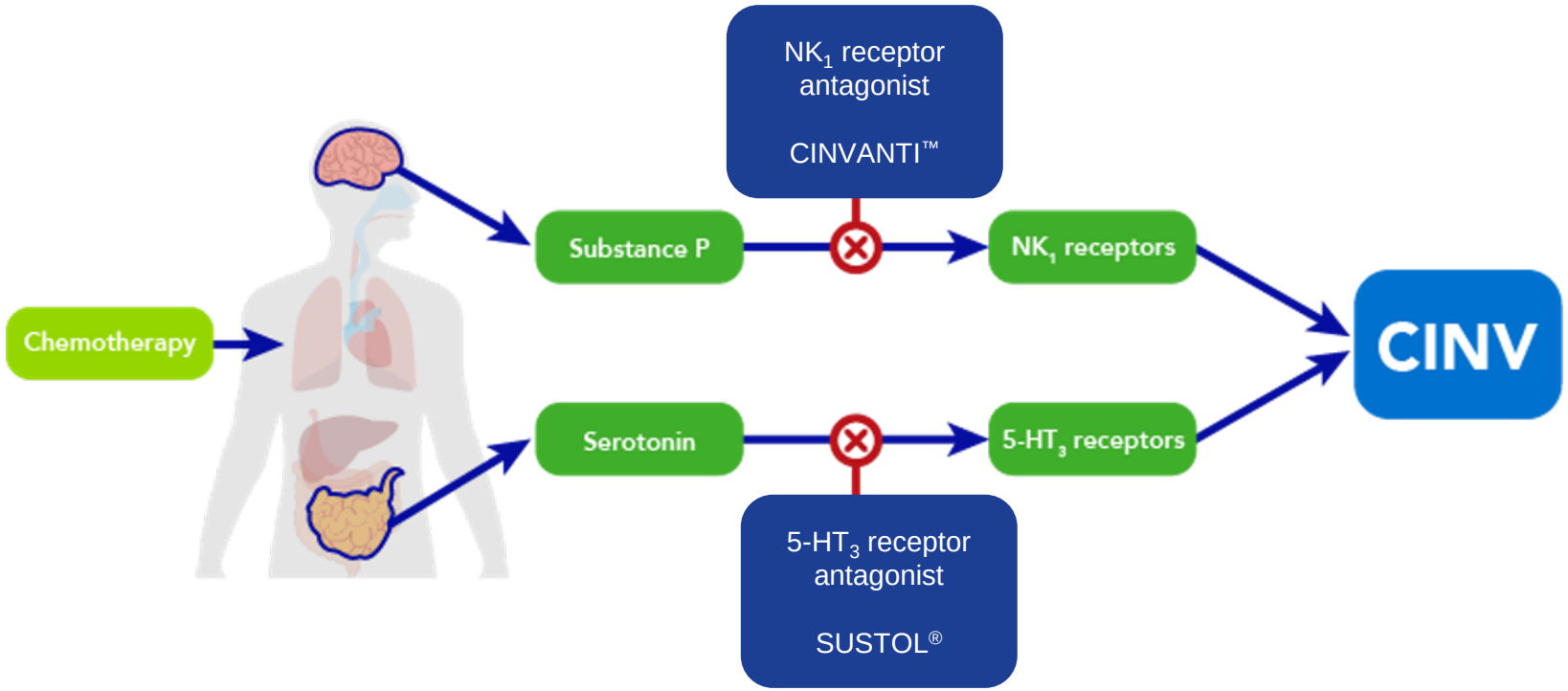
CINV Prophylaxis Typically Requires Two Complimentary Mechanisms of Action



NK_1 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 NK_1 market, contains the synthetic surfactant polysorbate 80 that has been associated with serious hypersensitivity and infusion site reactions

