Heron Therapeutics Update

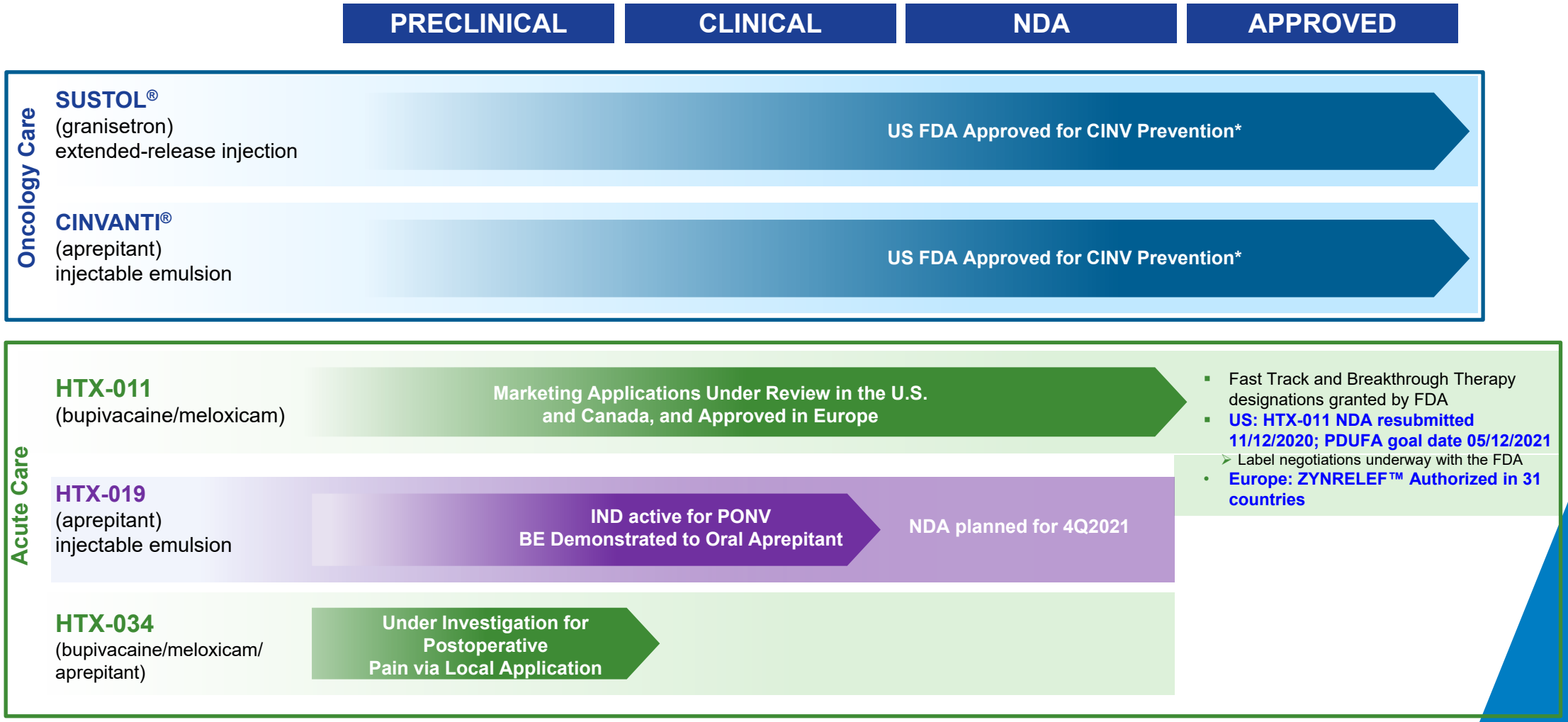
May 10, 2021

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: risks associated with achieving the full-year 2021 net product sales guidance for the CINV franchise; whether the FDA approves the NDA for HTX-011; whether the scope of the label for HTX-011, if approved, will be as desired; the timing of the commercial launch of HTX-011 in the U.S., if approved; the timing of the commercial launch of ZYNRELEF in Europe; the timing of Health Canada's NDS review process for HTX-011; whether Health Canada issues a Notice of Compliance for the NDS for HTX-011; the timing and results of studies for HTX-011, the HTX-034 development program, and the HTX-019 development program; the expected future balances of Heron's cash, cash equivalents and short-term investments; the expected duration over which Heron's cash, cash equivalents and short-term investments balances will fund its operations; the extent of the impact of the ongoing Coronavirus Disease 2019 (COVID-19) pandemic on our business; 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 THERAPEUTICS®

Heron Pipeline



*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 agentsis 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 as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI has not been studied for treatment of established nausea and vomiting.

HTX-011, HTX-034 and HTX-019 are investigational new drugs and are not approved by the FDA

NDA Resubmitted Based on Guidance at Type A Meeting

- Pharmacokinetic data generated for 3 excipients in toxicology animals and patients receiving HTX-011 400 mg in TKA and C-section studies
- Cmax of excipients at doses administered in reproductive toxicology studies are >50- to >200-fold higher than observed in patients receiving highest dose of HTX-011
  - Substantially higher exposures observed in toxicology species validates acceptability of submitted studies
  - Submitted pharmacokinetic data expected to address 3 of the 4 issues in CRL
- Fourth issue addressed by lowering impurity specification for final drug product to FDA agreed upon level
- **Class 2 resubmission with 6-month review clock: PDUFA goal date of 05/12/2021**
  - **Label negotiations underway**

HERON THERAPEUTICS

HTX-011 Commercialization Plan

Advancing Pain Management

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

Established Platform With Experienced Teams in Place

We are prepared for the potential launch of HTX-011. Critical teams are already in place, with extensive experience in successful hospital launches.

