Corporate Update

November 7, 2018

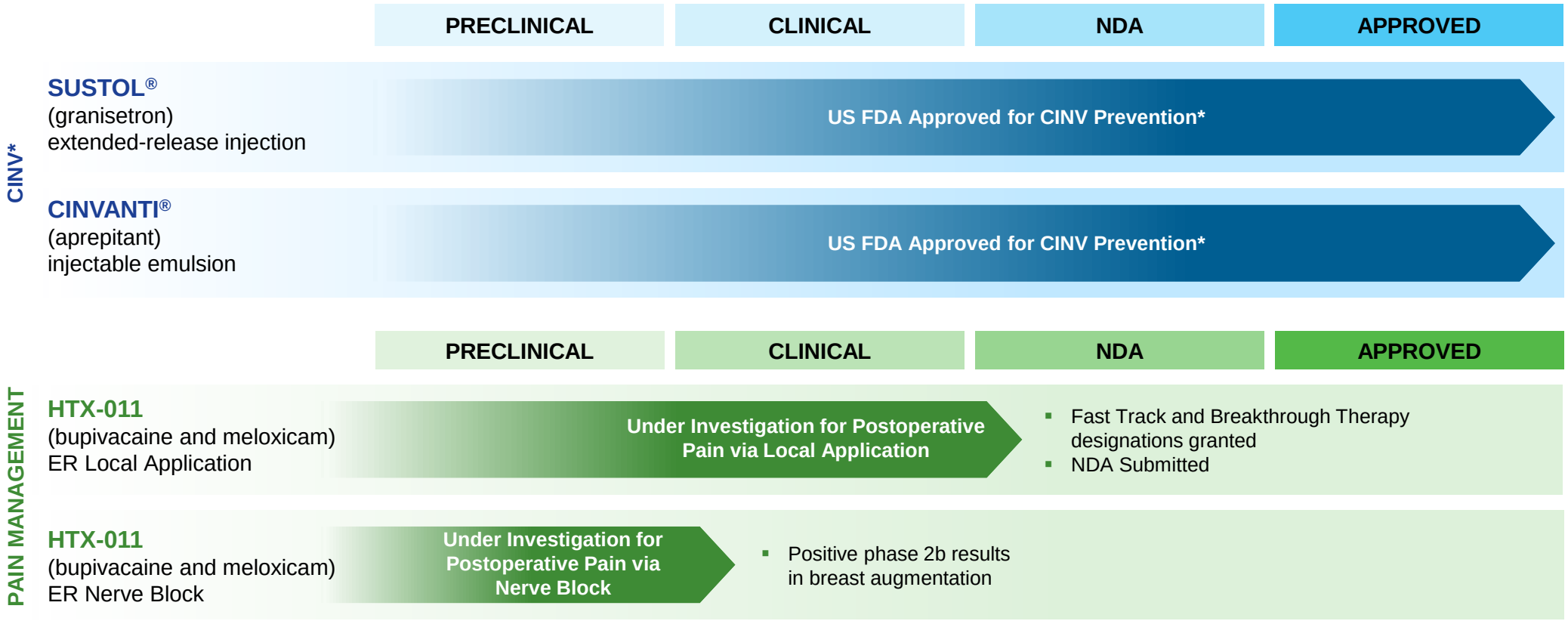
HERON THERAPEUTICS

Forward-Looking Statements

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: the full-year 2018 net product sales guidance for the CINV franchise; acceptance of the HTX-011 NDA as submitted; whether the FDA approves the HTX-011 NDA as submitted; the anticipated commercial launch of HTX-011; the potential market opportunity 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.

Heron Pipeline

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



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

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

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

- Breakthrough Therapy designation (BTD) 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 completed Phase 2 studies and Phase 3 studies
  - HTX-011 produced significant reductions in both pain intensity through 72 hours and need for opioids post-surgery compared to placebo and bupivacaine solution, the standard of care
- Based on BTD, FDA also granted a Rolling Review of HTX-011 new drug application (NDA) to facilitate their timely review
  - NDA submitted in October

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Postoperative Pain and its Impact on the Opioid Crisis

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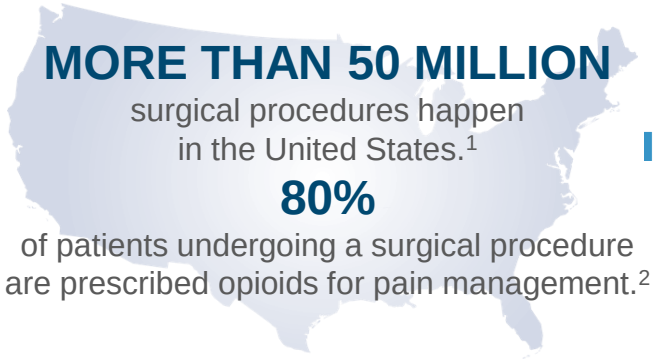
The Cost of Opioids
How Postoperative Opioids Can Be a Doorway to Addiction



MORE THAN 50 MILLION
surgical procedures happen in the United States.[1]

80%
of patients undergoing a surgical procedure are prescribed opioids for pain management.[2]

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

That equals about
2.6 MILLION PEOPLE.[1]

Of these 2.6 million persistent opioid users, approximately
440,000
will become addicted to opioids.[3]

In addition, opioid discharge prescriptions filled by recovering surgical patients result in more than
1 billion unused pills.[4,5]

70% of all these opioid tablets go unused.[2]

90% of these pills remain inside the home in unsecured locations.[6]

32% of all opioid addicts report first opioid exposure through leftover pills.[7]

More than
$13 billion
of the annual healthcare costs associated with addiction can be attributed to postoperative pain management.[1,3,8]

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

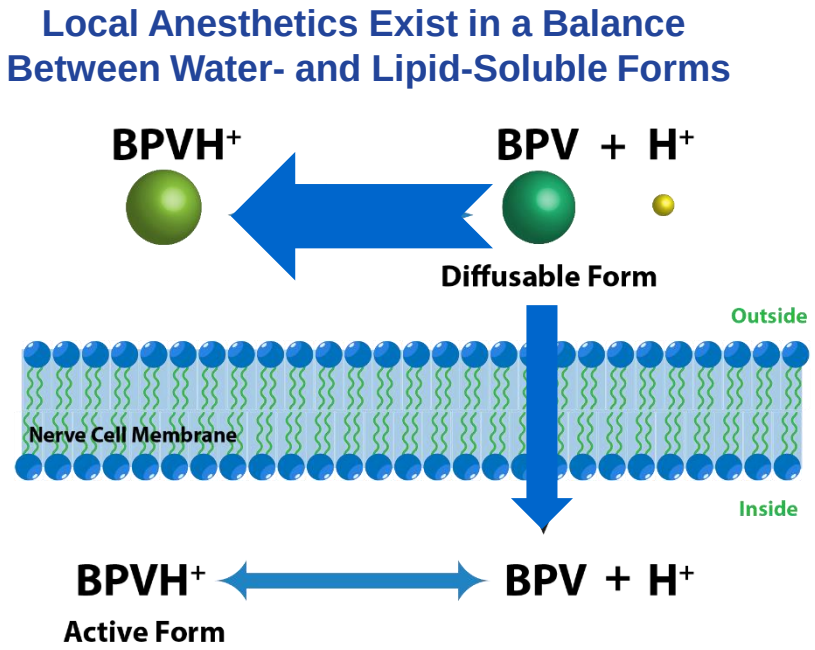
HERON THERAPEUTICS

Heron's Goals For Postoperative Pain Program

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

HTX-011 Mechanism of Action

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



Inflammation produces an acidic environment

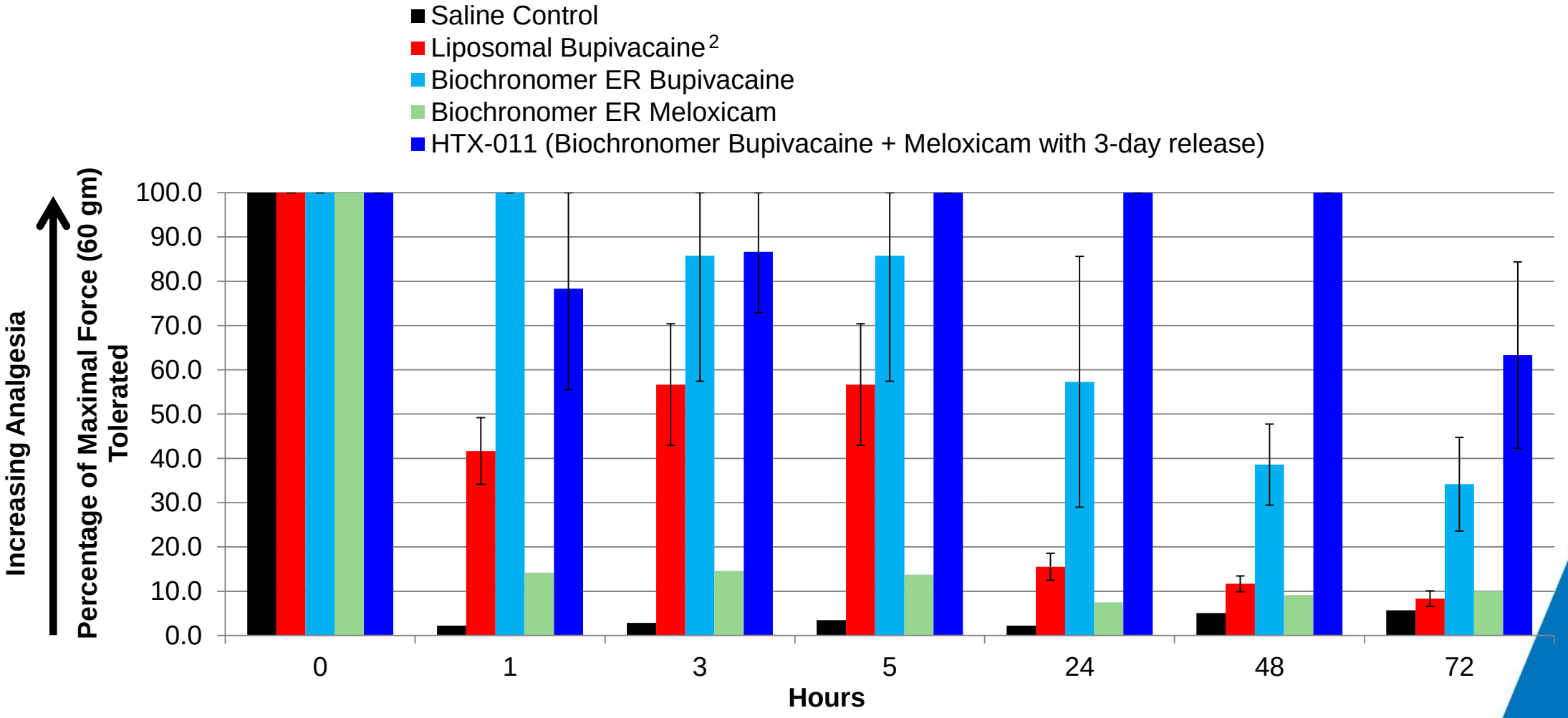
With a one pH unit drop, 10-fold less bupivacaine is able to penetrate the nerve cell membrane

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

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

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

HTX-011 is Designed to Produce Marked Analgesia Through the First 72 Hours After Surgery as Demonstrated in this Preclinical Model[1]



[1] Postoperative pain model in pigs from Castle et al, 2013 EPJ
[2] Human dose of liposomal bupivacaine with 40% smaller incision

(n=4 pigs in each arm)

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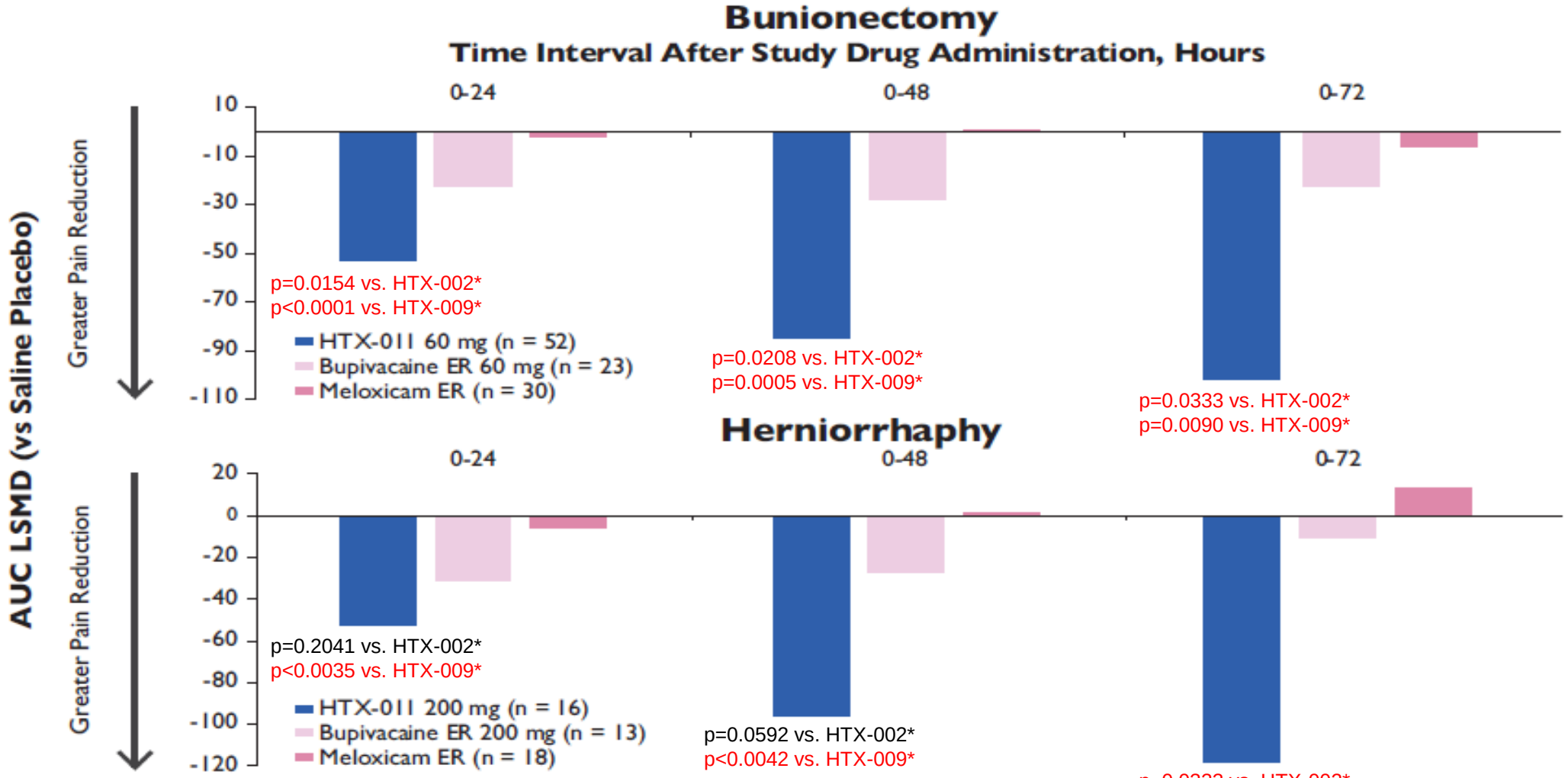
HTX-011 Reduces Pain Better Than the Individual Components in Both Bunionectomy and Herniorhaphy Phase 2 Studies