$5\text{-}HT_3$ 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

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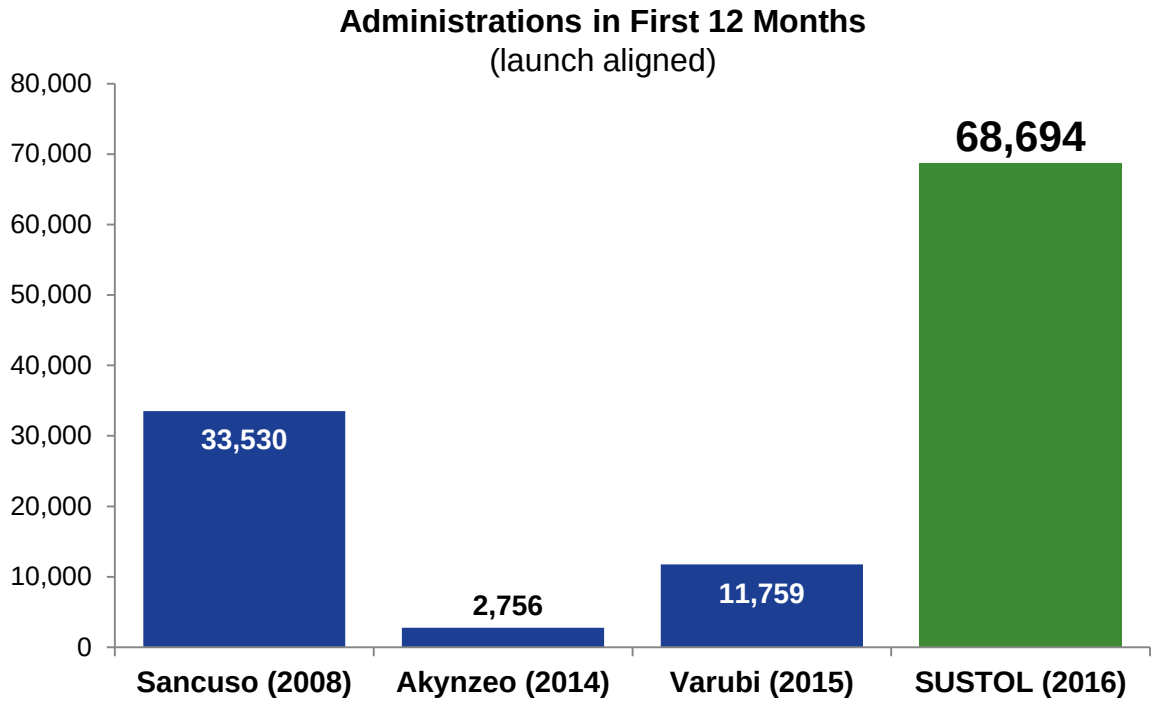
SUSTOL® Outperformed ALL Recent CINV New Brand Launches

CINV New Brand Launches Since 2008



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

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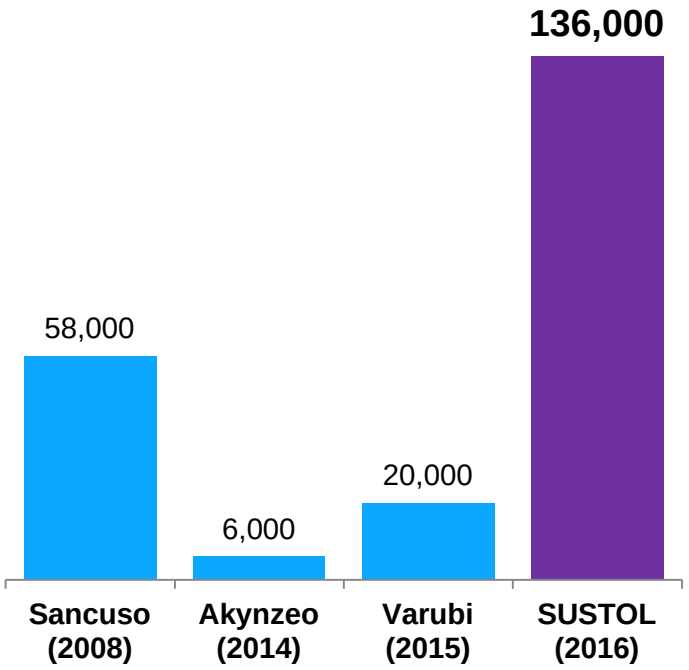
Heron's CINV Portfolio Continues to Outperform All Recent CINV Branded Launches