Existing Platform Advantages

- Strong KOL relationships
- Successful hospital and pain management launch experience
- IDN/hospital/ASC expertise and relationships
- Reimbursement infrastructure in place
- GPO contracts in place
- Full-line wholesaler agreements and 3PL in place
- Safety monitoring structure in place
- Proven compliant execution
- Robust systems in place and pressure tested for launch

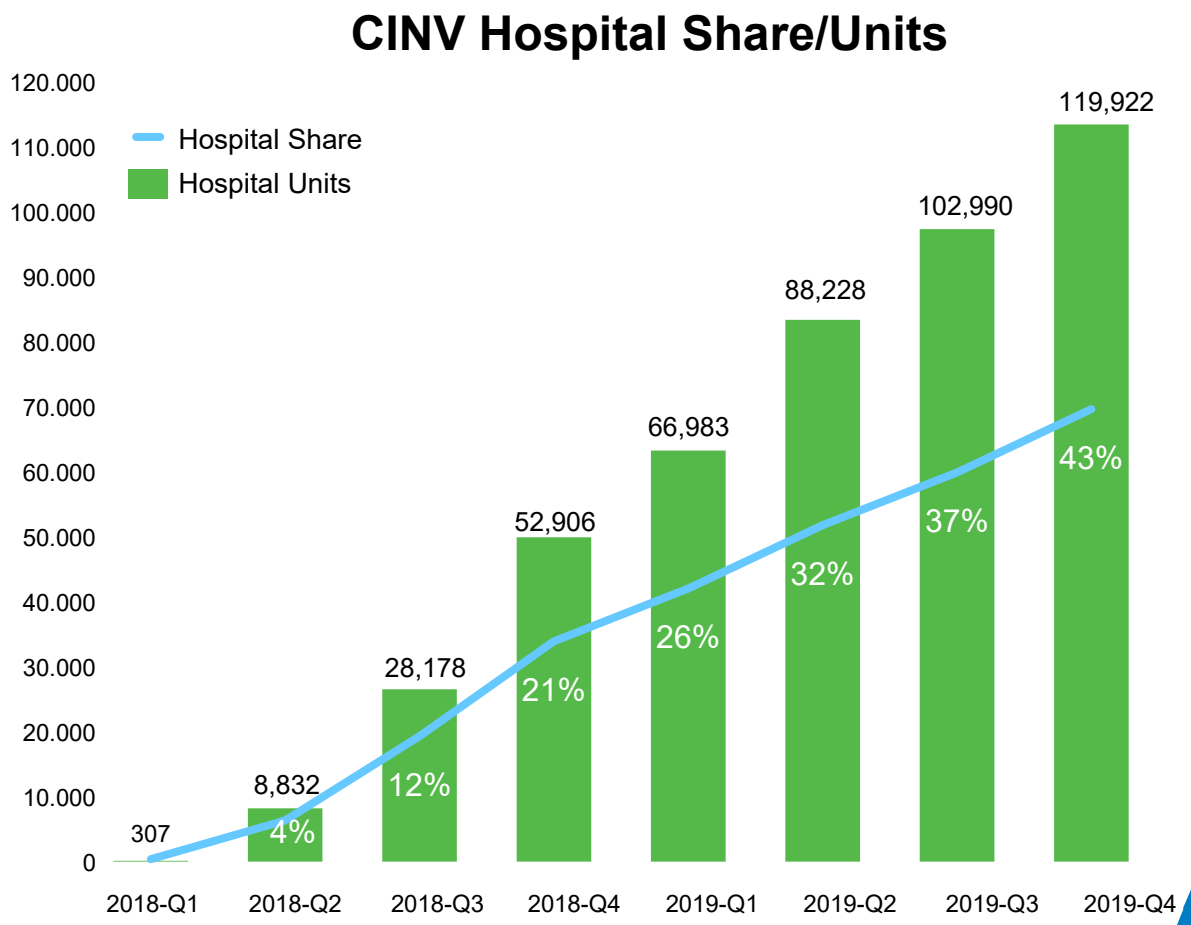
HTX-011 is an investigational new drug and not approved by the FDA

A Proven Track Record of Hospital Launch Success

Achieved >40% Market Share From Entrenched Competitor

- Heron launched CINVANTI in January 2018
- Achieved significant market share, in a very short time period
- Outstanding execution:
  - Superior pricing and contracting
  - Providing 340B discount
  - Differentiated product attributes
  - Rapid formulary adoption
  - Accelerated account pull-through
  - Trade and reimbursement expertise

We will leverage the success and experience gained from CINVANTI as we enter the postoperative pain management landscape with HTX-011.



Source: IMS DDD12.25.20, 867 1.5.21

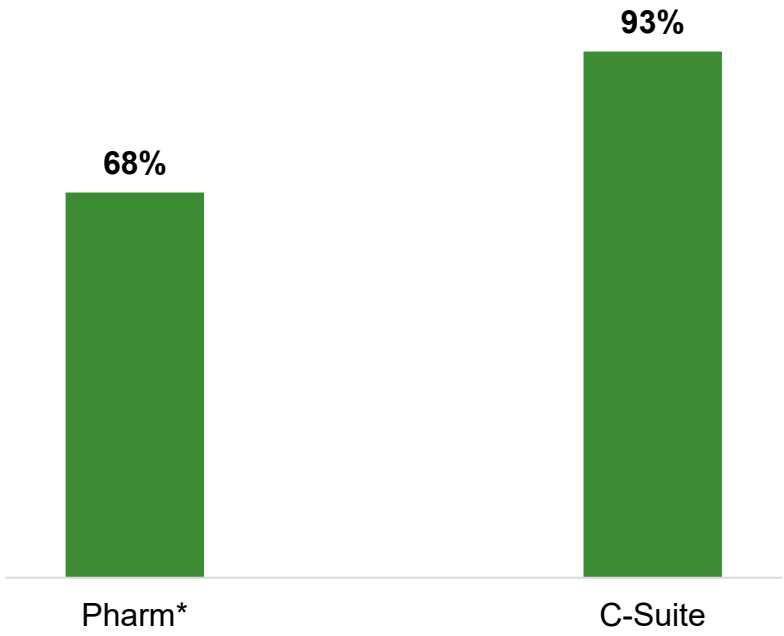
HTX-011 is an investigational new drug and not approved by the FDA

HTX-011 Is Well Positioned on Core Drivers to Create Fast Access and Uptake

Heron is positioned for a successful launch

- High Awareness with key formulary decision makers
- Outperforms both branded and generic competition on every important core attribute for a local anesthetic (LA)
  - Reduction in Severe Pain
  - Elimination of Opioid Discharge Prescriptions
  - 72 Hour Duration

HTX-011 Aided Awareness P&T Decision Makers



Source: Company-sponsored ATU Study July 2020 – Survey of 386 surgeons, anesthesiologists, pharmacists, NP/Pas of potential use of an approved product with the attributes for which we are developing HTX-011

*Pharmacists were required to be involved in formulary decisions to qualify for the survey

