

HTX-011

Postoperative Pain Program

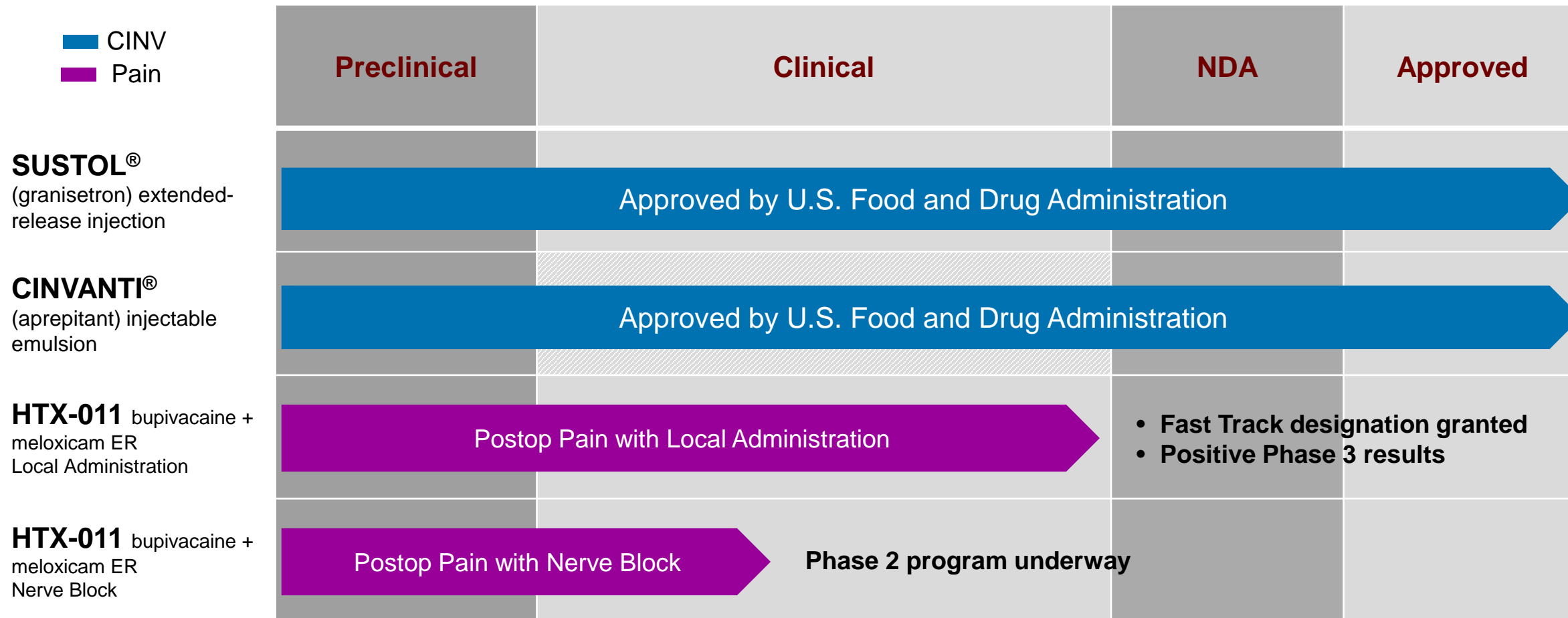
Topline Results From Phase 3

March 19, 2018

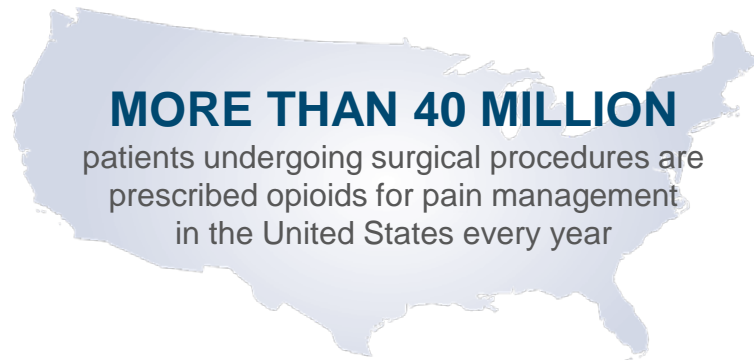
Forward-Looking Statements

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 trials for HTX-011; the 2018 net product sales guidance for the CINV franchise; the projected sufficiency of our capital position for future periods; 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



Postoperative Opioids: A Doorway to Addiction



As many as
2.6 MILLION PEOPLE
that take
opioids to manage pain
after surgery may become persistent opioid
users.



Up to 440,000/yr
will become addicted to opioids.



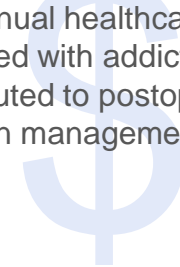
In addition
>BILLION OPIOID PILLS
are taken home from the hospital after surgery

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.



Large US Market Opportunity

Theoretical and Target Market







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



*Based on the current WAC of Exparel

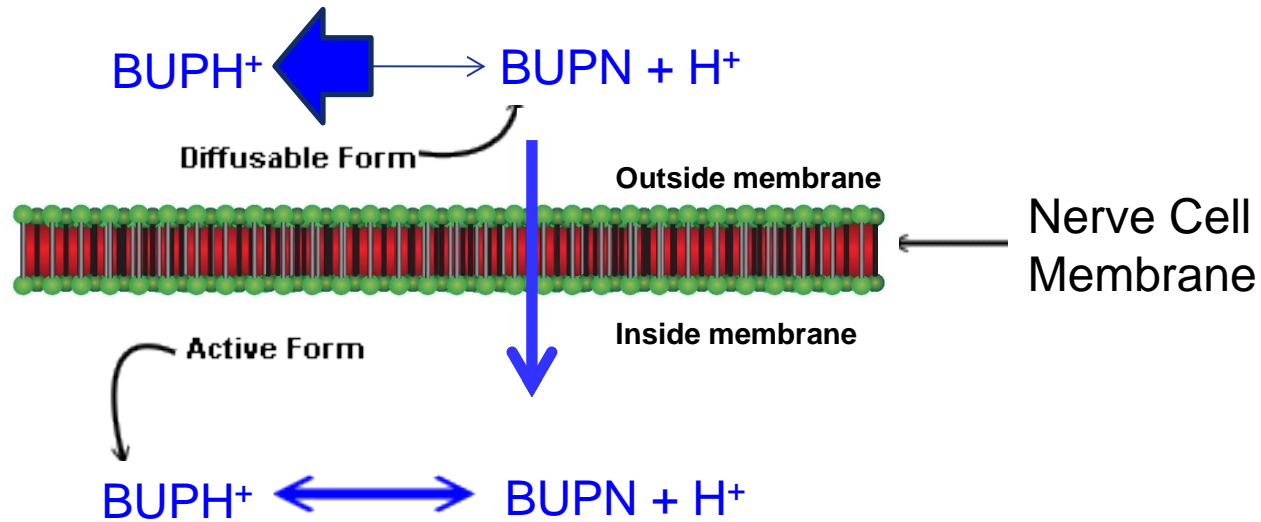
High Procedure Volume in Target Markets Provides a Robust RoW Market Opportunity