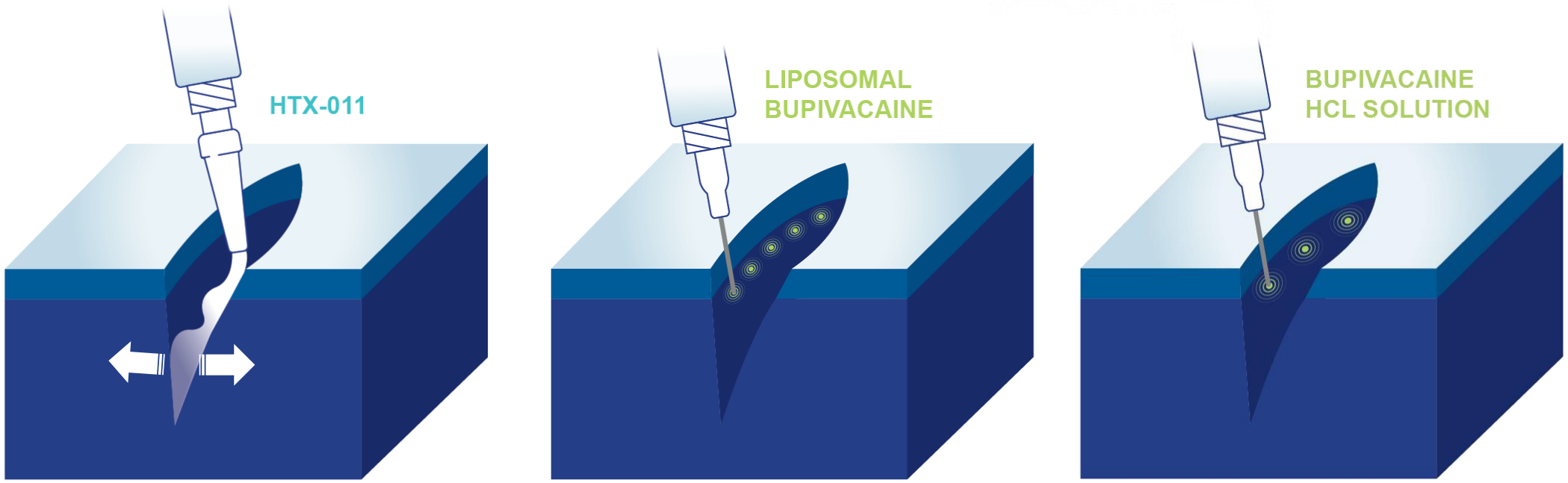


*p-value from ANOVA, LSMD of area under the curve for HTX-011 vs. HTX-002 or HTX-009

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

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

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



Reference: Data on file.

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

Study	Phase	Surgical Model	Tissue Type	Significant for Pain Reduction vs. PBO	Significant for Pain Reduction vs. BPV	Significant Reduction in Opioid Use
202	2	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; TKA = total knee arthroplasty

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HTX-011 Clinical Development

EPOCH 1: Bunionectomy Results

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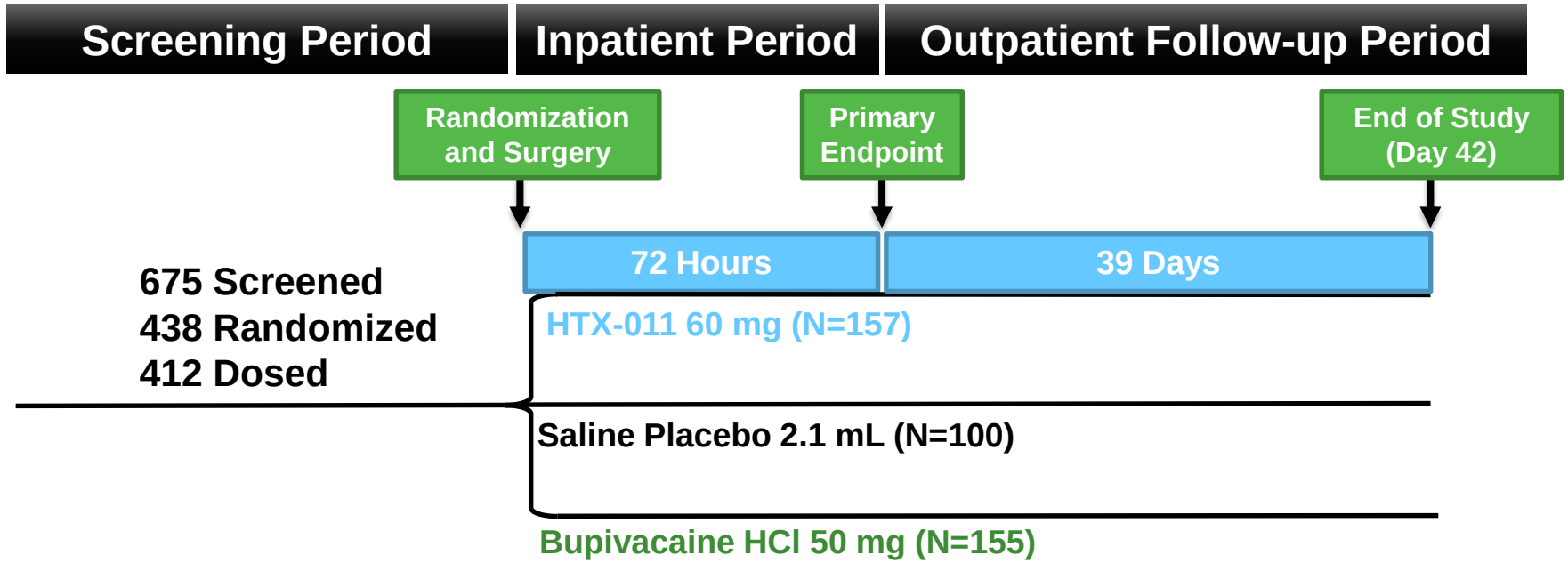
EPOCH 1 Bunionectomy: Study Design

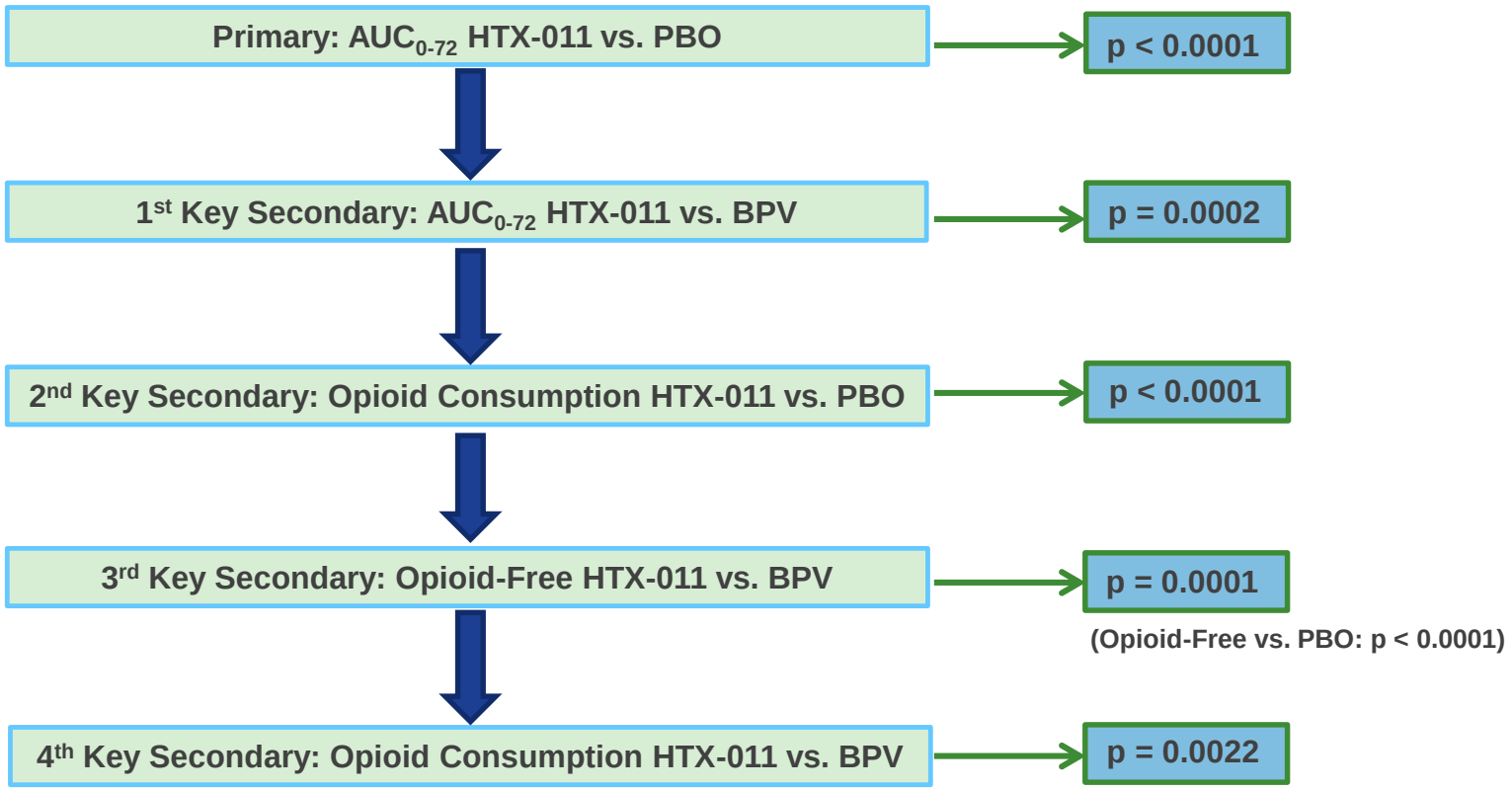
- N = 412 (3:2:3 to HTX-011 60 mg, saline placebo, or bupivacaine HCl 50 mg)
- 438 subjects were randomized and 412 were dosed (ITT Population)
- 13 sites in the United States