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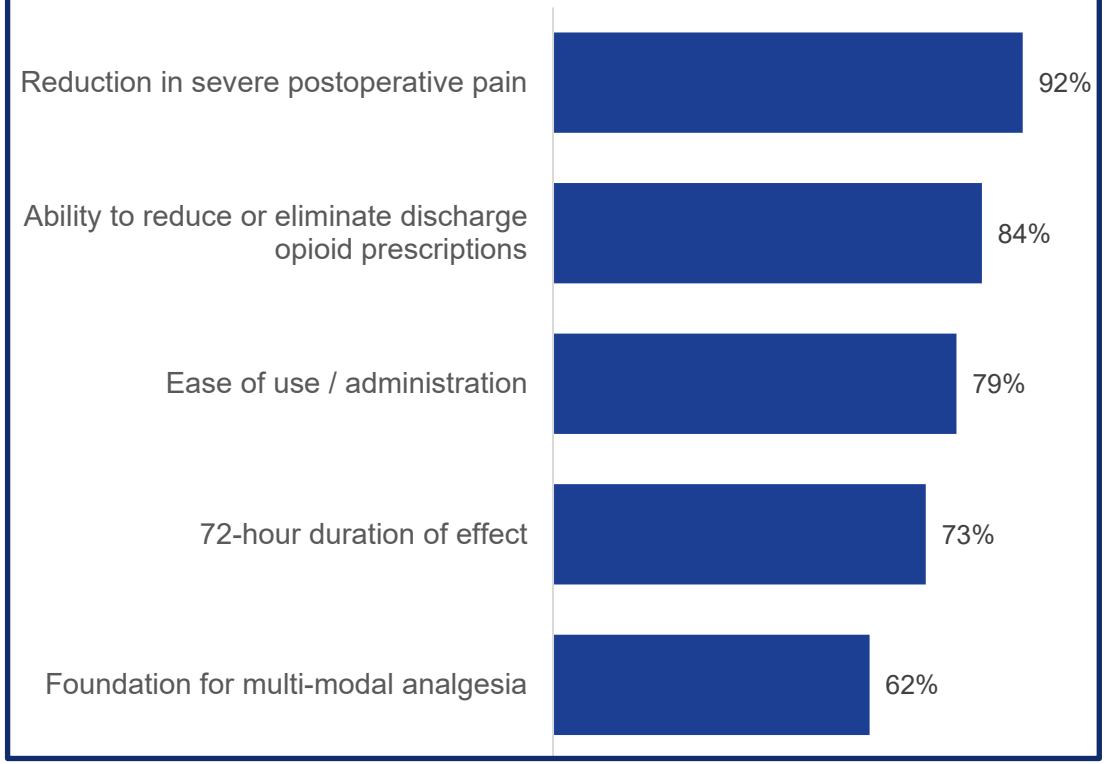
HTX-011 Is Well Positioned on Core Drivers to Create Fast Access and Uptake

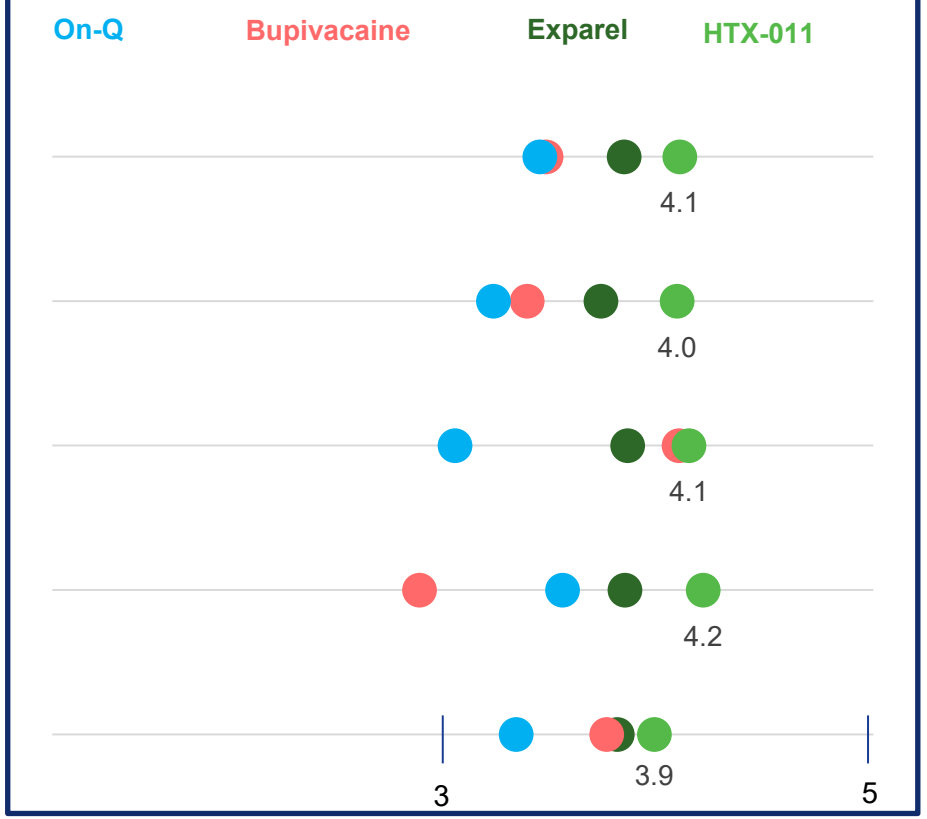
Importance of Core Attributes in Selecting a LA

Top 2 Boxes



Mean Product Rating on Core Attributes

1-5 Scale



Source: Company-sponsored ATU Study July 2020 – Survey of 386 surgeons, anesthesiologists, pharmacists, NP/Pas of potential use of an approved product with the attributes for which we are developing HTX-011

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Large Body of Peer-Reviewed Data for Launch

- Published Peer-Reviewed Manuscripts
  - EPOCH 1 Bunion (301), *Regional Anesthesia & Pain Medicine*
  - EPOCH 2 Hernia (302), *Hernia*
  - EPOCH 1 Follow-on Bunion (218), *J. Am Podiatric Med Assoc* (JAPMA)
  - EPOCH 2 Follow-on Hernia (215), *Surgery*
  - EPOCH TKA (209), *Journal of Arthroplasty*
  - Mechanism of Action, *Regional Anesthesia & Pain Medicine*
  - Truven HEOR (Opioid Naïve Users), *Journal of Managed Care & Specialty Pharmacy (JMCP)*
  - Truven HEOR, *JMCP* (*Persistent Opioid Users*), *Journal of Managed Care & Specialty Pharmacy (JMCP)*
- 38 posters and abstracts have been accepted and presented at key Congresses*

*Includes congress publications from 2016-2020 based on Preclinical and Phase 2 studies (2016-2017) and Phase 3, Phase 3 Follow-On and Retrospective studies (2018-2020). 2020 congress publications include video/audio presentations at virtual congresses.