Country		Total Surgical Procedures	Total Procedures Requiring Postop Pain Management	Initial Target Procedures	Remaining Secondary, Lower Volume & Procedures Currently Not Using Local Anesthetics
	Germany	22,545,000	6,838,000	3,649,000	3,189,000
	France	14,545,000	4,357,000	2,292,000	2,065,000
	UK	13,882,000	3,835,000	1,790,000	2,045,000
	Italy	5,637,000	2,530,000	1,919,000	611,000
	Canada	3,416,000	1,638,000	1,282,000	356,000
	Japan	25,959,000	6,600,000	2,668,000	3,932,000
Total		85,984,000	25,798,000	13,600,000	12,198,000

Inflammation Can Reduce the Activity of Local Anesthetics

HTX-011 is Different Because It Blocks Both Pain and Local Inflammation



- 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

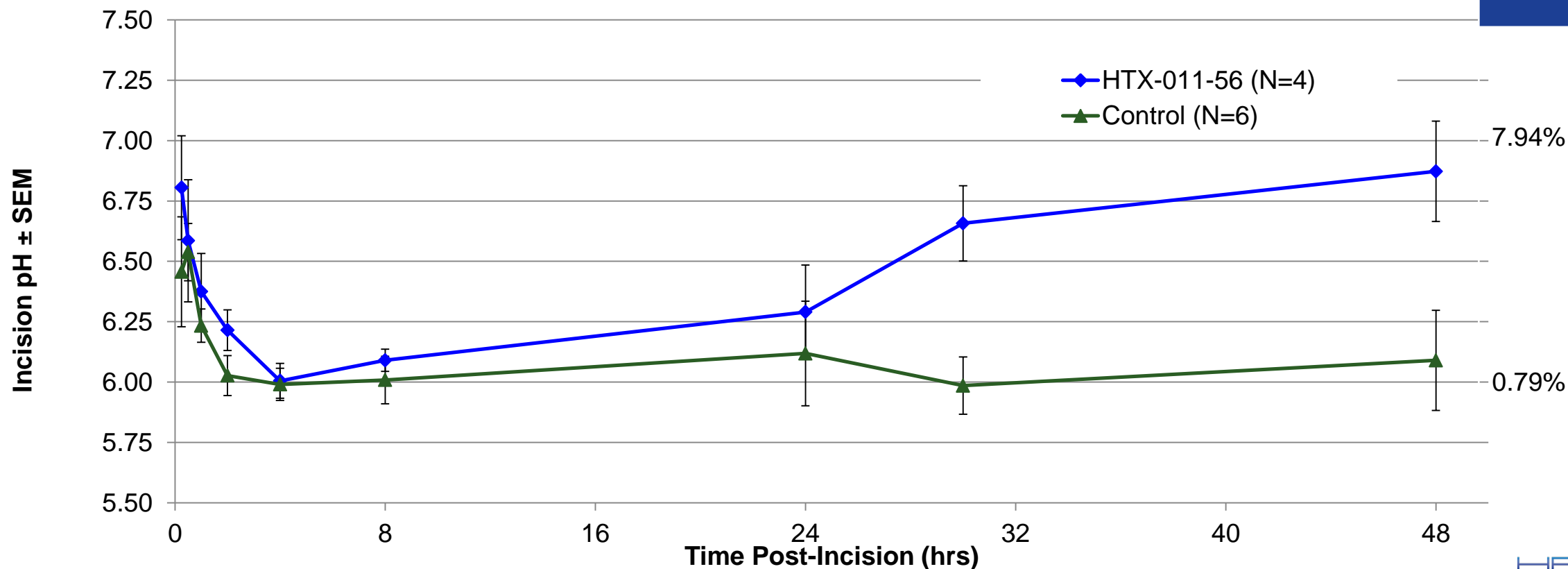
1. Ueno, et al. J of Inflammation Research 1:41-48 2008.

2. Local anesthetic nerve penetration model adapted from Becker and Reed, Anesth Prog 53:98–109 2006

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

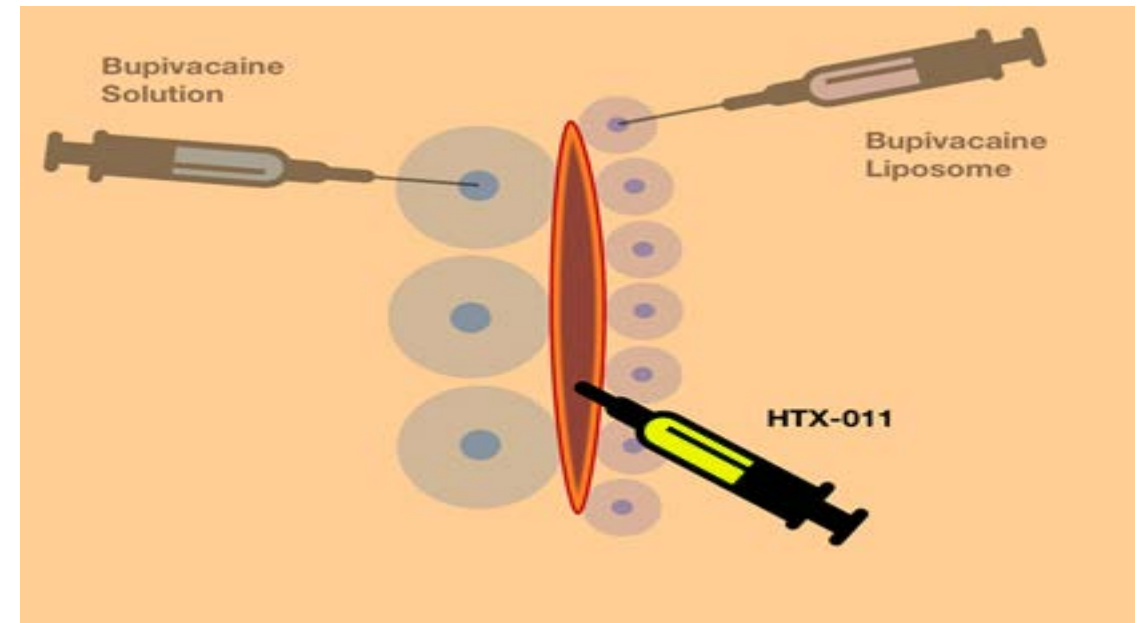
The normalization of pH starting at 8 hours with HTX-011 allows almost 10x more bupivacaine (BPV) to enter the nerve to block the pain signal