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

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

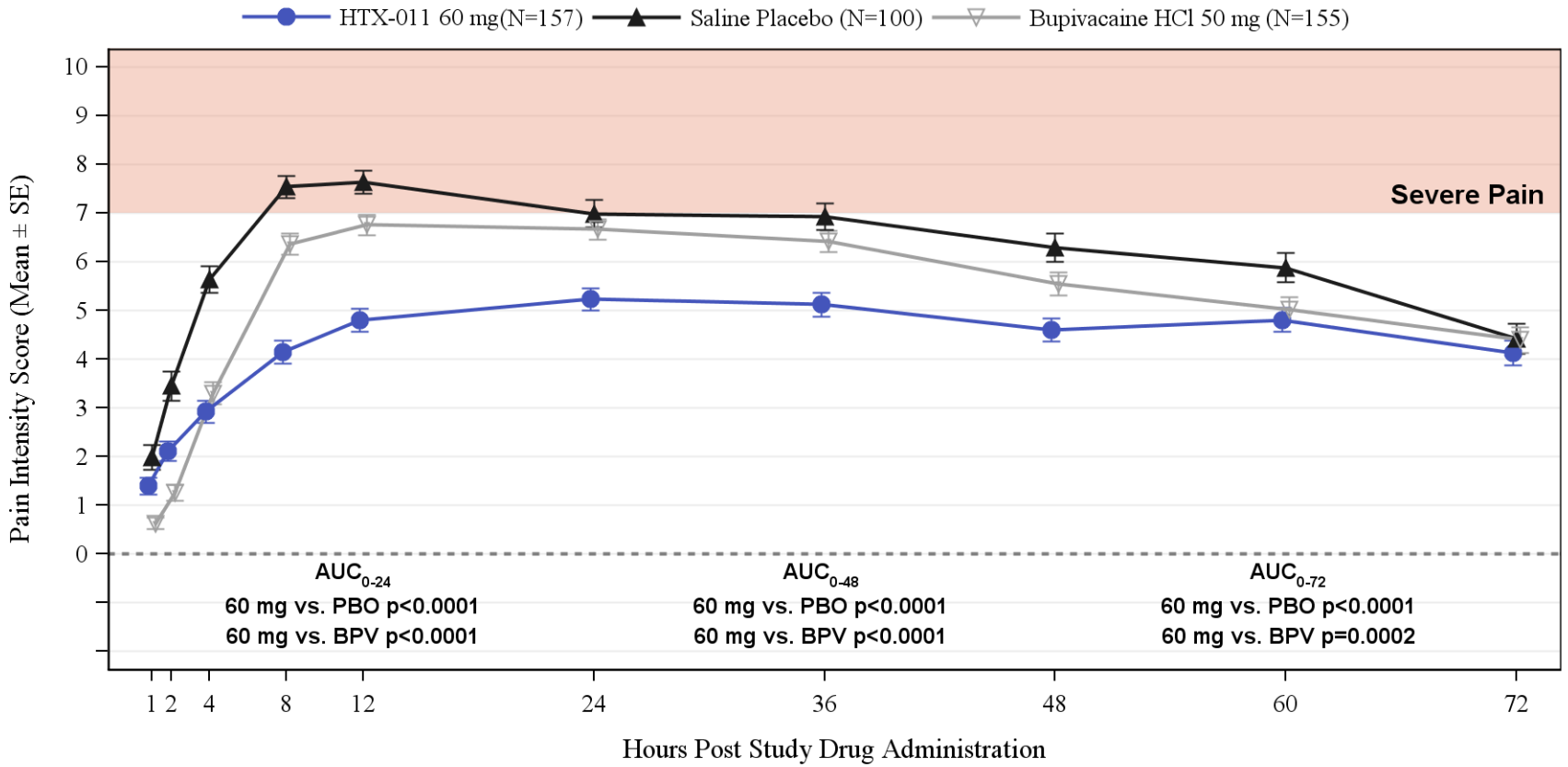
EPOCH 1 Bunionectomy: Results Hierarchy



PBO: saline placebo; BPV: bupivacaine HCl

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

EPOCH 1 Bunionectomy: Mean Pain Intensity

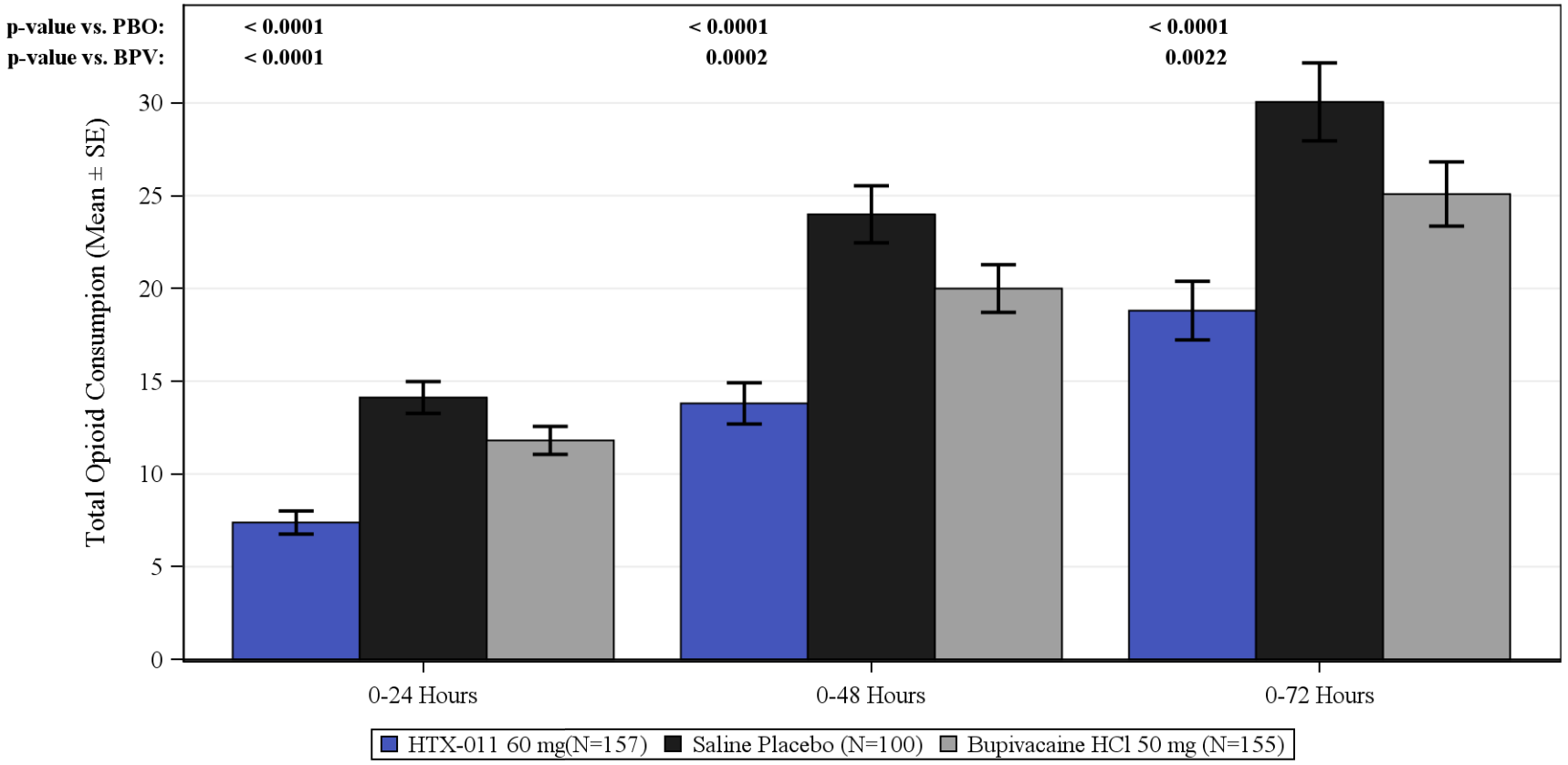


wWOCF – window worst observation carried forward

Source: Figure 14.2.7

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

EPOCH 1 Bunionectomy: Total Postoperative Opioid Consumption (MME)

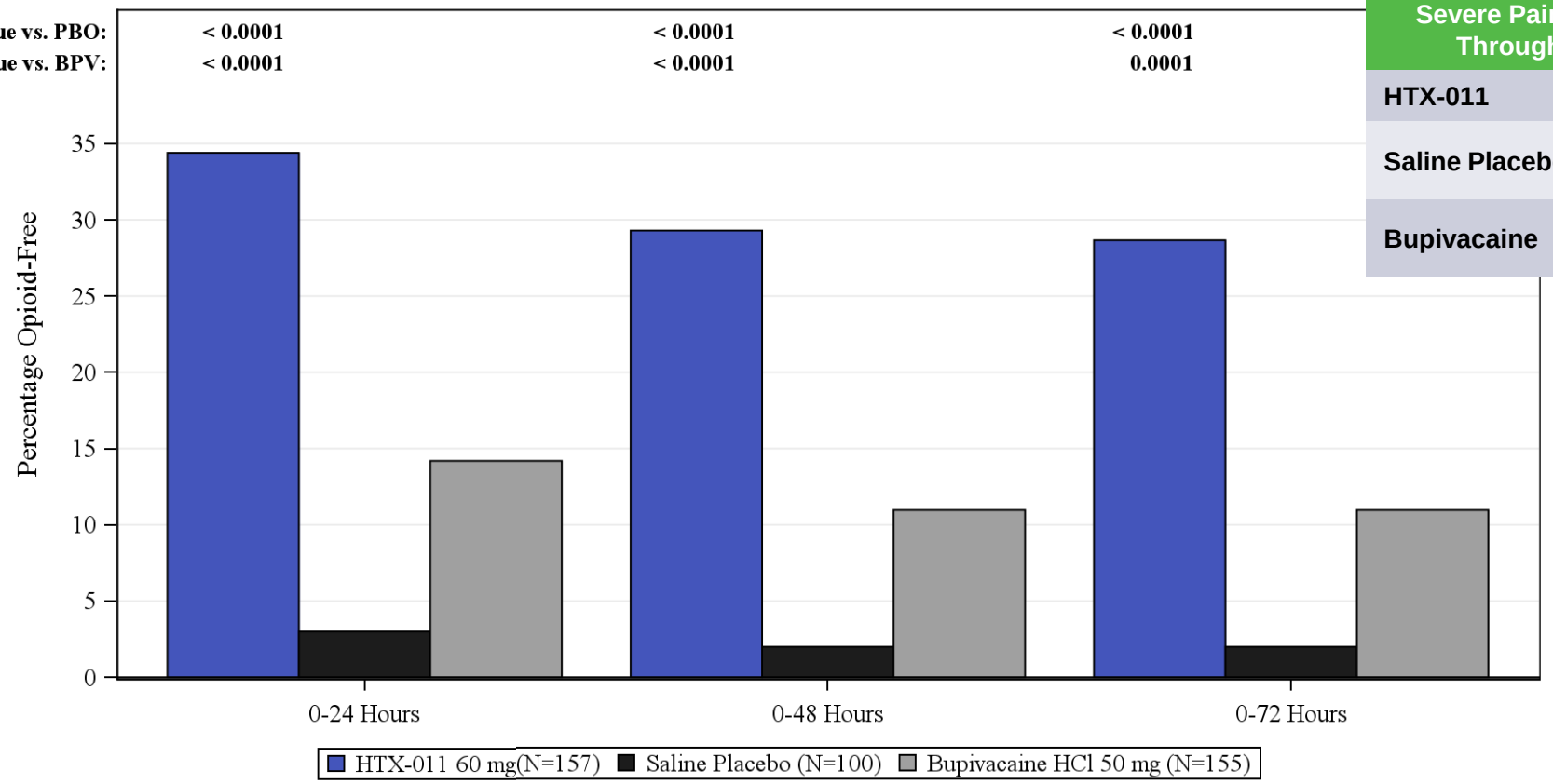


Key Secondary Endpoint
Source: Figure 14.2.2

MME = morphine milligram equivalents

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

EPOCH 1 Bunionectomy: Percentage of Subjects Who Are Opioid-Free

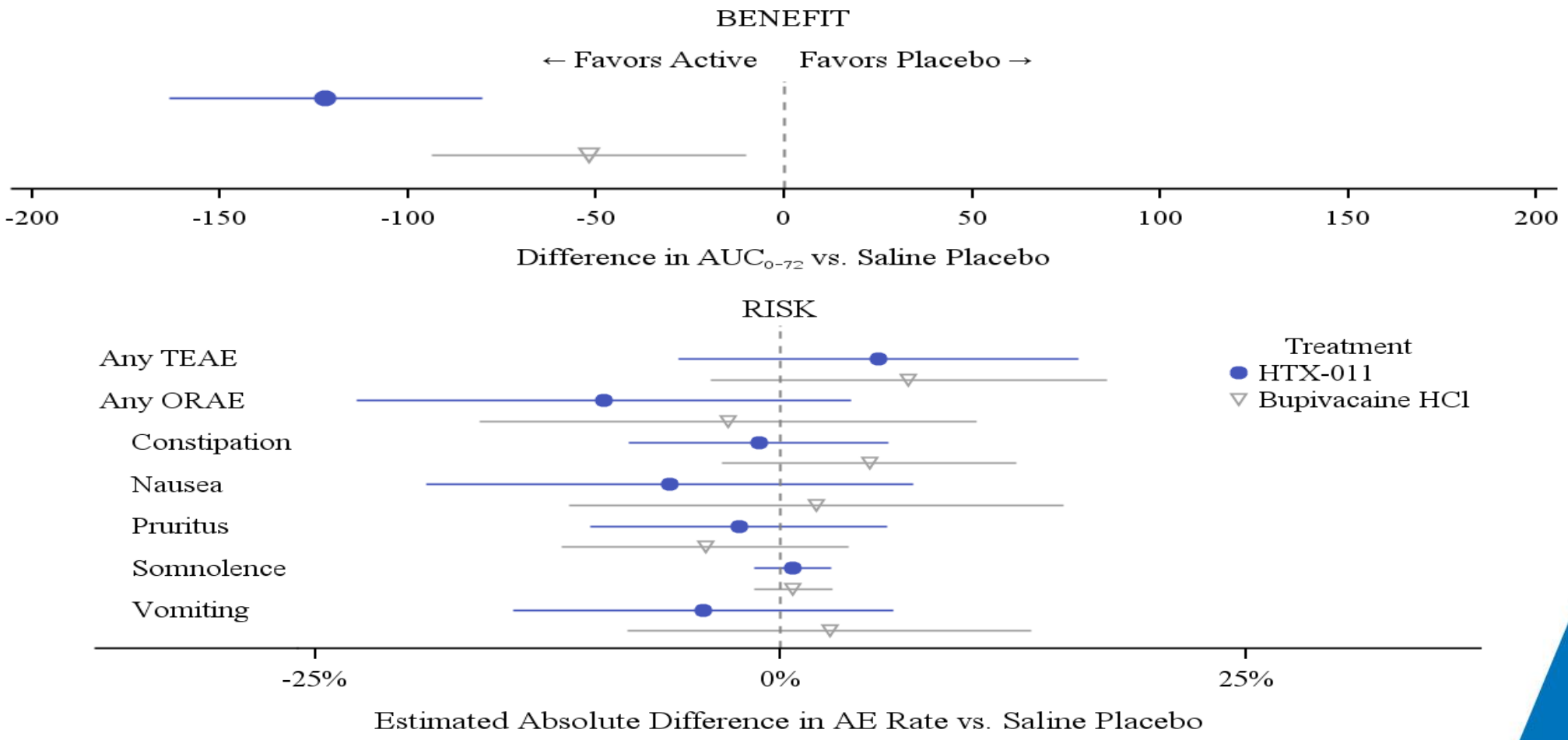


Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011	53.5%
Saline Placebo	83.0% p<0.0001
Bupivacaine	75.5% p<0.0001

Key Secondary Endpoint
Source: Figure 14.2.3

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

EPOCH 1 Bunionectomy: Benefit – Risk for HTX-011



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

HTX-011 Clinical Development

EPOCH 2: Hernia Repair Results

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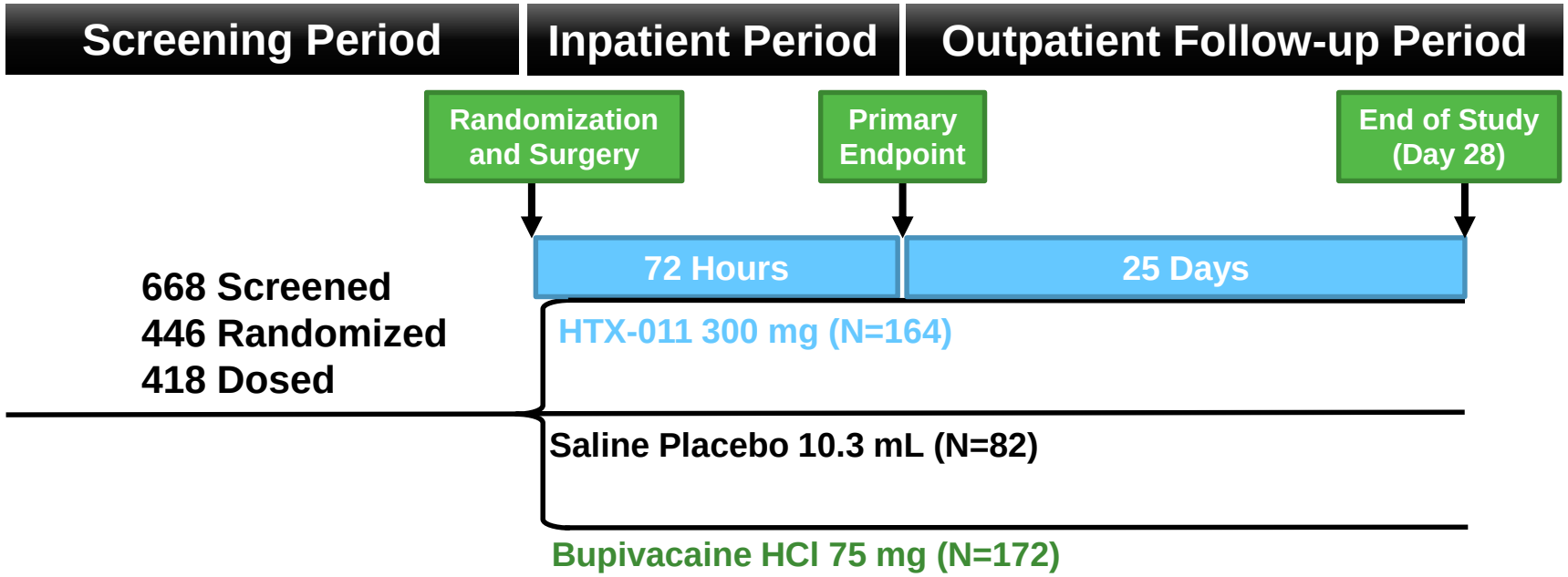
EPOCH 2 Herniorrhaphy: Study Design