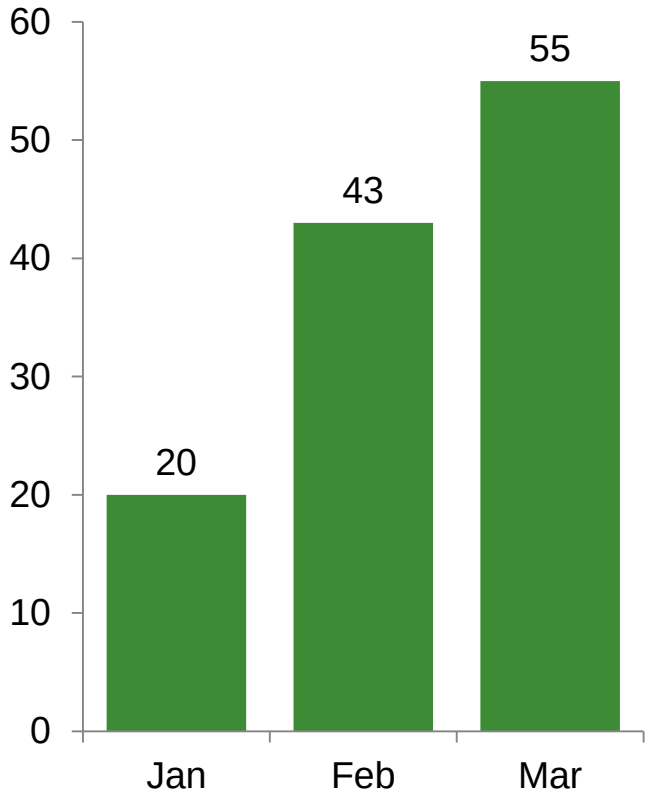
CINV Brand Launches Since 2008

Approximate administrations in <u>First 18 Months</u> (launch aligned)



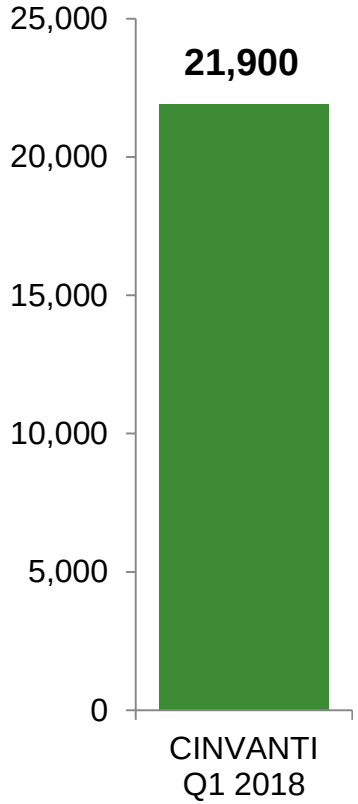
Sources: IMS DDD; Heron actuals (distributor 867 reports); due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2; Varubi includes actuals for launch months 1-15 and estimates for months 16-18