% of un-ionized BPV available to enter nerve



The Properties of HTX-011 Are Ideally Suited for Needle-Free Administration to Coat the Affected Tissue

- HTX-011 is a single dose application of a viscous solution administered directly via needle free syringe to coat the affected tissue within the surgical site prior to suturing
- HTX-011 releases its active ingredients simultaneously over 72 hours
- Release of bupivacaine/meloxicam from polymer is not modulated by where it is administered
- Compared to injection, simply coating the affected tissue is:
 - Easier to administer and less invasive
 - Avoids up to 120 injections
 - Potentially safer, eliminating the risk of venous puncture and accidental needle sticks
 - Since HTX-011 cannot be admixed with bupivacaine solution, there is a low risk of overdose

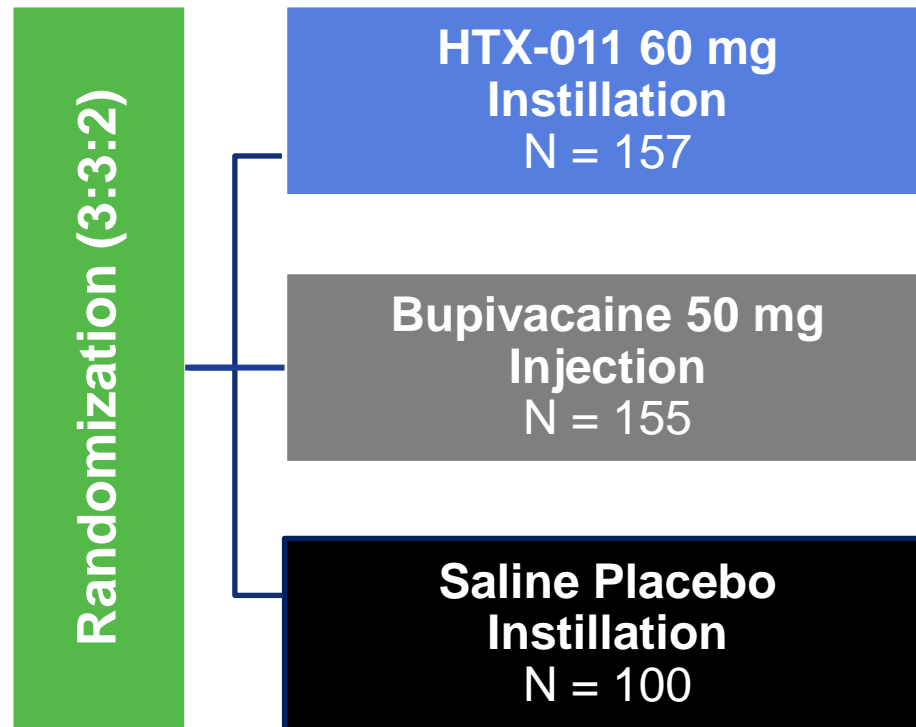




HTX-011 ACHIEVED ALL PRIMARY AND KEY SECONDARY ENDPOINTS IN BOTH PHASE 3 TRIALS