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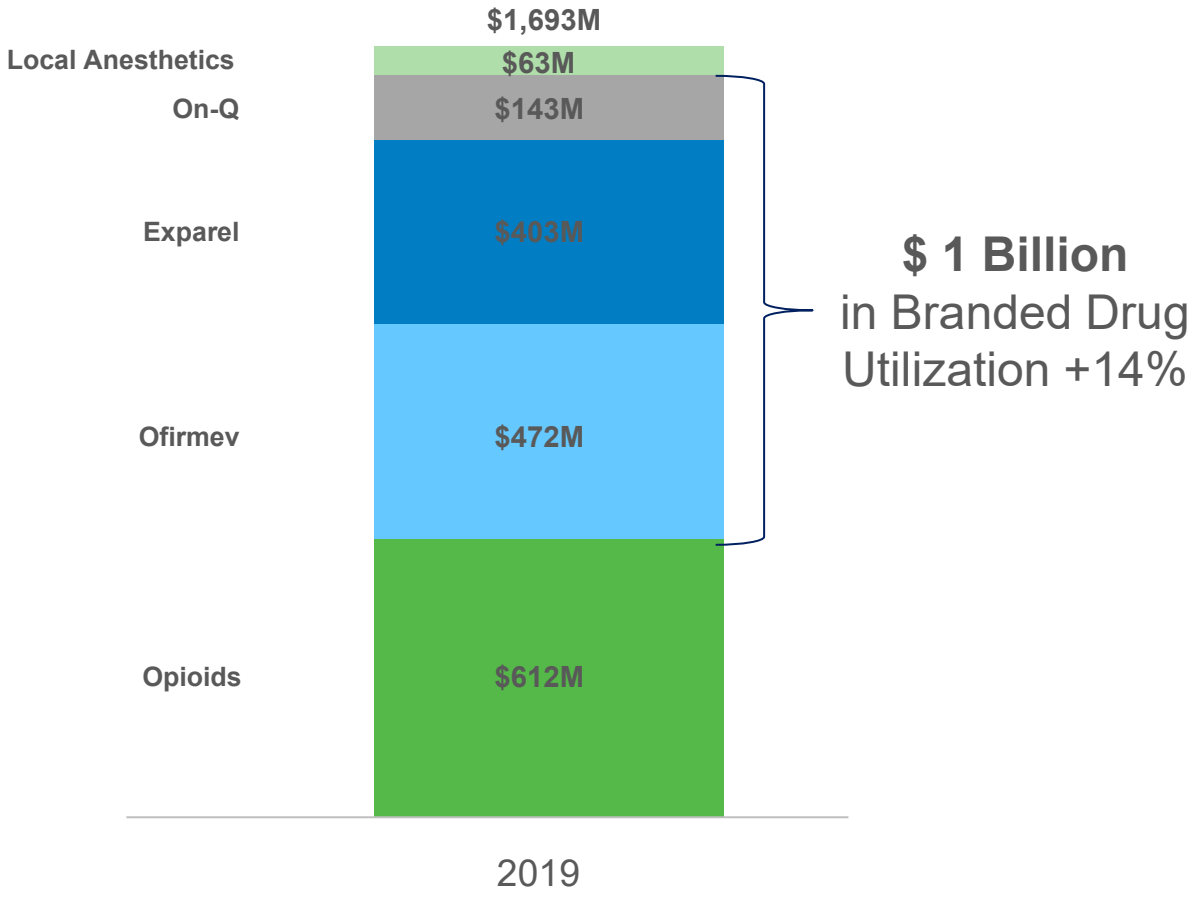
HERON THERAPEUTICS®

In 2019 Branded Use Grew to Over $1B, however, 2020 has been Impacted by COVID 19



$ 1 Billion
in Branded Drug Utilization +14%

COVID IMPACT: FY 20 vs 19				
Product	Pack Units	% Change	WAC	% Change
Bupivacaine	14.7M	11%	$31.7M	12%
Ropivacaine	1.9M	7%	$48.5M	40%
Exparel	1.3M	-4%	$386.7M	-4%
OFIRMEV	8.4M	-23%	$400.3M	-15%
Opioids	150.7M	-3%	$649.1M	6%

On-Q sales are estimated at ~$150M (down mid-single digits) / Avanos Earnings Call 11/05/19

Source: SHA Symphony Health Drug Data FY 2019, SHA Symphony Health Drug Data through 12-25-2020 – FY data forecasted

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Market Dynamics are Shifting in Favor of HTX-011 and Will Accelerate Outpatient Growth

New CMS OPPS* Rules

- CMS is eliminating the Inpatient Procedure Only (IPO) list over 3 years starting in CY 2021
  - In CY 2021 266 musculoskeletal-related procedures were removed from IPO
- CMS will continue to package non-opioid pain management products in the hospital outpatient setting but products will remain unpackaged in ASC setting at ASP plus 6 percent.
- CMS indicated they will consider outpatient unbundling with real world peer reviewed evidence of opioid prescription elimination

	HOPD* Reimbursement	ASC Reimbursement
Market Size	~6.0M Procedures	~1.3M Procedures
HTX-011	YES 3 year pass-through	YES
Exparel	NO	YES

*OPPS: Outpatient Perspective Payment System, HOPD: Hospital Outpatient Department

Source: Heron estimate for procedure volume by site of care based on 2018 DRG Claims (data 2017) / DRG revised Claims Data 2020 (data 2017).