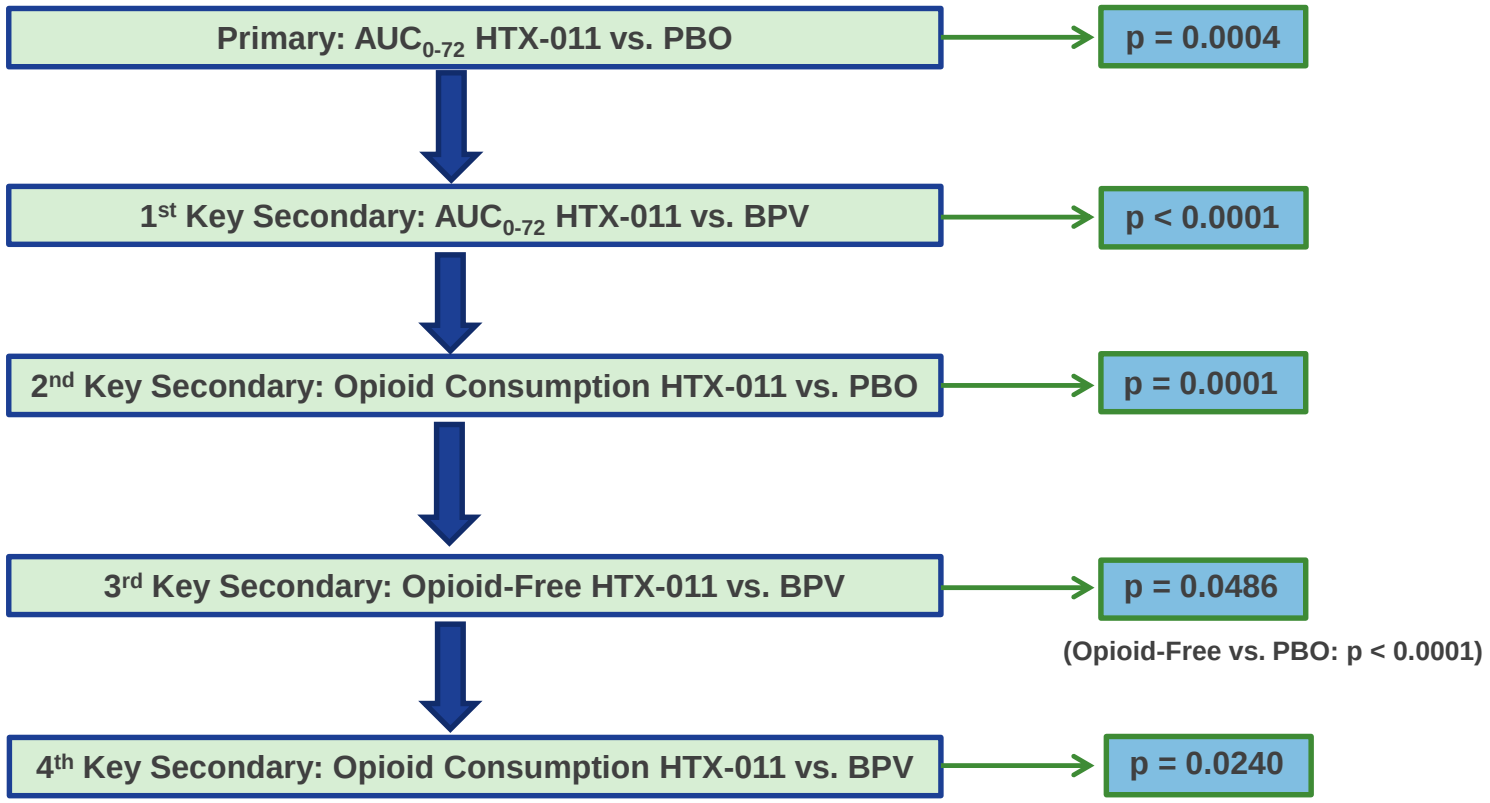
- N= 418 (2:1:2 to HTX-011 300 mg, saline placebo, or bupivacaine HCl 75 mg)
- 446 subjects were randomized and 418 were dosed (ITT Population)
- 17 sites in 2 countries (United States, Belgium)



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

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

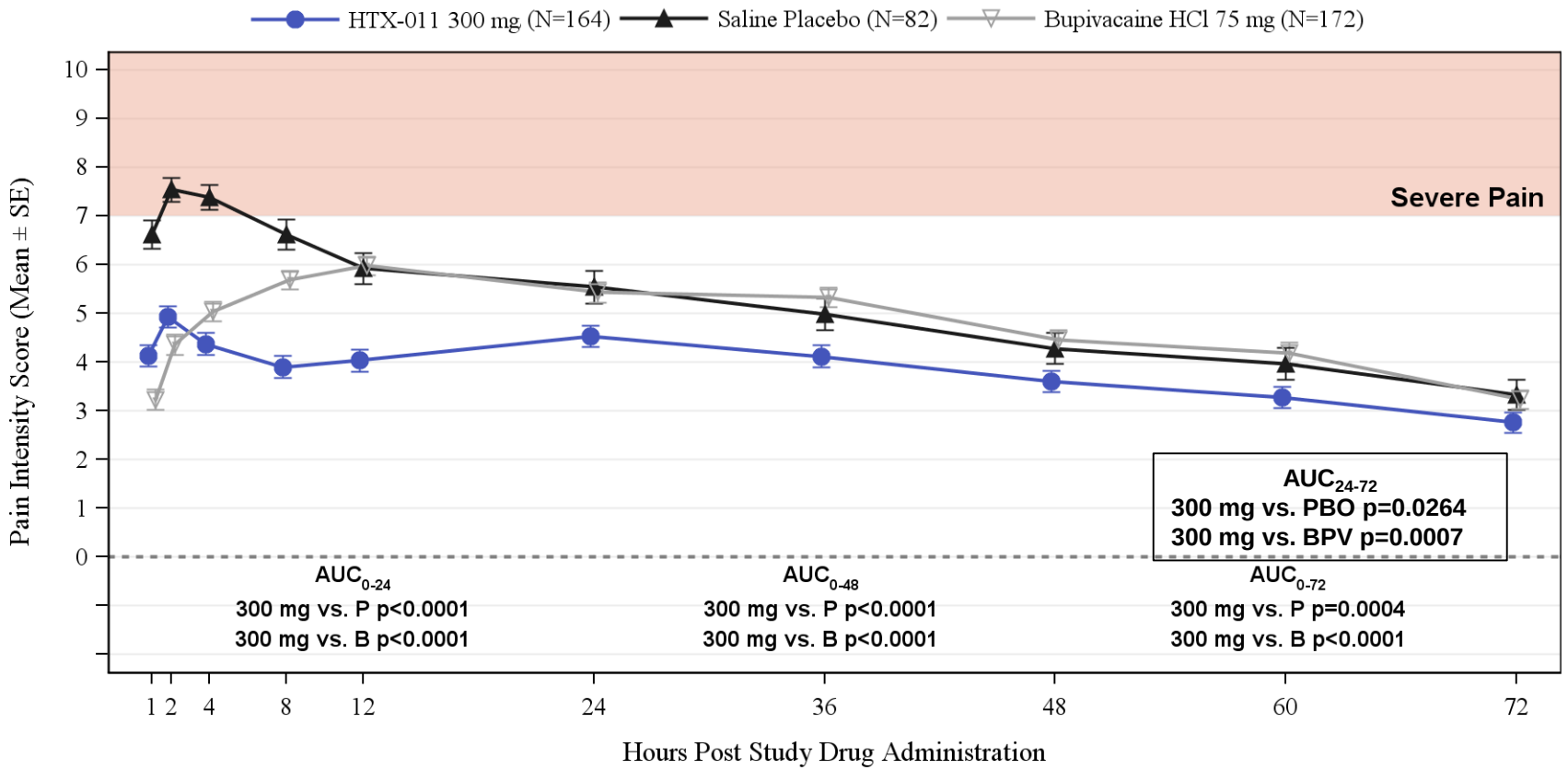
EPOCH 2 Herniorrhaphy: Results Hierarchy



PBO: saline placebo; BPV: bupivacaine HCl

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

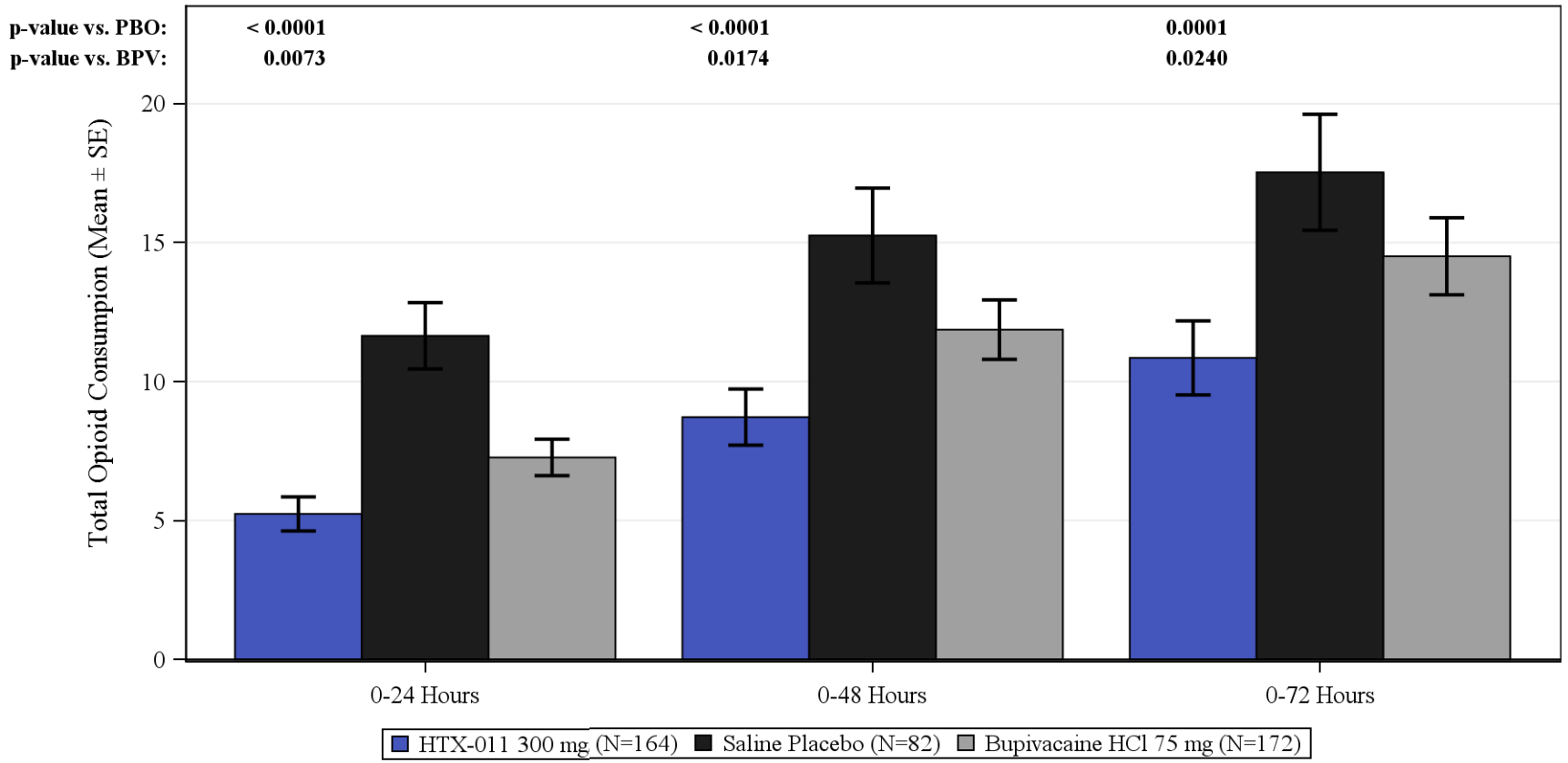
EPOCH 2 Herniorrhaphy: Mean Pain Intensity



Source: Figure 14.2.7

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

EPOCH 2 Herniorrhaphy:
Total Postoperative Opioid Consumption (MME)