Study 301/EPOCH1: Phase 3 Bunionectomy

Study Design



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

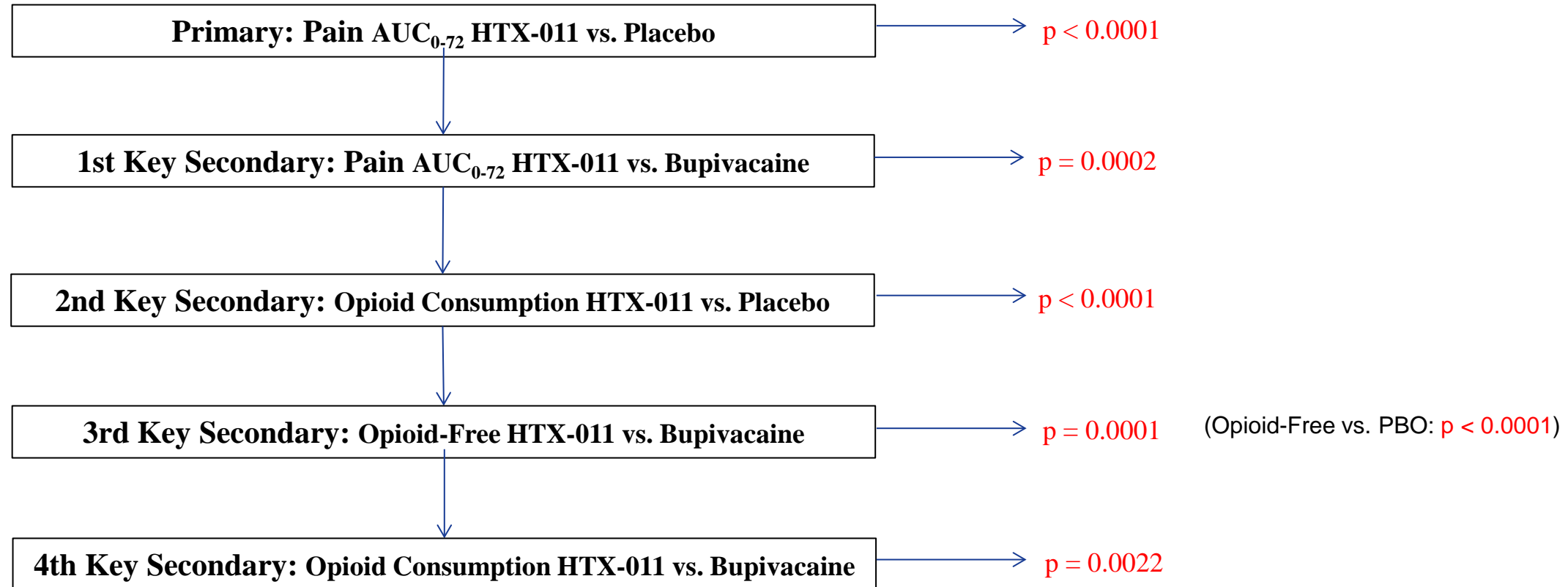
Study 301: Subject Demographics

	HTX-011 60 mg (N=157)	Saline Placebo (N=100)	Bupivacaine HCl 50 mg (N=155)	Total (N=412)
Age (years) – mean (SD)	48.0 (14.47)	47.3 (12.83)	45.5 (14.79)	46.9 (14.22)
Sex – %				
Female	87.9%	86.0%	85.2%	86.4%
Male	12.1%	14.0%	14.8%	13.6%
Race – %				
American Indian or Alaskan Native	0.6%	0%	1.3%	0.7%
Asian	5.1%	2.0%	0.6%	2.7%
Black or African Descent	15.3%	12.0%	14.2%	14.1%
Native Hawaiian or Other Pacific Islander	0%	0%	0.6%	0.2%
White	78.3%	86.0%	82.6%	81.8%
Other	0.6%	0%	0.6%	0.5%
Ethnicity – %				
Hispanic or Latino	29.9%	32.0%	31.6%	31.1%
Not Hispanic or Latino	70.1%	68.0%	68.4%	68.9%

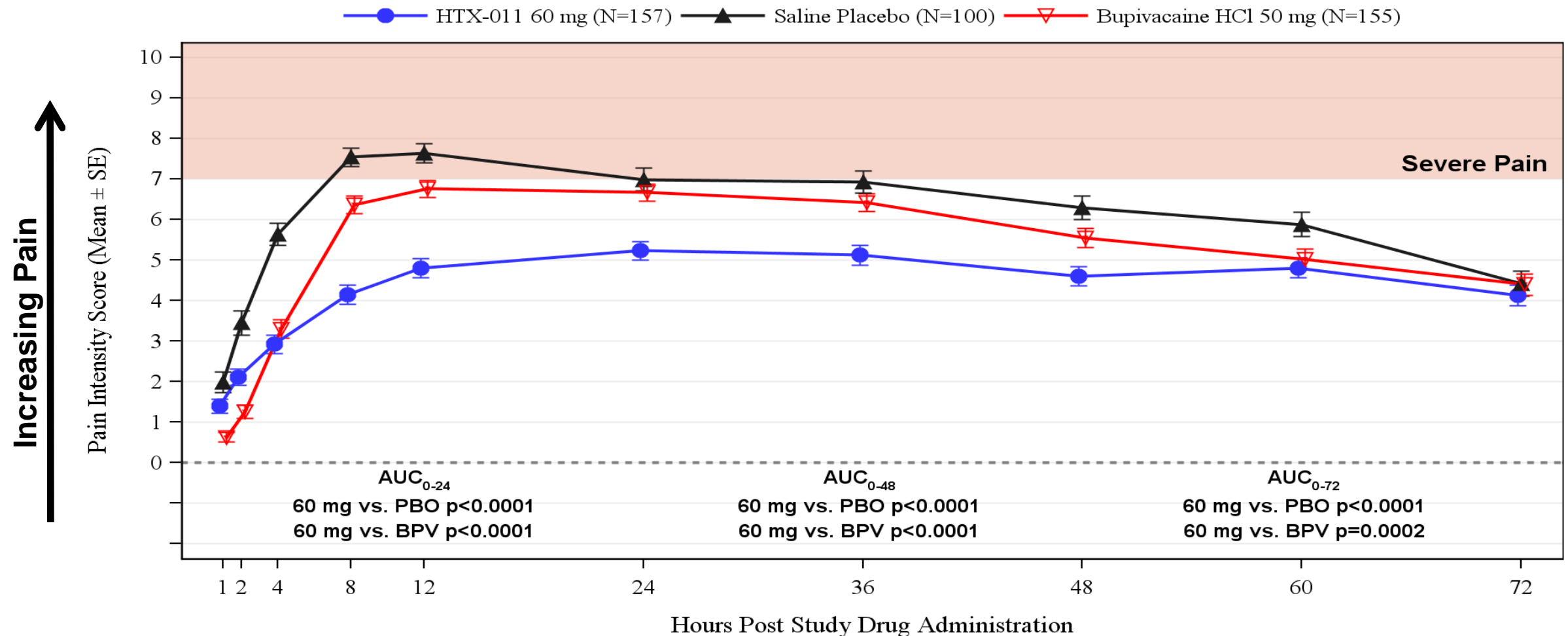


Study 301: Results Hierarchy

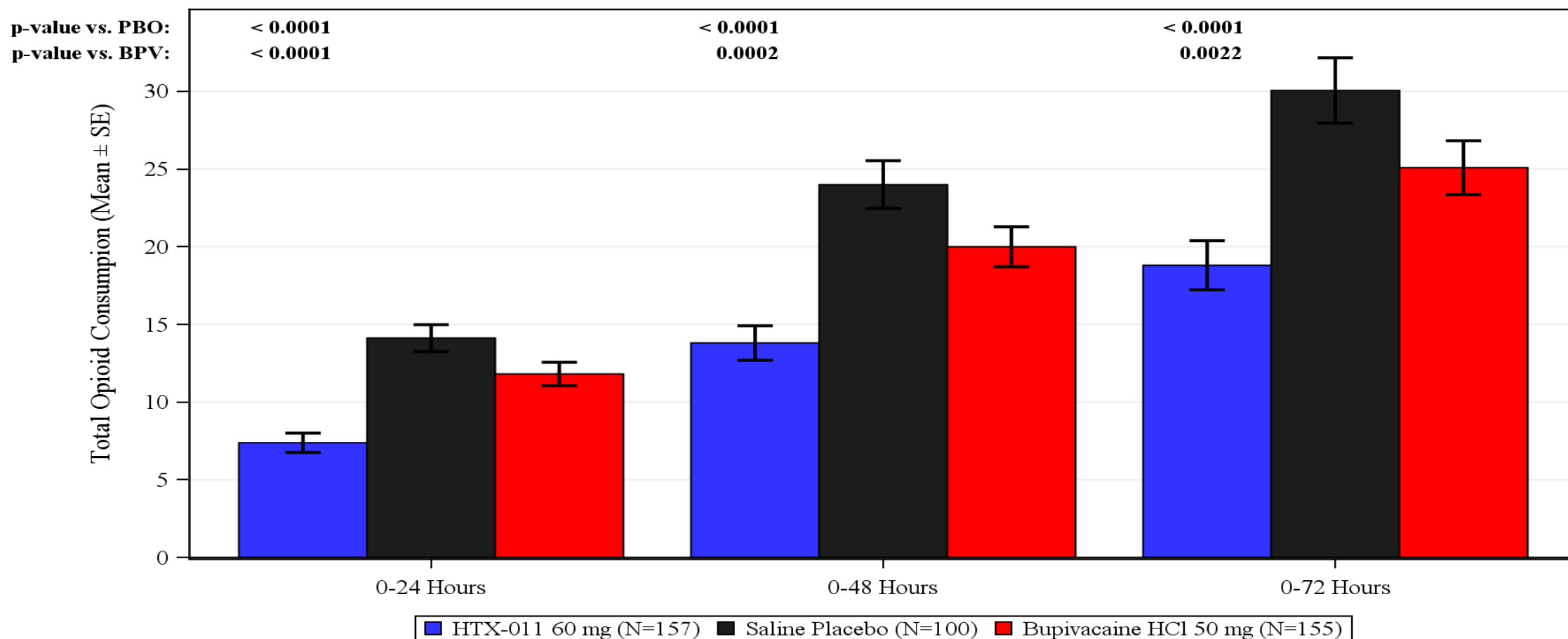
Primary and ALL Key Secondary Endpoints Significant