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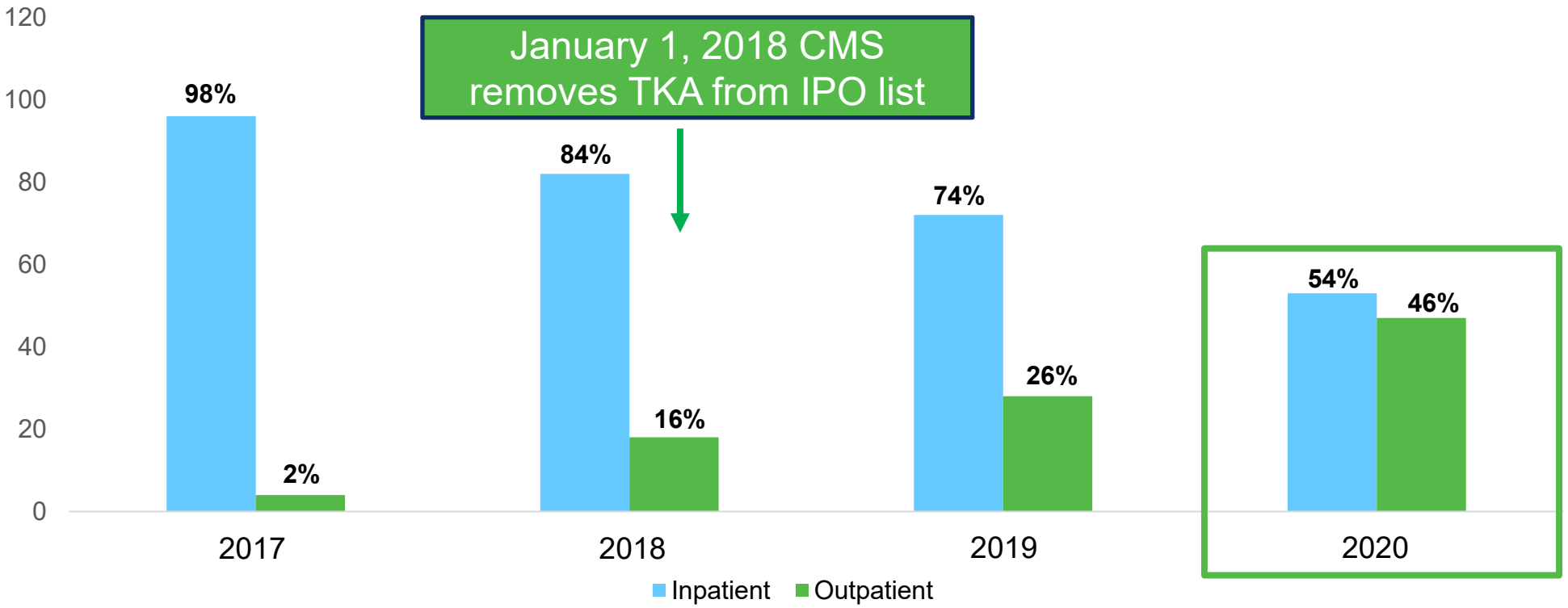
Impact of Previous CMS Rule Change on TKA

Outpatient Moved from 4% of TKA Procedures to 46% in Less Than 3 Years



Source: LexisNexis Procedure data full year 2017, 2018, 2019, 2020 data January – 12/27/20

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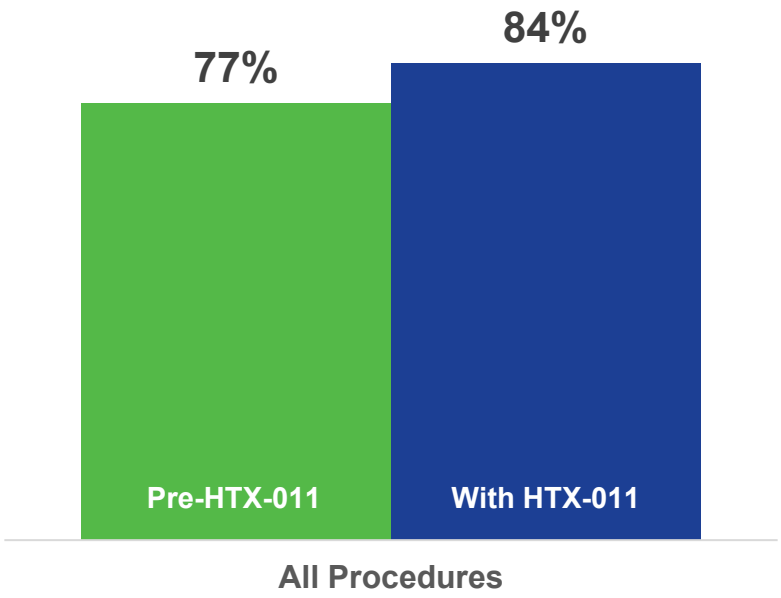
Physicians and Pharmacists Surveyed Believe HTX-011 Will Grow the Local Anesthetics Market

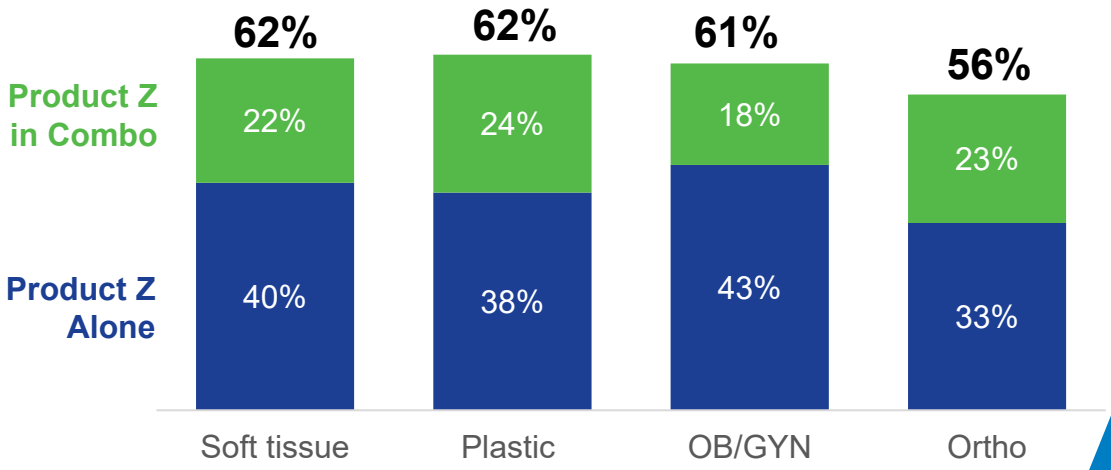
With the option of using Product Z available, respondents preferred using a local anesthetic 7% more of the time across their procedures

Across all 4 specialty groups, respondents indicate a preference for using HTX-011 (either alone or in combination*) in ~60% of procedures.

% of time LA used - all procedures



HTX-011 Usage by Specialty Group



Source: Company-sponsored ATU Study July 2020 – Survey of 386 surgeons, anesthesiologists, pharmacists, NP/Pas of potential use of an approved product with the attributes for which we are developing HTX-011

* Used in combination with other local anesthetics (LA); for example, where another LA is used as a nerve block

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Highly Focused Launch Approach: Targeting the Top 2 Specialties – Orthopedics and General Surgeons

~14M Target Procedures

Initial Targets

Highest-volume procedures in 2 major specialties

- ~6.0M Orthopedic procedures
- ~4.5M General surgery procedures
- ~2.6M OB/GYN procedures
- ~900K Plastic surgery procedures

- Ortho and general surgeons account for 10.5M procedures or 75% of the 14M initial targets
- Ortho and general surgeons account for 82% of Exparel market utilization
- Ortho surgeons are heavy influencers (P&T, new drugs, profitability) across all settings of care