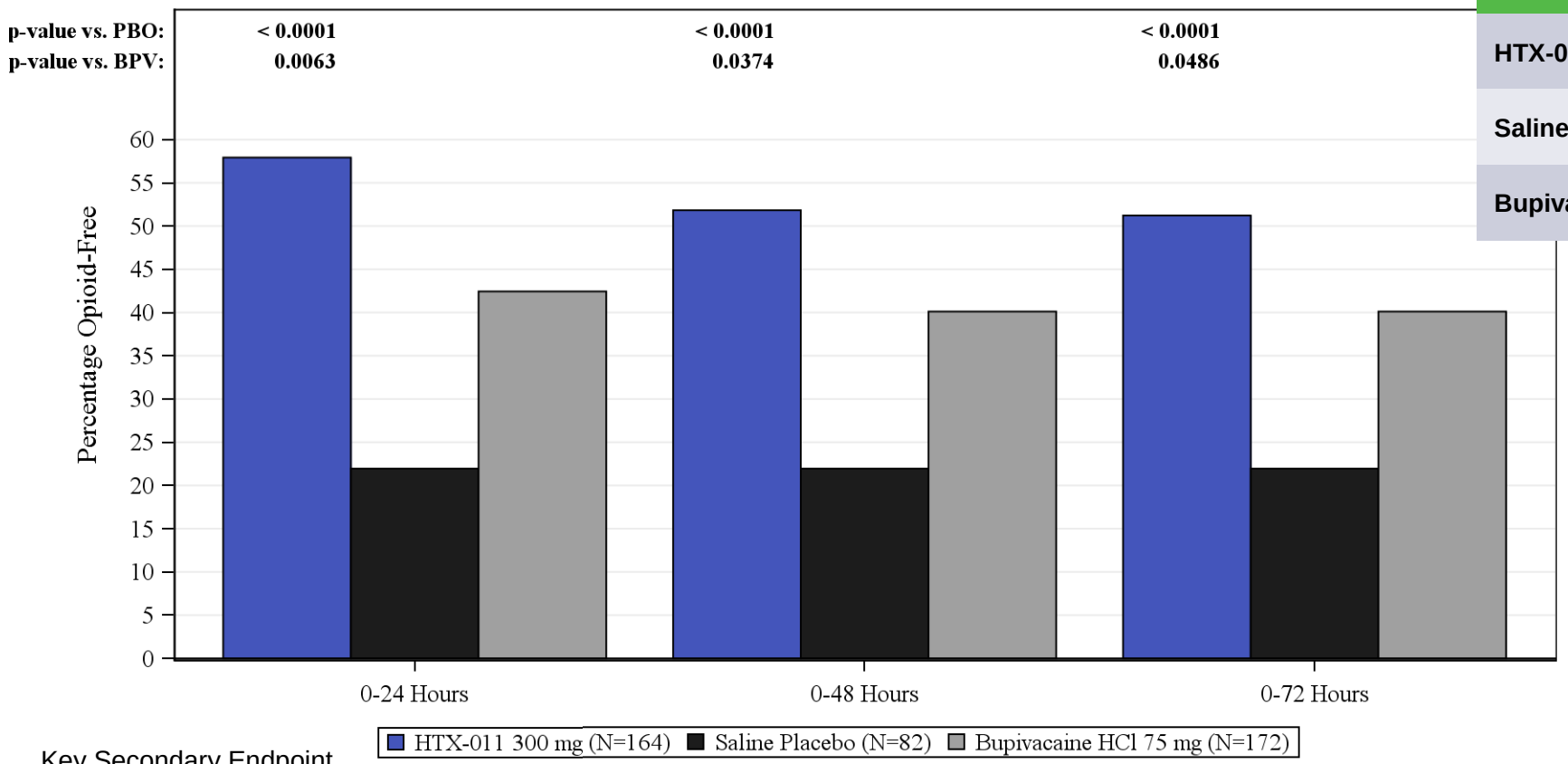


Key Secondary Endpoint
Source: Figure 14.2.2

MME = morphine milligram equivalents

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

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

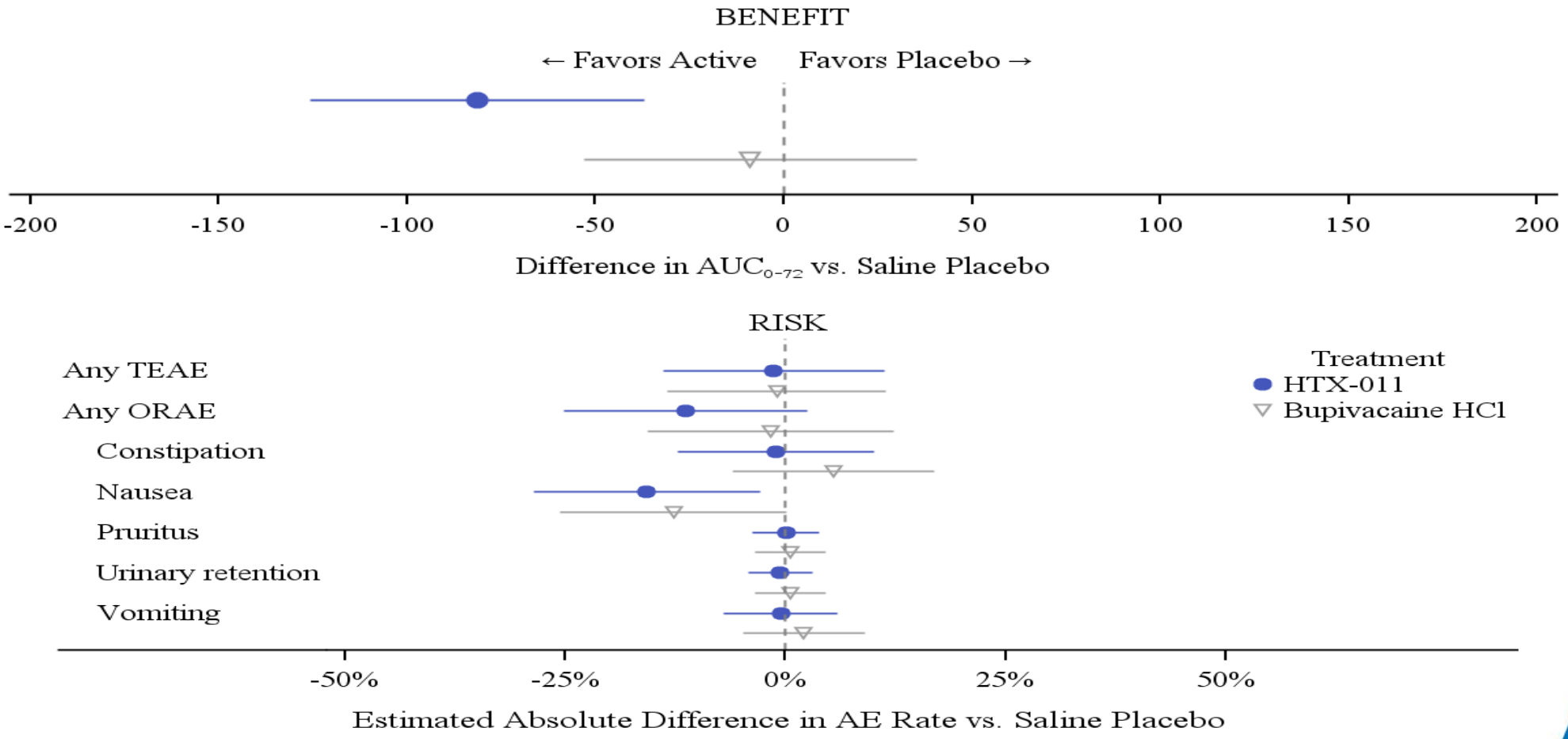


Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011	48.8%
Saline Placebo	81.7% p<0.0001
Bupivacaine	60.5% p=0.0372

Key Secondary Endpoint
Source: Figure 14.2.3

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

EPOCH 2 Herniorrhaphy: Benefit – Risk for HTX-011



← Favors Active Favors Placebo →

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HTX-011 Clinical Development

Phase 2b Total Knee Arthroplasty (TKA) Study

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Study 209 Phase 2b: Total Knee Arthroplasty

HTX-011 400 mg
Instillation
N = 58

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

Saline Placebo
Injection
N = 53

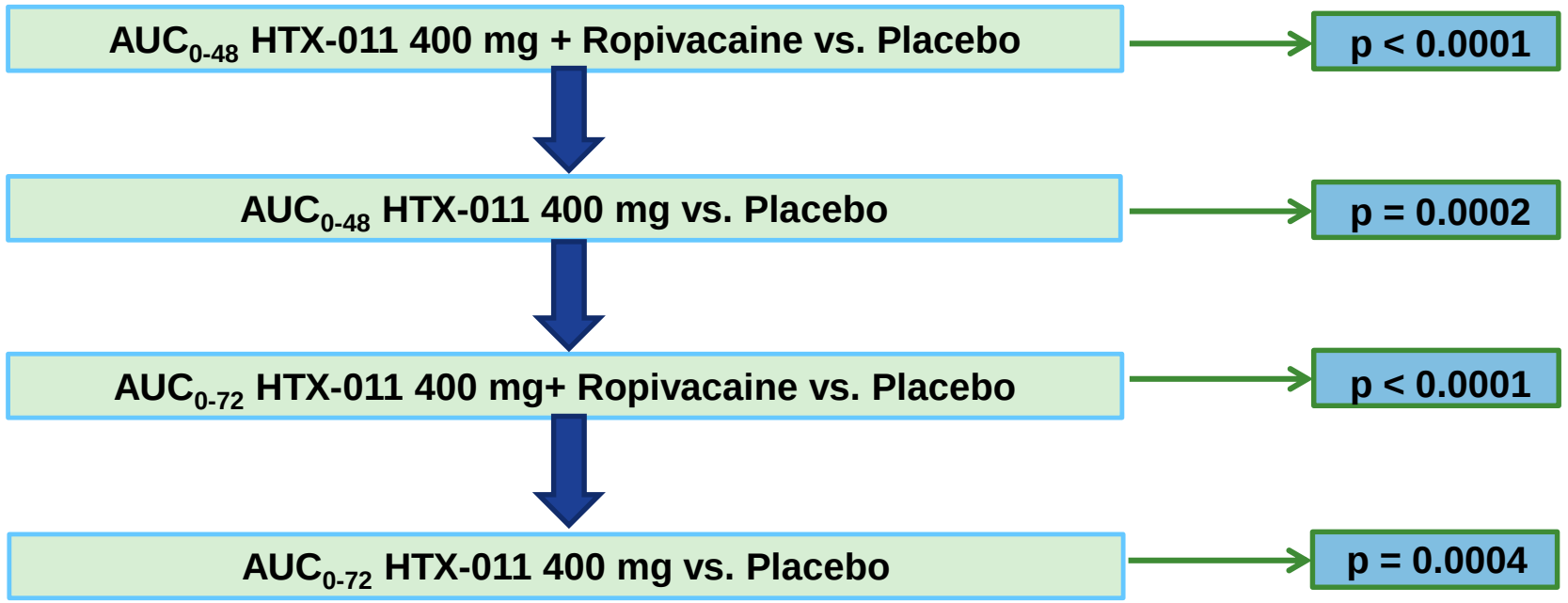
Bupivacaine 125 mg
Injection
N = 55

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

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

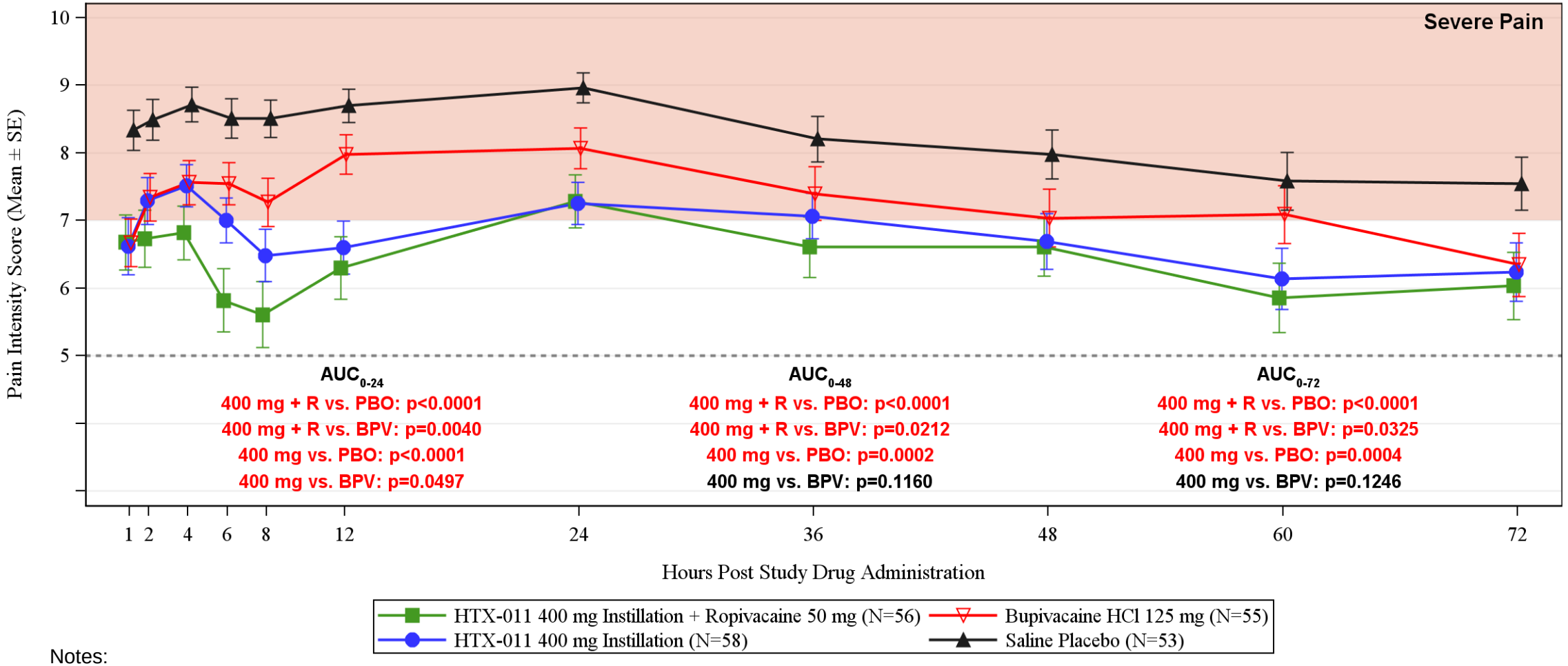
Study 209 TKA: Results Hierarchy

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



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

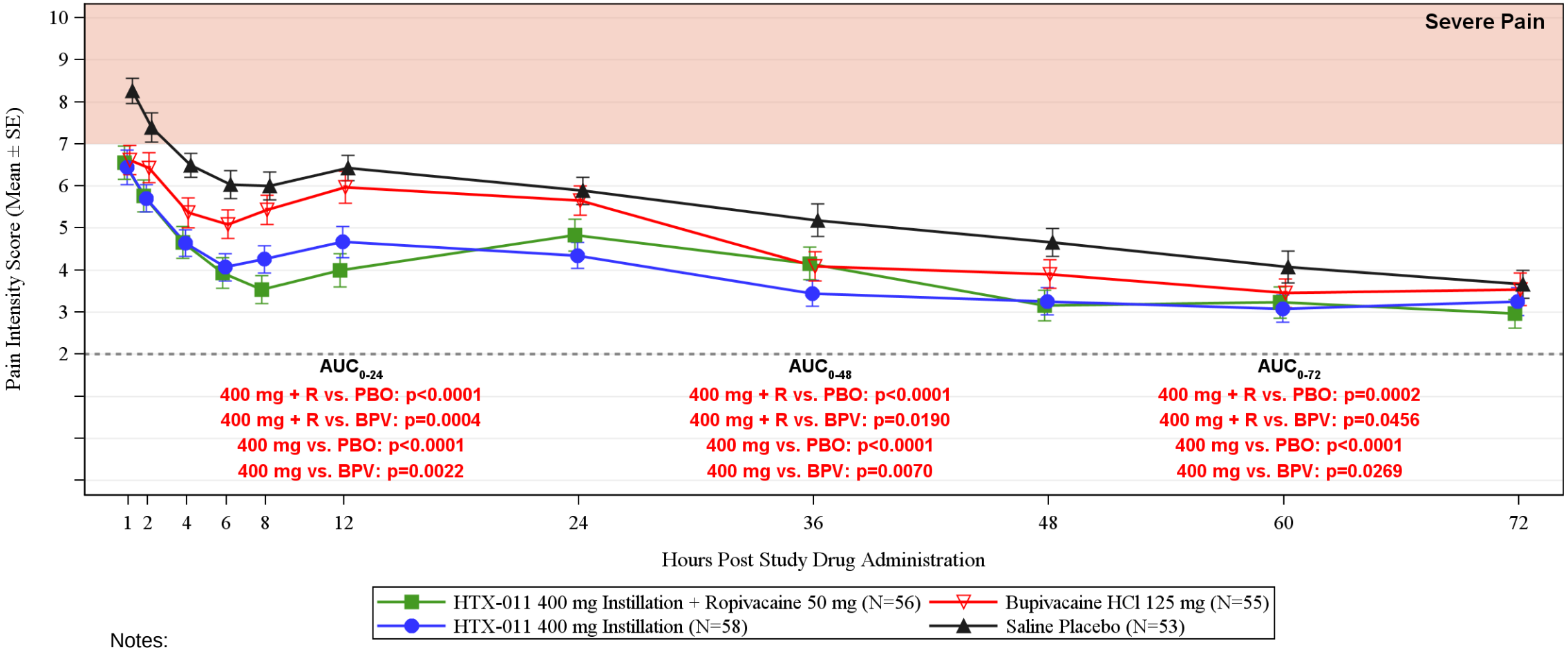
Study 209: Significant Separation between HTX-011 Arms and Placebo through 72 Hours for Pain at Rest