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



Study 301: HTX-011 Significantly Reduces Total Opioid Use vs Bupivacaine and Placebo

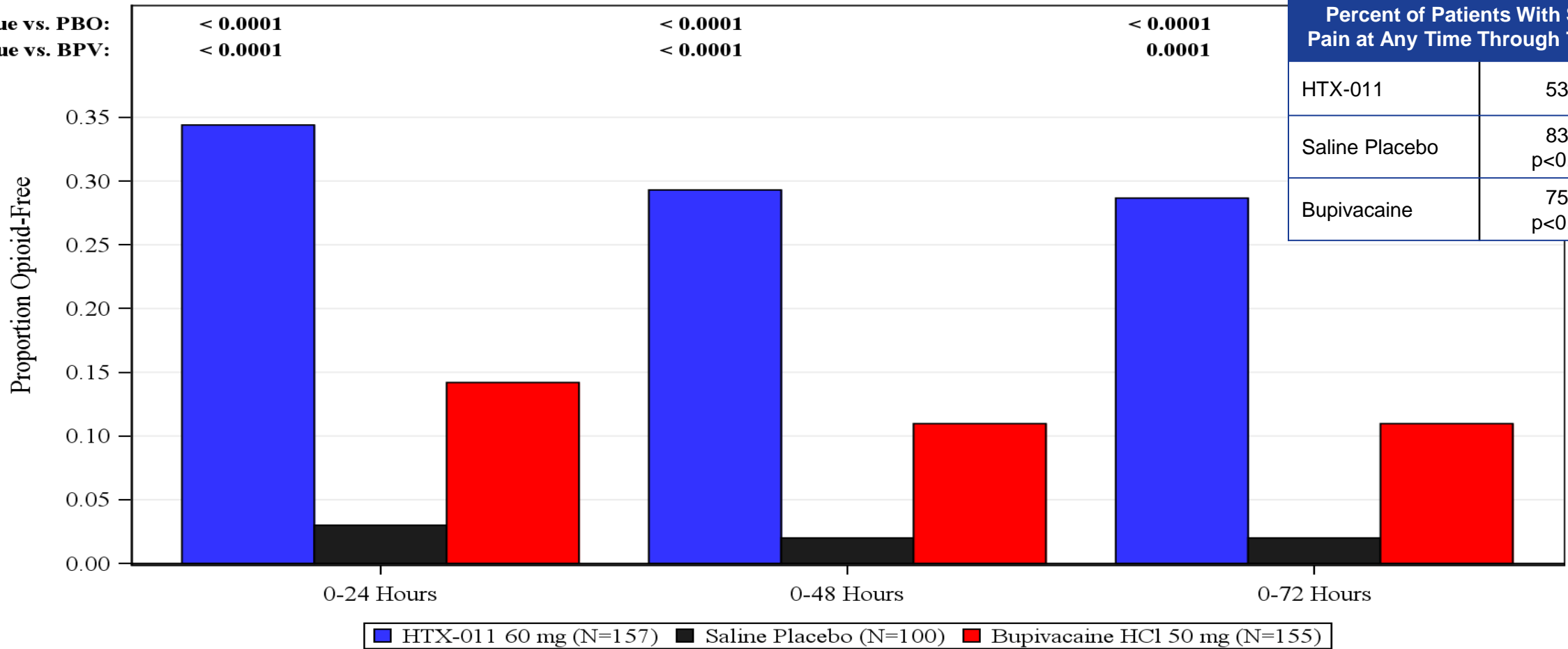


Opioid consumption is presented in mean milligrams of morphine equivalents

Source: Figure 14.2.2

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

p-value vs. PBO:
p-value vs. BPV:



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 SAFETY

Study 301: Incidence of Treatment Emergent Adverse Events Occurring in $\geq 5\%$ 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%

Study 301: HTX-011 Lowers the Incidence of Opioid-Related Adverse Events

Preferred Term	HTX-011 60 mg (N=157)	Saline Placebo (N=101)	Bupivacaine HCl 50 mg (N=154)
Any ORAE	43.9%	53.5%	50.6%
Nausea	37.6%	43.6%	45.5%
Vomiting	14.6%	18.8%	21.4%
Pruritus	7.6%	9.9%	5.8%
Constipation	5.7%	6.9%	11.7%
Somnolence	0.6%	0%	0.6%