New CINVANTI Accounts By Month



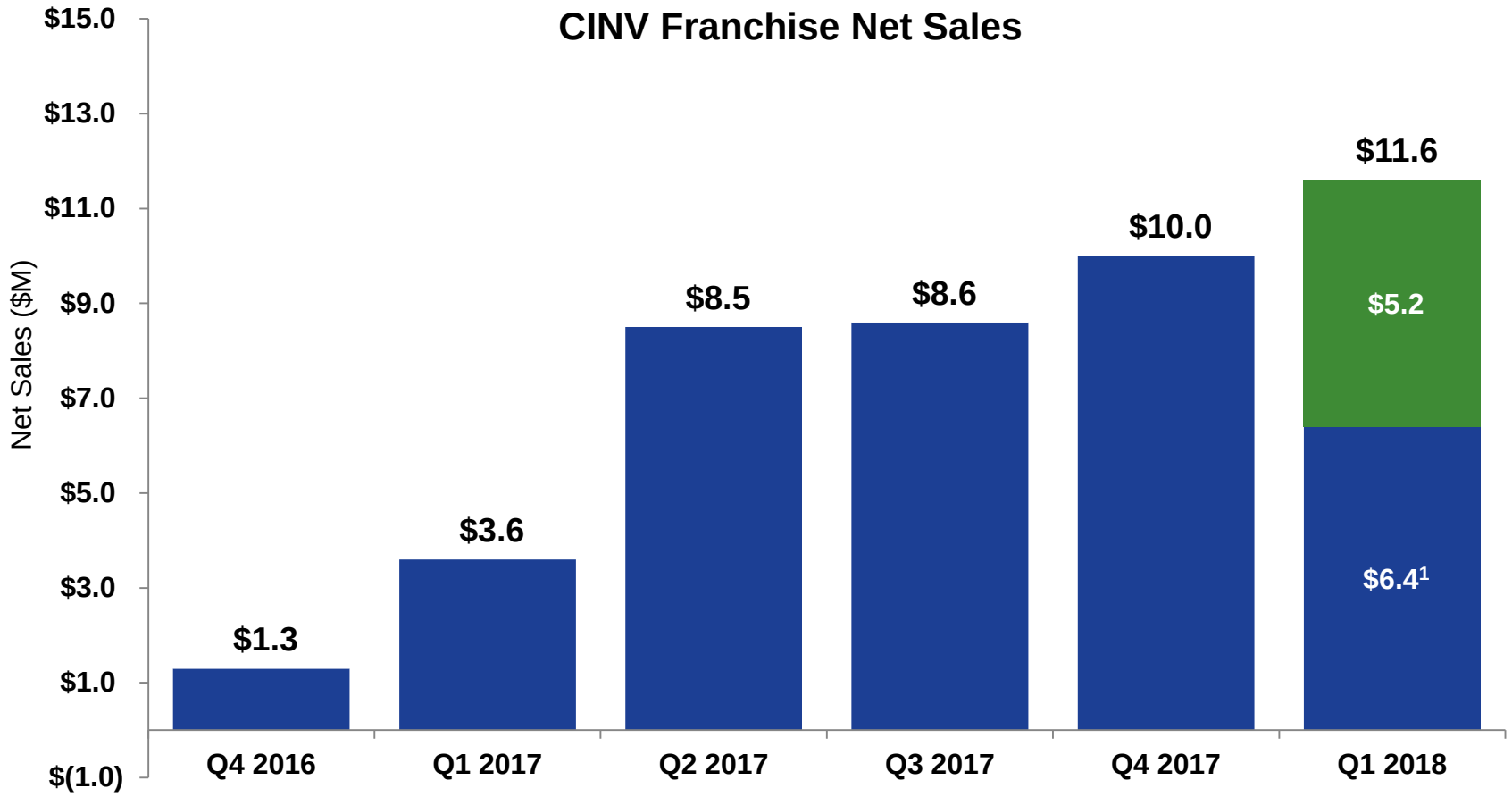
Source: Heron 867 data

Q1 CINVANTI Provider Demand Units



Source: Heron 867 data

Heron CINV Portfolio achieved $11.6M Q1 2018 Net Sales



[1]If it were not for the fact that the Company adopted the required revenue recognition rules (Topic 606) on January 1, net sales would have been $7.7M

Source: Heron 867 data

2018 CINV Franchise Outlook

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

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

CINVANTI®

- Commercially available in the US
- We believe it has the best overall profile compared to the other available NK_1 antagonists
- Offers strong strategic and operational fit with existing commercial organization to win in a branded CINV market with ~3.6M annual units

CINV Franchise

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

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Financial Summary

As of March 31, 2018, pro-forma cash, cash equivalents and short-term investments, adjusting for the April 2018 public offering, were $282.6 million.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share data)	Three Months Ended March 31, 2018
Net product sales	$ 11,567
Operating expenses[1]	63,557
Other expenses, net	(275)
Net loss[1]	$ (52,265)
Net loss per share[2]	$ (0.81)
Net cash used in operations	$(61,713)

Condensed Balance Sheet Data (In thousands)	March 31, 2018
Cash, cash equivalents and short-term investments	$ 113,938
Accounts receivable, net	$ 37,713
Total assets	$ 183,383
Promissory note payable	$ 25,000
Total stockholders' equity	$ 92,206

Common shares outstanding at March 31, 2018 totaled 65.0 million.

[1] Includes $7.7 million of non-cash, stock-based compensation expense for the three months ended March 31, 2018.
[2] Based on 64.7 million weighted-average common shares outstanding for the three months ended March 31, 2018.

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Key Catalysts in Pain Management & CINV Franchises

HTX-011 for Postoperative Pain	CINVANTI ® and SUSTOL® for CINV
✓ Fast Track designation granted	2018 net sales guidance for CINV franchise: $60M - $70M
✓ Completed enrollment in Phase 3 pivotal trials	
✓ Top-line Pivotal Phase 3 results 1H 2018	
✓ Topline results from breast augmentation and TKA studies late 1H 2018	
✓ Breakthrough Therapy designation received from FDA	
NDA filing 2H2018	