Source: DRG Claims Analysis, 2016 and 2019

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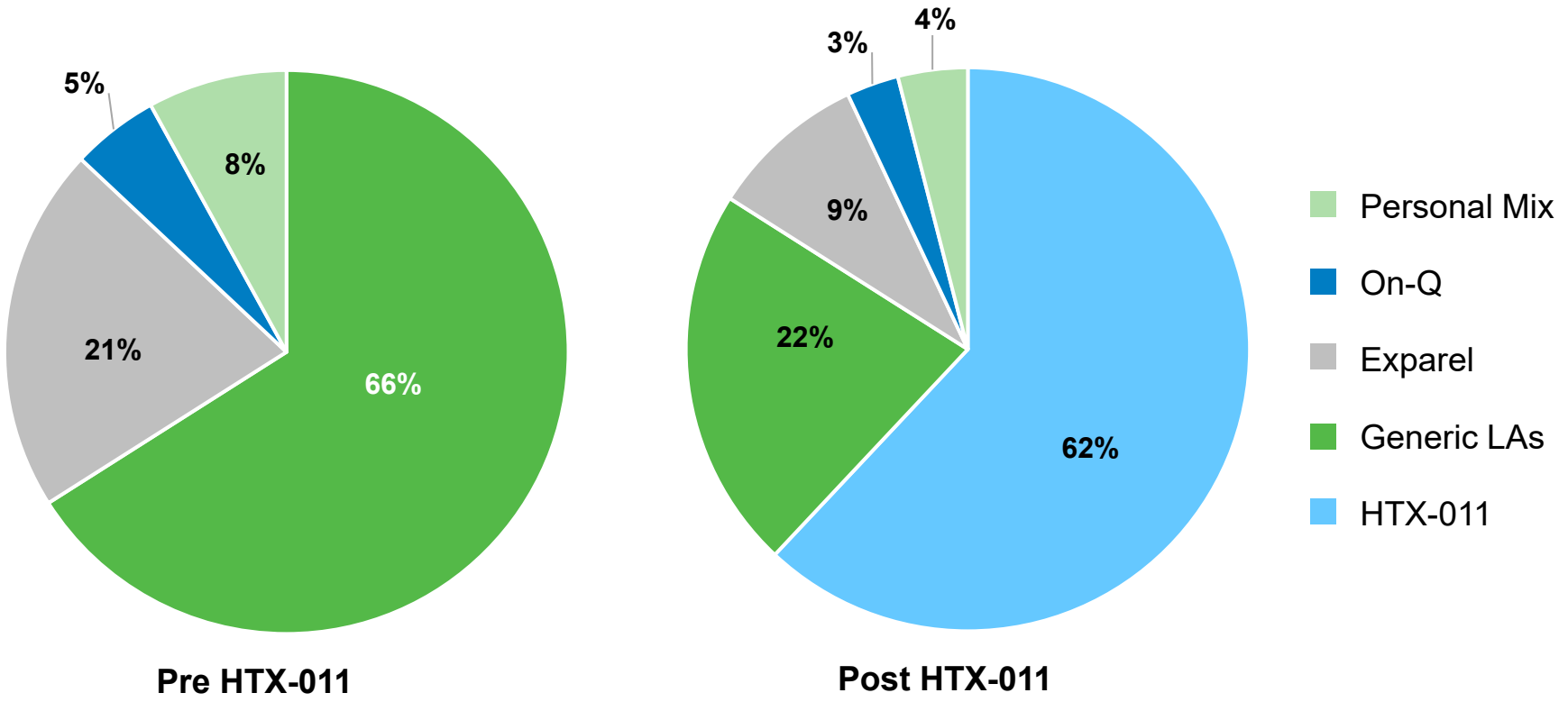
General Surgeons: HTX-011 Expected to Take Share from Other Treatment Options, With the Most Significant Being from Generic LAs

Anticipated Local Anesthetic Use - Soft Tissue Procedures



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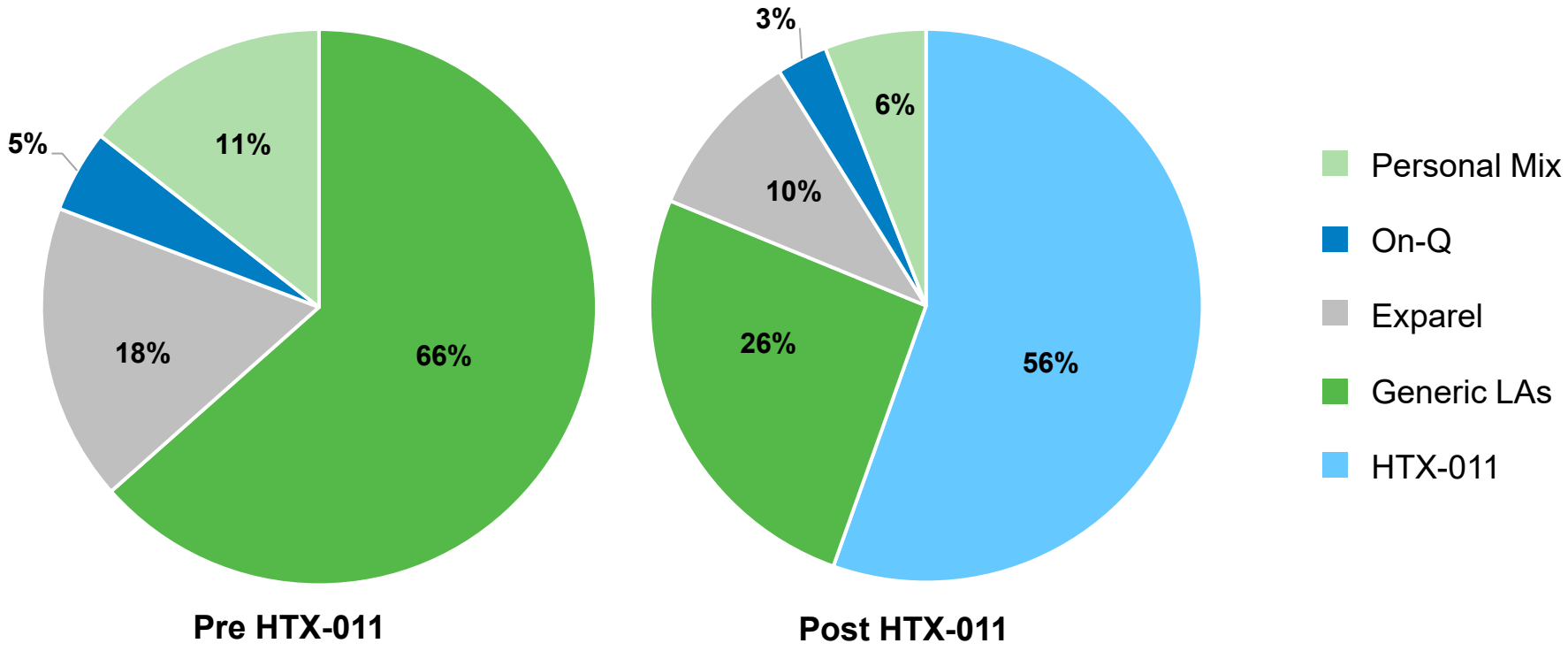
Orthopedic Surgeons: HTX-011 Expected to Take Share from Other Treatment Options, With the Most Significant Being from Generic LAs