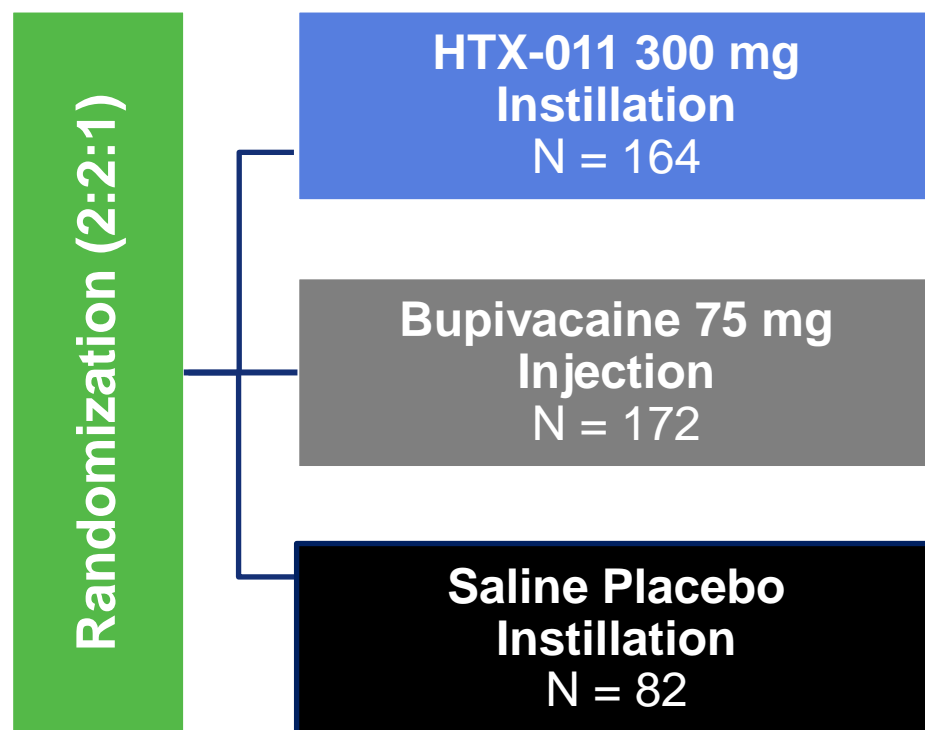
HTX-011 Safety in Bunionectomy

HTX-011 was generally well tolerated with:

- No drug-related serious adverse events
- No premature discontinuations due to drug-related adverse events
- No deaths (one death on BPV)
- Fewer opioid-related adverse events
- No evidence of drug-related LAST

Study 302/EPOCH2: Phase 3 Herniorrhaphy

Study Design



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

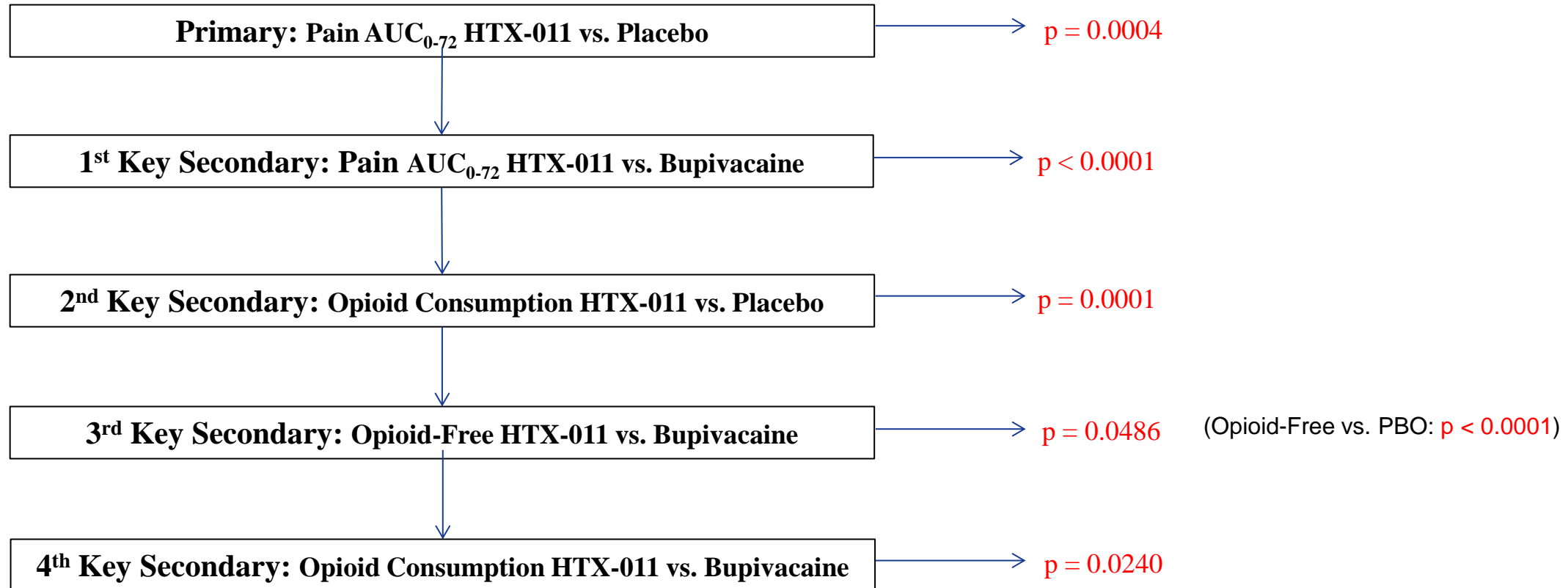
Study 302: Subject Demographics

Number of subjects:	HTX-011 300 mg (N=164)	Saline Placebo (N=82)	Bupivacaine HCl 75 mg (N=172)	Total (N=418)
Age (years) – mean (SD)	48.9 (13.29)	48.0 (14.59)	49.4 (11.26)	48.9 (12.75)
Sex – %				
Female	7.3%	3.7%	4.7%	5.5%
Male	92.7%	96.3%	95.3%	94.5%
Race – %				
American Indian or Alaskan Native	1.2%	0%	0%	0.5%
Asian	1.2%	1.2%	1.2%	1.2%
Black or African Descent	10.4%	3.7%	9.3%	8.6%
Native Hawaiian or Other Pacific Islander	2.4%	0%	0.6%	1.2%
White	84.8%	95.1%	89.0%	88.5%
Ethnicity – %				
Hispanic or Latino	26.2%	36.6%	29.7%	29.7%
Not Hispanic or Latino	73.8%	63.4%	70.3%	70.3%