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

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

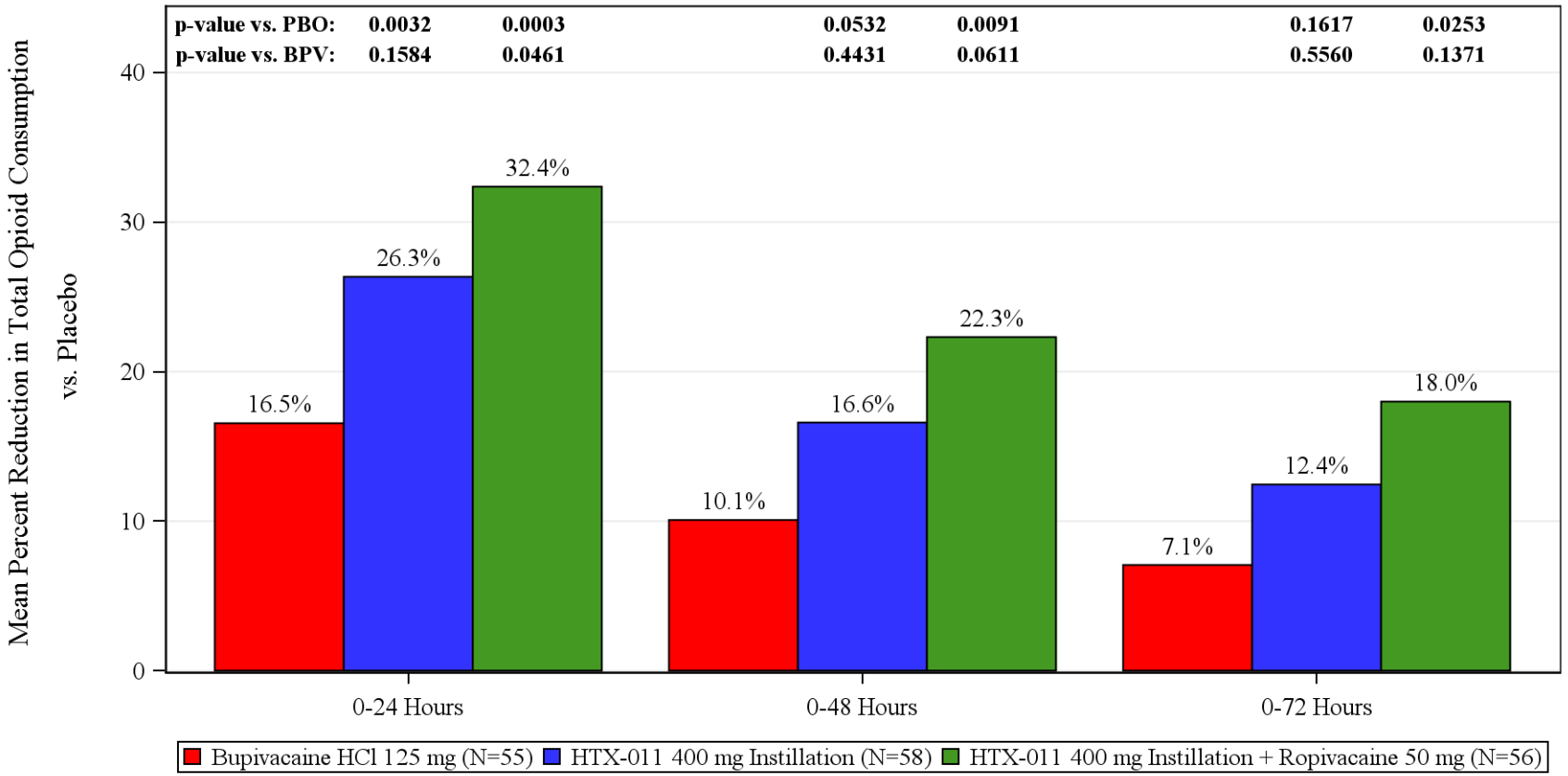
Study 209: HTX-011 Significantly Superior to Both Placebo and Bupivacaine Through 72 Hours Without Adjusting for Opioid Use



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

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

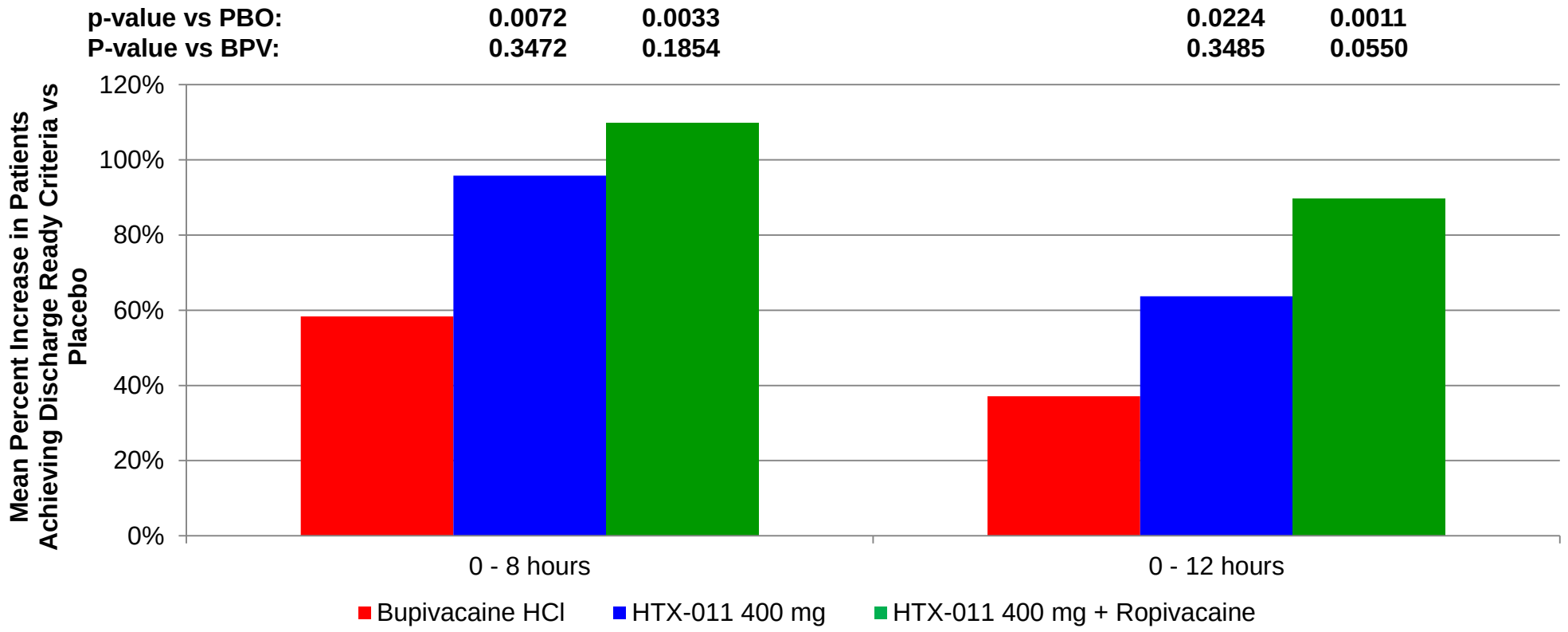
Study 209 TKA: HTX-011 plus Ropivacaine Significantly Reduces Opioid Use vs. Placebo through 72 Hours



Source: Figure 14.2.2.2

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

Study 209 TKA: Significant Increase Compared to Placebo in Patients Achieving “Discharge Ready” MPADDS Criteria* in First 12 Hours

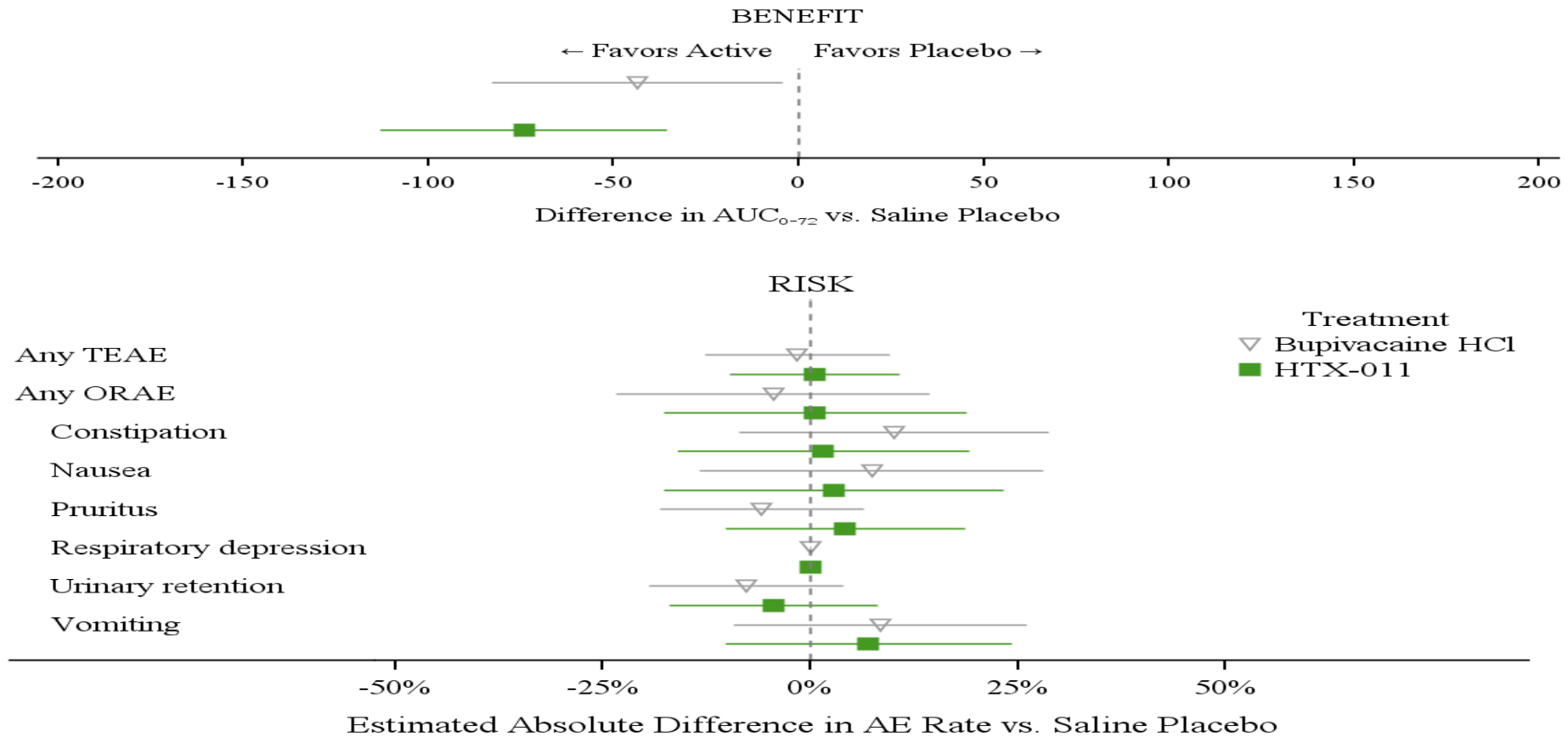


*MPADSS, modified postanaesthetic discharge scoring system. The proportion of subjects who first achieve an MPADSS score ≥9 at each timepoint was analyzed cumulatively. P-values from Fisher's exact test.