Anticipated Local Anesthetic Use - Orthopedic Procedures



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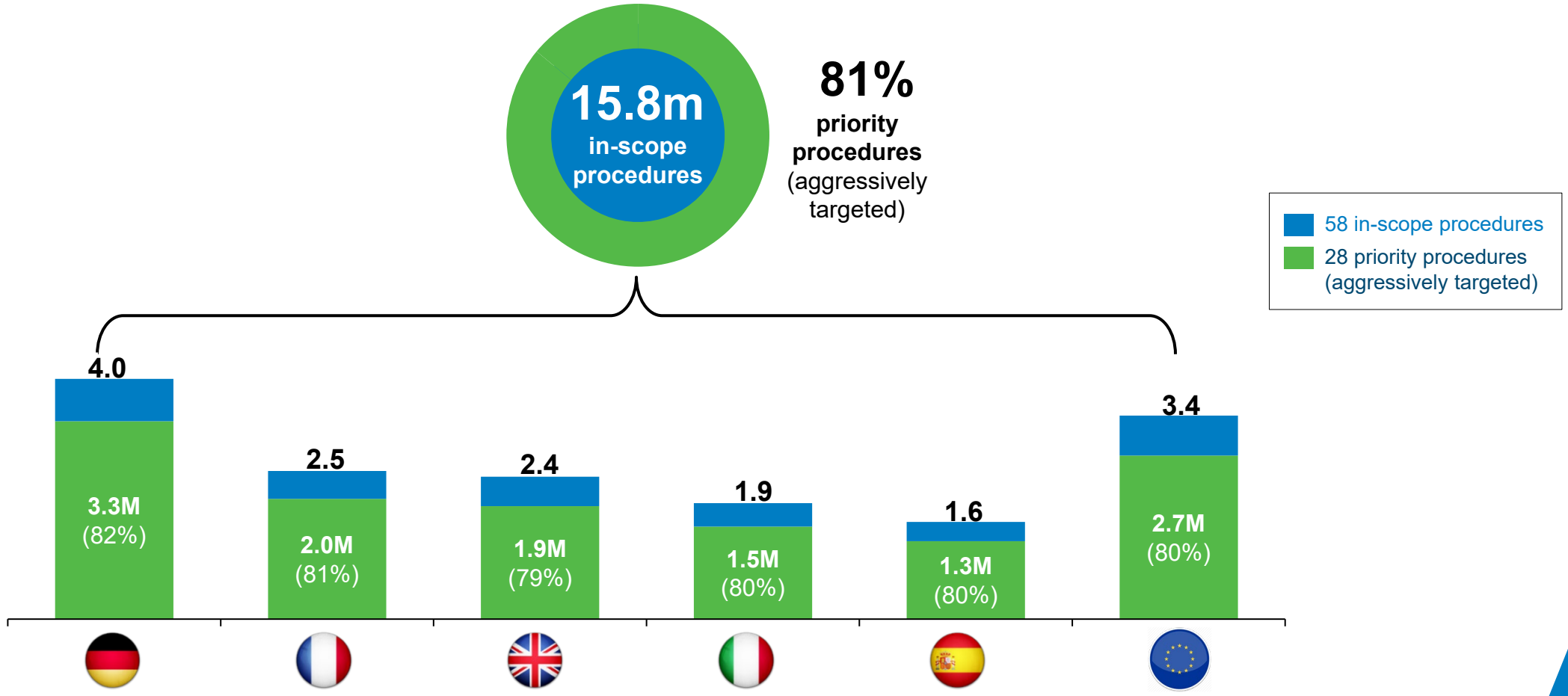
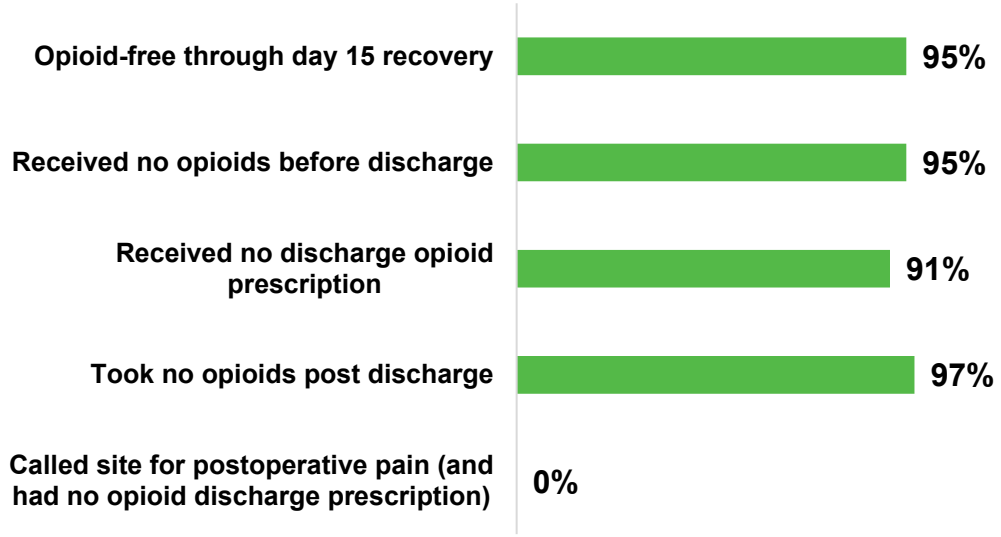
Market Opportunity for Zynrelef in Europe is ~15.8M Procedures of Which ~80% are Priority Procedures