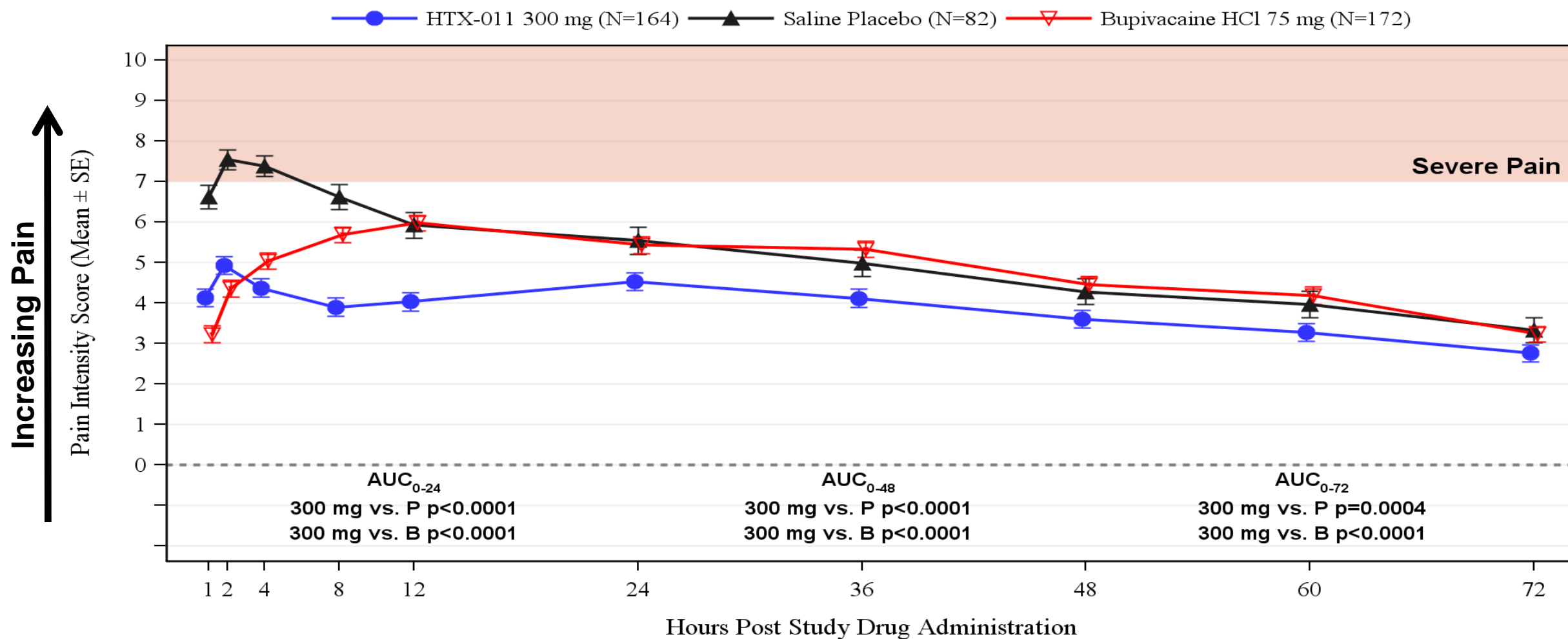
Source: Table 14.1.5.1

Study 302: Results Hierarchy

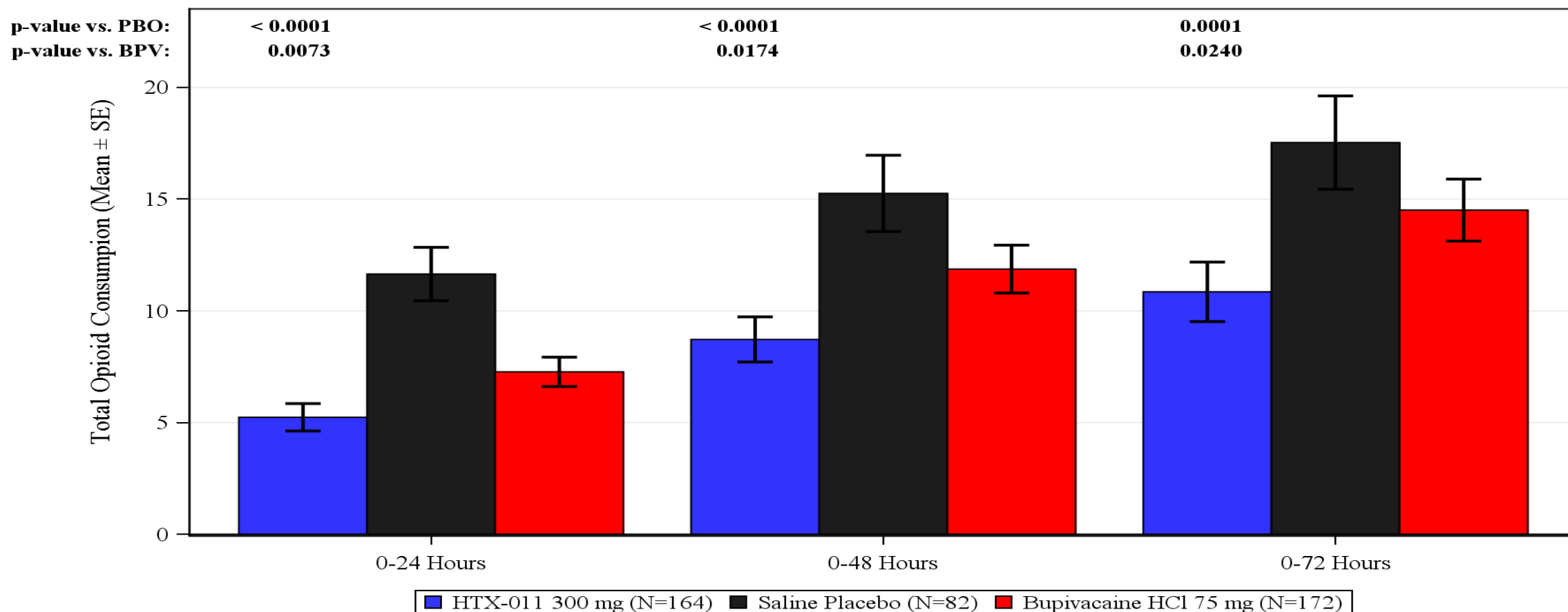
Primary and ALL Key Secondary Endpoints Significant