Source: Table 14.2.13.2

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

Study 209 TKA: Benefit – Risk for HTX-011



← Favors Active Favors Placebo →

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

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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9.7 Million Out of the 15 Million Initial Target Procedures (65%) Will Have ASP+6% Reimbursement At Launch*

Hospitals account for 76%
[11.4 M procedures]

35% Inpatient
[5.3M procedures]

- **MS-DRG / Bundled Payment**

41% Hospital Outpatient
[6.1M procedures]

- **C-Code / J-Code – 3-year pass through at ASP+6%**
- **340B Drug Discount Program**
- **During 3-year C-Code period, plan to work with CMS to make pass-through permanent based on ability to significantly increase opioid-free patients**

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

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

- **C-Code / J-Code separately billable at ASP+6%**

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

- **J-Code**
- **Fee-for-service/reimbursed separately at ASP+6%**

**Based on obtaining a C-Code within 90 days of approval*

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340b Hospital Summary

- ~2258 hospitals (excluding children's & psych)
  - Perform 8.4M outpatient surgeries
  - 4.4M inpatient surgeries/year
- Manufacturers required to provide 23.1% discount off ASP/WAC
- Effective January 1, 2018, CMS reimbursement to hospitals for 340B drugs changed significantly from ASP+6% to ASP–22.5%
- Change enables CMS to capture most of the discounts manufacturers provide eligible hospitals
- **Products with pass-through status are exempt from this reimbursement change**

340B Drug Reimbursement

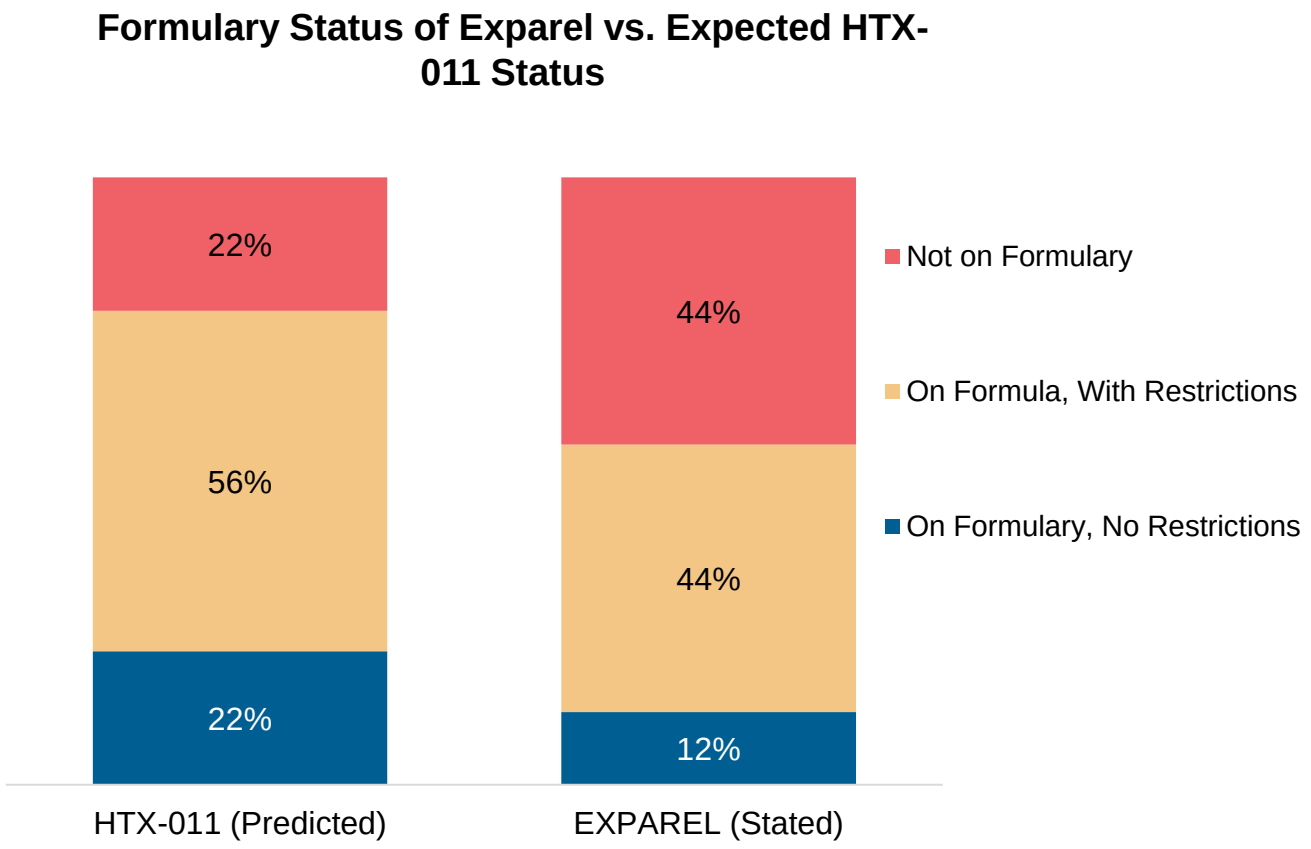
Without C-Code	With C-Code
ASP – 22.5%	ASP + 6%

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

- Penetration of Exparel is so low (<6% of the addressable market), that it provides a similarly small obstacle to the acceptance of HTX-011
  - Across most product attributes, surveyed surgeons and pharmacy directors consistently prefer HTX-011 over Exparel based on their view of:
    - Unique mechanism of action
    - Superior efficacy profile of HTX-011, with significant benefit over bupivacaine HCl
    - Significant reduction in severe pain resulting in significant increase in opioid-free patients
    - Simple route of administration eliminating the need for up to 120 injections, with no need for extensive training
  - Surveyed pharmacy directors state that they would be provide better access to HTX-011 than the access currently enjoyed by EXPAREL

Sources: DRG Pharmacy Director Surveys

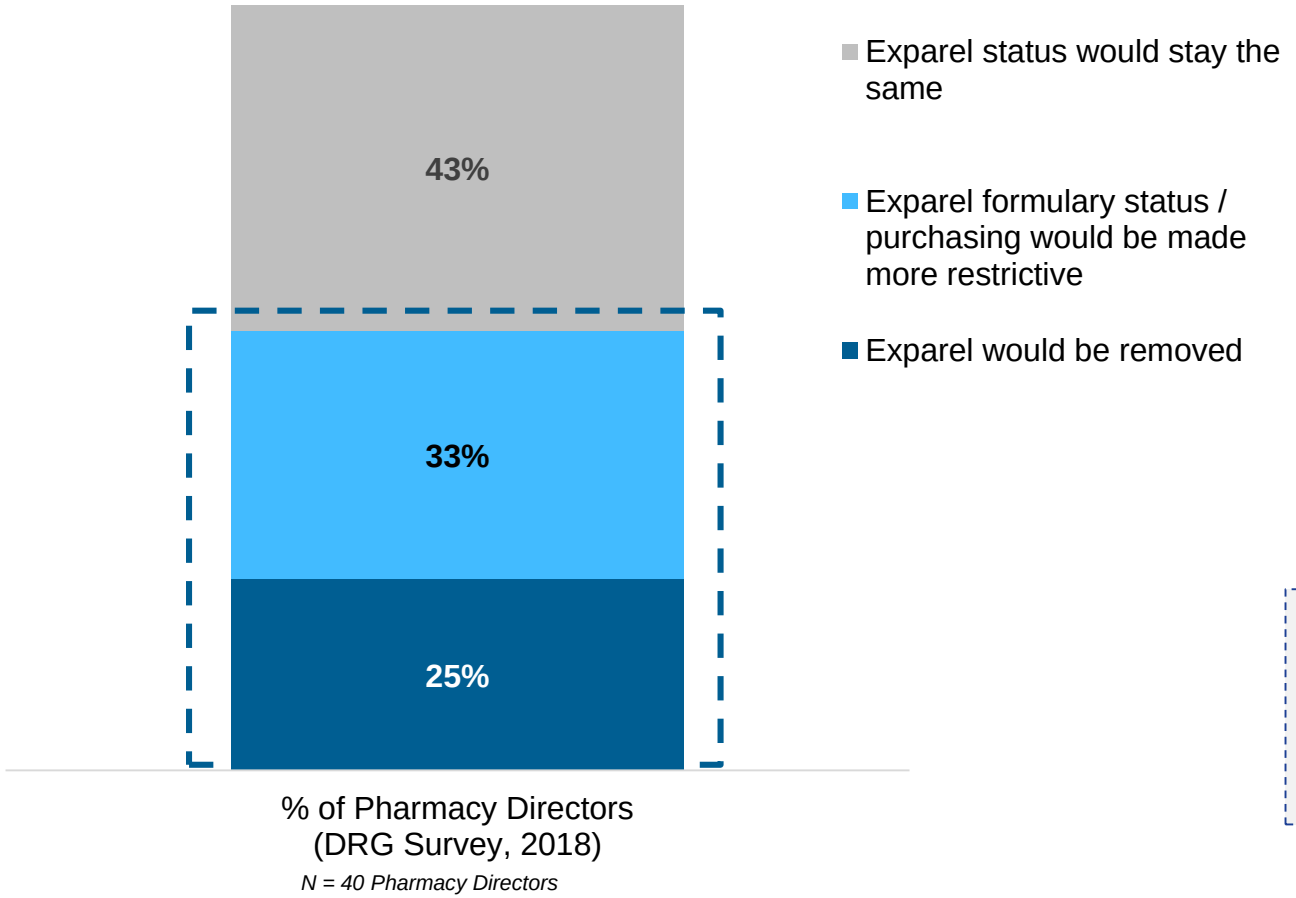
Pharmacy Directors State That They Would Provide Better Access to HTX-011 Than Currently Available to EXPAREL



Sources: DRG Pharmacy Director Surveys

Up to 25% of Pharmacy Directors Report That Exparel Would be Removed From Formulary When HTX-011 Becomes Available

Impact of HTX-011 Launch on Exparel Formulary Status



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

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

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

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

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

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

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

$4.9B **$1.9B** **$2.3B**

Theoretical Market Size*

*Based on the current WAC of Exparel

High-Value Procedures in Initial Target Market

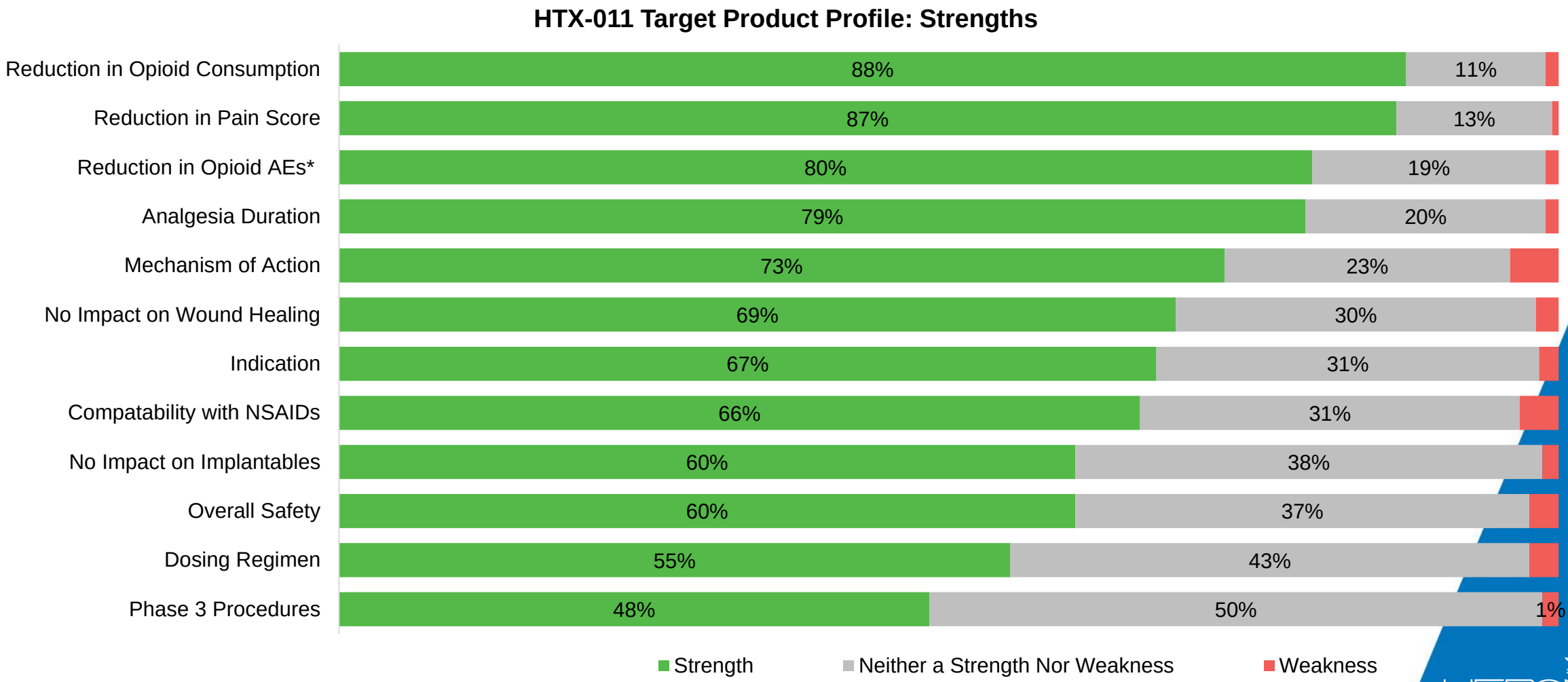
	Procedure	Annual Volume ('000s, US, 2015)						Overall % Local Anesthetic Use
		Total Procedures	*Inpatient*	*Outpatient (C-code)*	*ASC (C-Code)*	*Medicare*	*Non-Medicare*	*Survey*
Ortho Surgery	Knee arthroplasty	815	721	65	28	41%	59%*	87%
	Hip arthroplasty	337	325	7	5	43%	57%*	81%
	Shoulder arthroplasty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

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

Completed studies

HERON THERAPEUTICS

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

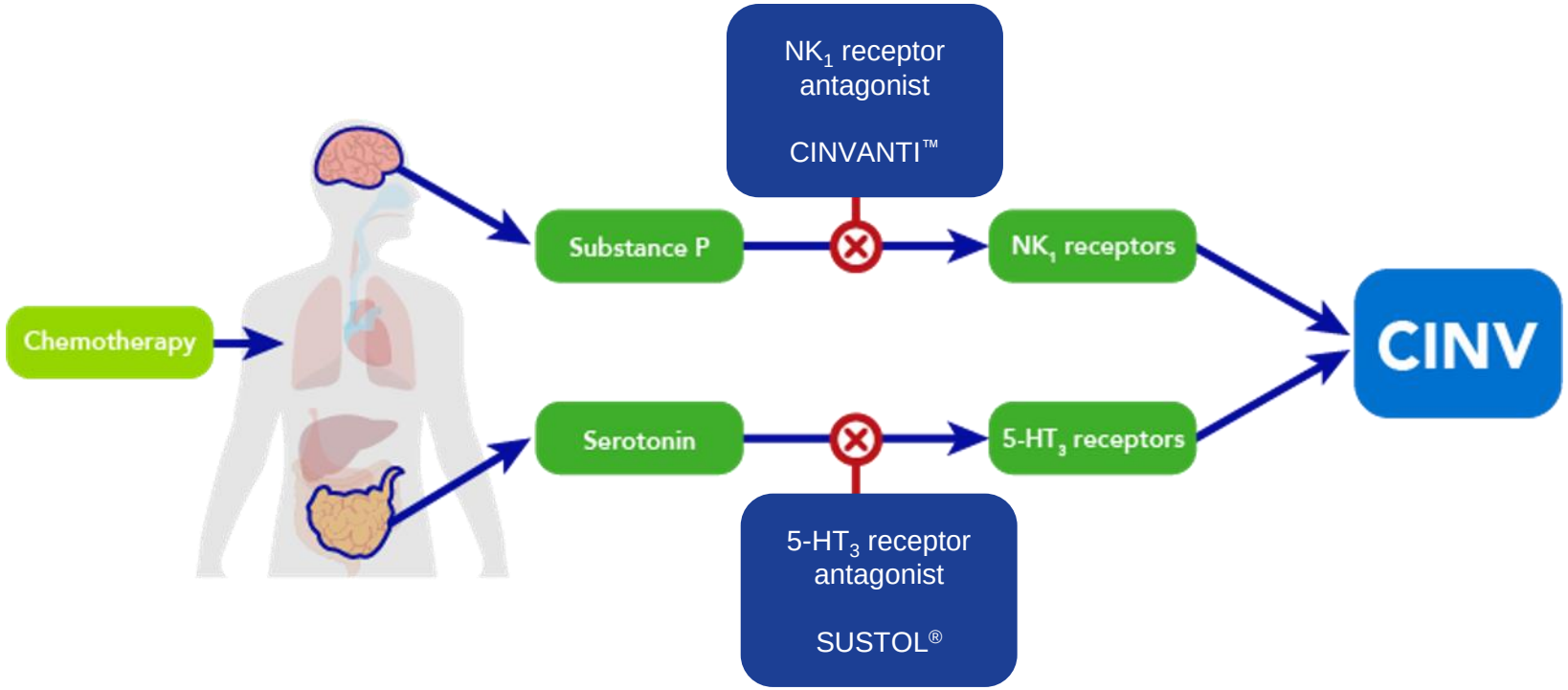


n = 376 total (101 anesthesiologists, 51 general surgeons, 122 orthopedic surgeons, 50 plastic surgeons, 52 pharmacy directors)

CINV Commercial Products

HERON THERAPEUTICS

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

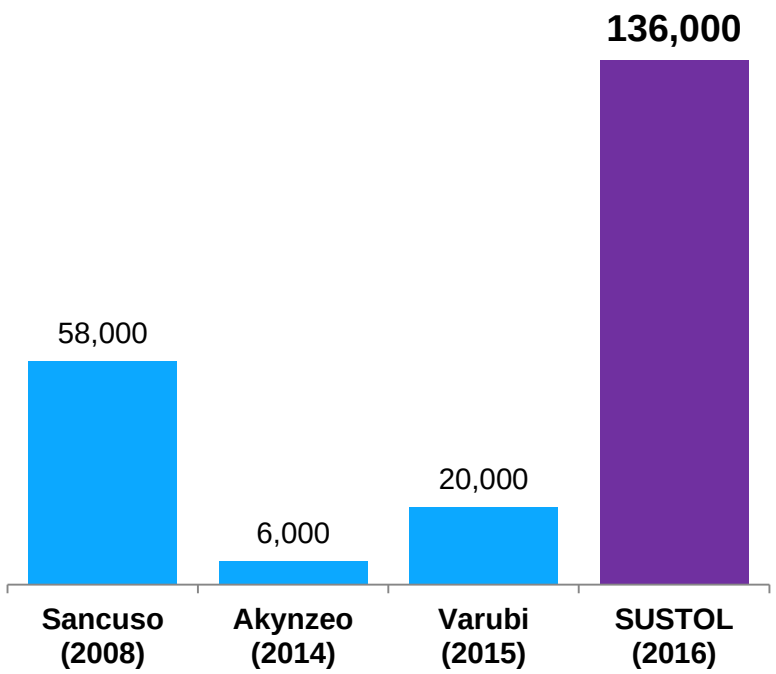
5-HT_3 receptor antagonists

- 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

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

CINV Brand Launches Since 2008

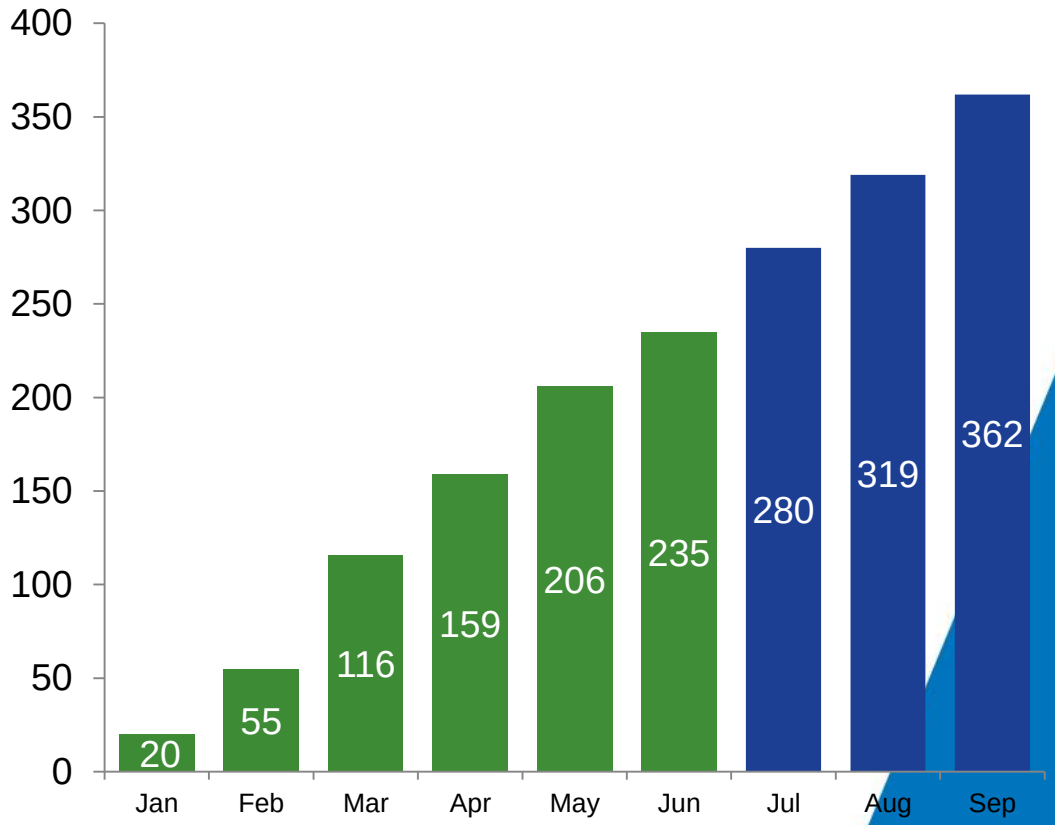
Approximate administrations in <u>First 18 Months</u> (launch aligned)



CINVANTI administrations in first <u>9 months</u>:

154,000

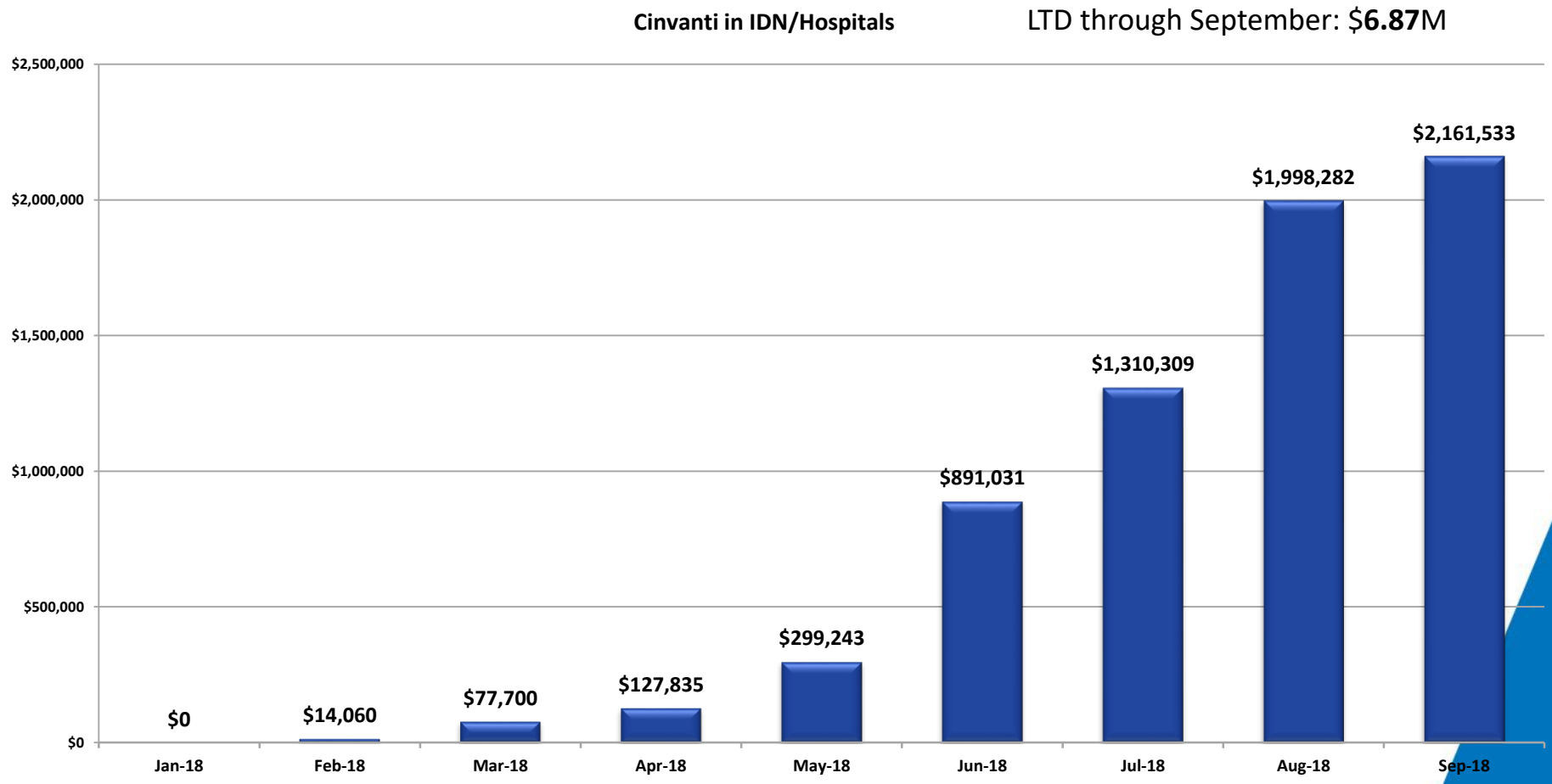
CINVANTI Ordering Accounts Since Launch



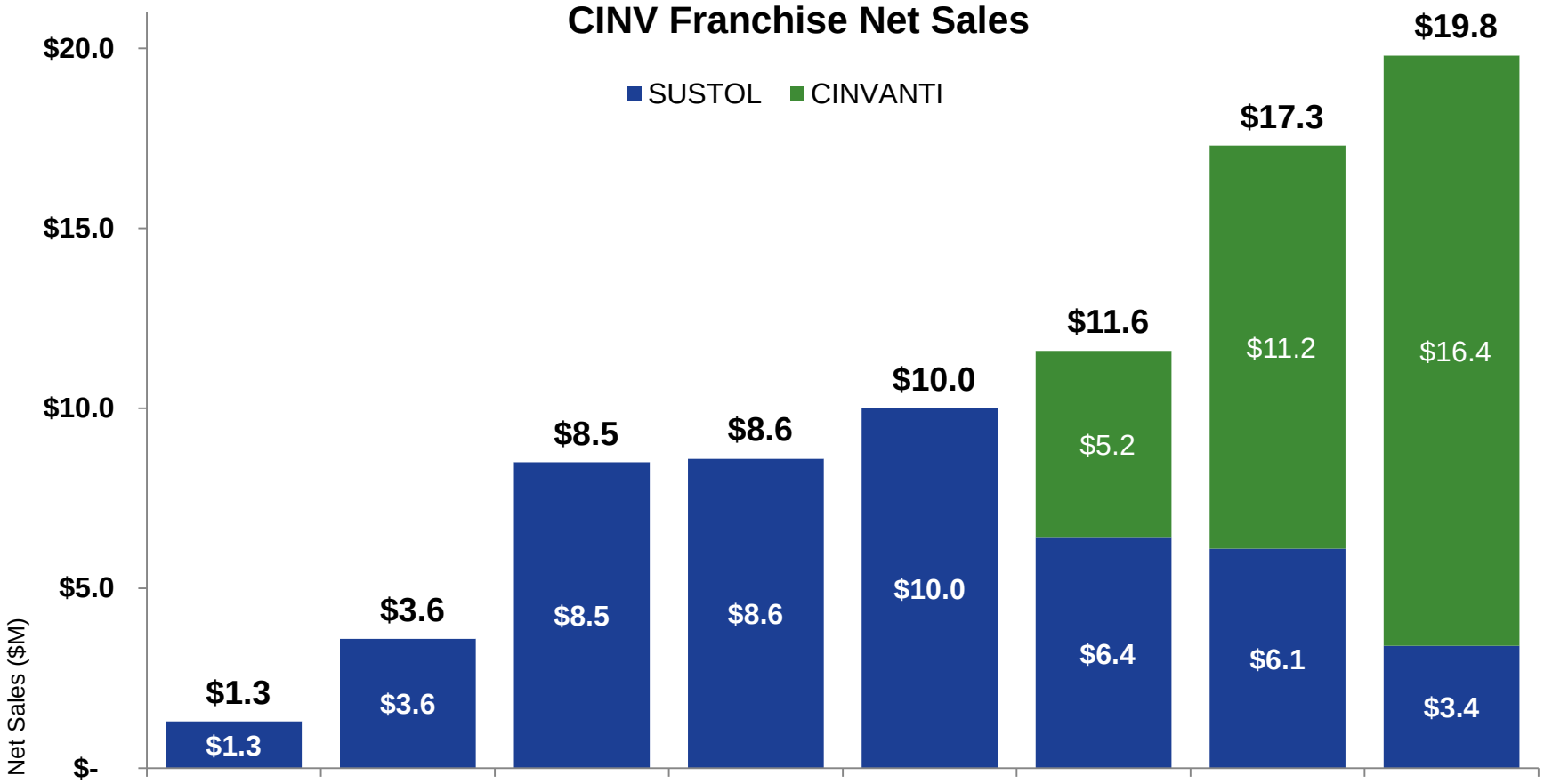
Sources: IMS DDD; Heron actuals (distributor 867 reports); due to data availability, Sancuso data includes actuals for launch months 3-12 and estimates for months 1-2; Varubi includes actuals for launch months 1-15 and estimates for months 16-18

Hospital Success Driven by Leveraging Pass Through Status

51% *of units sold were derived from 340B and Pass through Status*



Heron CINV Portfolio achieved $19.8M Q3 2018 Net Sales



Source: Heron data

2018 CINV Franchise Outlook

SUSTOL®: We continue to expect core SUSTOL business to be weak during the palonosetron arbitrage with growth thereafter

CINVANTI®

- 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
- We continue to see steady growth in the marketplace
- CINVANTI (aprepitant)injectable emulsion receives unique J-Code J0185 effective January 1, 2019
- Expect updated label in Q1 for IV push

CINV Franchise

- **2018 guidance: raising from $60M-70M to $70M-$72M**

Financial Summary

CINV Net Product Sales Guidance Raised to $70 Million to $72 Million.

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

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

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

[1] Includes $8.1 million and $23.6 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2018, respectively.
[2] Based on 77.8 million and 71.5 million weighted-average common shares outstanding for the three and nine months ended September 30, 2018, respectively.

HERON THERAPEUTICS