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



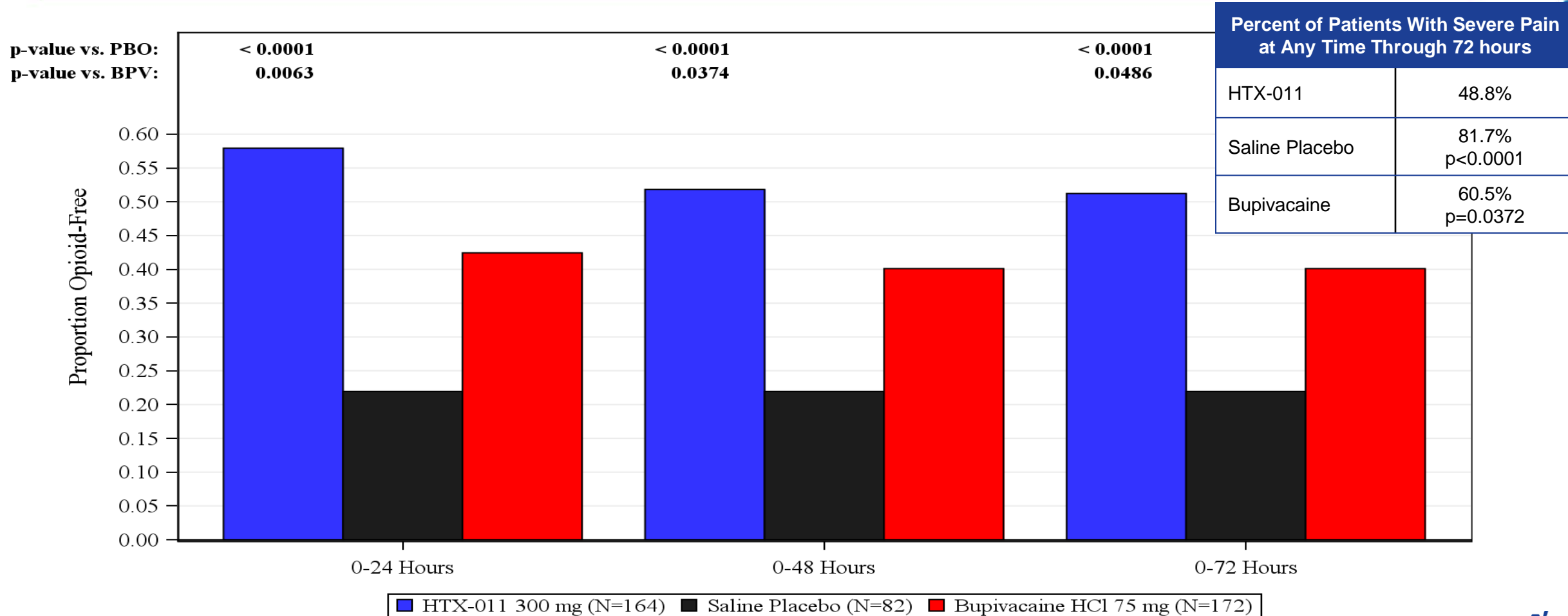
Study 302: HTX-011 Significantly Reduces Total Opioid Use vs Bupivacaine and Placebo



Opioid consumption is presented in mean milligrams of morphine equivalents

Source: Figure 14.2.2

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



Source: Figure 14.2.3

STUDY 302 SAFETY

Study 302: Incidence of Treatment Emergent Adverse Events Occurring in $\geq 5\%$ 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 odour abnormal	8.0%	1.2%	0.6%

Study 302: HTX-011 Lowers the Incidence of Opioid-Related Adverse Events

Preferred Term	HTX-011 300 mg (N=163)	Saline Placebo (N=82)	Bupivacaine HCl 75 mg (N=173)
Any ORAE	32.5%	43.9%	42.2%
Nausea	18.4%	34.1%	21.4%
Constipation	17.2%	18.3%	23.7%
Vomiting	4.3%	4.9%	6.9%
Pruritus	1.2%	1.2%	2.3%
Urinary retention	0.6%	1.2%	1.7%

HTX-011 Safety in Herniorrhaphy

HTX-011 was generally well tolerated with:

- No drug-related serious adverse events
- No premature discontinuations due to adverse events
- No deaths
- Fewer opioid-related adverse events
- No evidence of drug-related LAST

CONCLUSIONS

Overall Conclusions From Phase 3

- Phase 3 results show conclusively that HTX-011 is the first and only long-acting local anesthetic to demonstrate superior pain reduction and significantly reduce the need for opioids compared to the current standard of care, bupivacaine solution for the full 72 hours after surgery
- HTX-011 is the first and only long-acting local anesthetic designed to address both postoperative pain and inflammation in a single administration at the surgical site.
- The unique synergy of bupivacaine and meloxicam in HTX-011 has consistently demonstrated superiority in all 5 completed Phase 2 and Phase 3 studies that included a bupivacaine control group
- The significantly lower number of HTX-011 patients who experienced severe pain in both studies compared to placebo and bupivacaine patients corresponds directly to the significantly lower need for opioid rescue medication and the increase in opioid free patients who received HTX-011.
- This demonstrates the dramatic benefit of blocking pain signals at the source compared to using opioids to tell the brain the pain signal does not hurt
- HTX-011 has the profile to be the cornerstone of opioid-free postoperative pain management

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 a full 72 hours after surgery
- NDA will contain data from 5 surgical models to support a broad label:
 - Bunionectomy
 - Herniorrhaphy
 - TKA
 - Abdominoplasty
 - Breast augmentation

Financial Summary

Cash, cash equivalents, short-term investments, accounts receivable plus cash from projected net sales of SUSTOL and CINVANTI are expected to be sufficient to fund operations for at least one year.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share data)	Three Months Ended December 31, 2017	Twelve Months Ended December 31, 2017
Net product sales	\$ 10,053	\$ 30,767
Operating expenses ¹	71,943	225,325
Other expenses, net	(600)	(2,926)
Net loss ¹	\$ (62,490)	\$ (197,484)
Net loss per share ²	\$ (1.09)	\$ (3.65)
Net cash used in operations	\$ (47,149)	\$(170,300)

Condensed Balance Sheet Data (In thousands)	December 31, 2017
Cash, cash equivalents and short-term investments	\$ 172,379
Accounts receivable, net	\$ 41,874
Total assets	\$ 234,307
Promissory note payable	\$ 25,000
Total stockholders' equity	\$ 131,136

Common shares outstanding at December 31, 2017 totaled 64.6 million.

¹ Includes \$6.9 million and \$30.5 million of non-cash, stock-based compensation expense for the three and twelve months ended December 31, 2017, respectively.

² Based on 57.6 million and 54.0 million weighted-average common shares outstanding for the three and twelve months ended December 31, 2017, respectively.

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	
NDA filing 2H 2018	