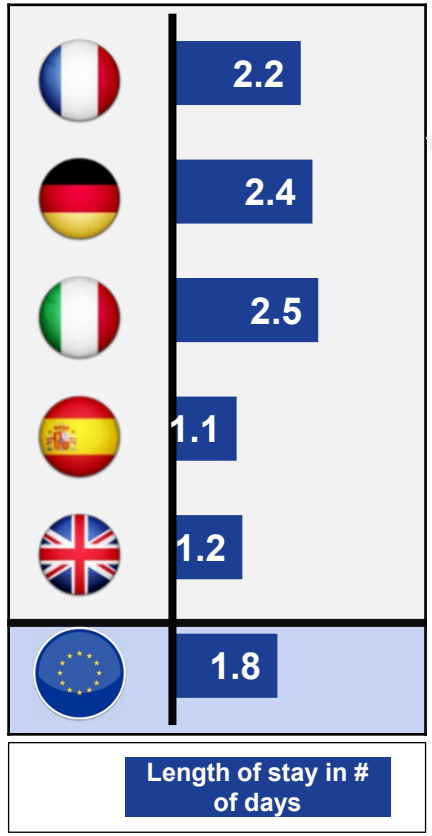
Notes: (1) In-scope procedures are those covered by current SmPC; (2) EU11 markets include Netherlands, Belgium, Luxembourg, Denmark, Sweden, Finland, Norway, Switzerland, Austria, Portugal, Ireland; (3) Based on 2018 procedure volumes data; **Sources**: National IQVIA data (2018); Regional hospital episodes data from public national statistics databases (2018); ZYNRELEF is authorized in 31 European countries for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults

There is an Opportunity in Europe to Demonstrate Significant Reductions in Hospital Length of Stay across Multiple Procedures Example: Hernia Repair (HOPE Data)

Zynrelef plus OTC analgesics resulted in patient discharged 2 to 3 hours after surgery with 95% of patients opioid-free through Day 15[1]



Average length of stay for hernia repair[2]



There is an opportunity to **demonstrate significant cost savings** through stay reductions for hernia repair and other procedures

Zynrelef may allow a **greater number of procedures to be preformed in the outpatient setting**

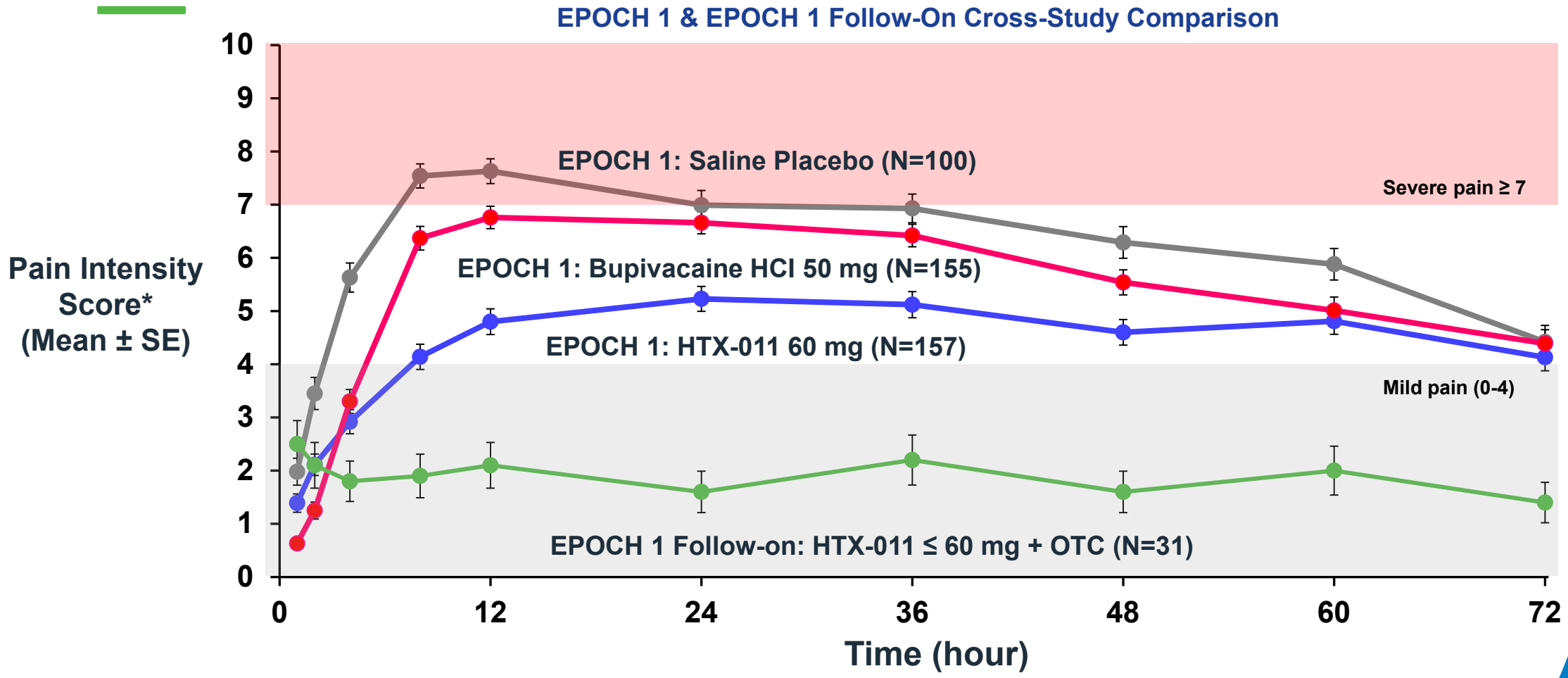
Notes: 1) Open inguinal hernia repair patients were treated with ZYNRELEF and a scheduled non-opioid oral over-the-counter (OTC) analgesic regimen (N = 93). 2) Two cohorts of patients were studied under Alternating or Concurrent multimodal analgesia (MMA) regimens. Alternating regimen (N=46): OTC regimen of ibuprofen 600 mg every 6 hours (q6h) alternated 3 hours later with acetaminophen 1 g q6h. Concurrent regimen (N=47): OTC regimen of ibuprofen 600 mg and acetaminophen 1 g, taken together q6h. 3) Opioids were only prescribed at discharge for patients who rated their pain at ≥6 (NRS) or received opioid rescue medication prior to discharge. 4) Average length of stay (LOS) for 58 surgical procedures Heron is initially targeted based ZYNRELEF's ability to address unmet needs and commercial considerations. In a survey of 304 physicians in EU5, 58 procedures were defined by wound size (small, medium and large), and classified by length of stay. The mean LOS was determined by market, specialty, and procedure.
Sources: 1) Data on file. Study ZYNRELEF-304. San Diego, CA: Heron Therapeutics Inc; 2019. 2) Heron Therapeutics EU Physician Survey (2020).

HTX-011 Clinical Development

Postoperative Pain

EPOCH 1 (Bunionectomy) and Follow-on Study

EPOCH 1 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours



Using Numeric Rating Scale (NRS) with window worst observation carried forward (wWOCF)
OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h
EPOCH 1: Reg Anesth Pain Med. 2019;44:700-706. EPOCH 1 Follow-on accepted for publication in J. Am Podiatric Med Assoc (JAPMA)

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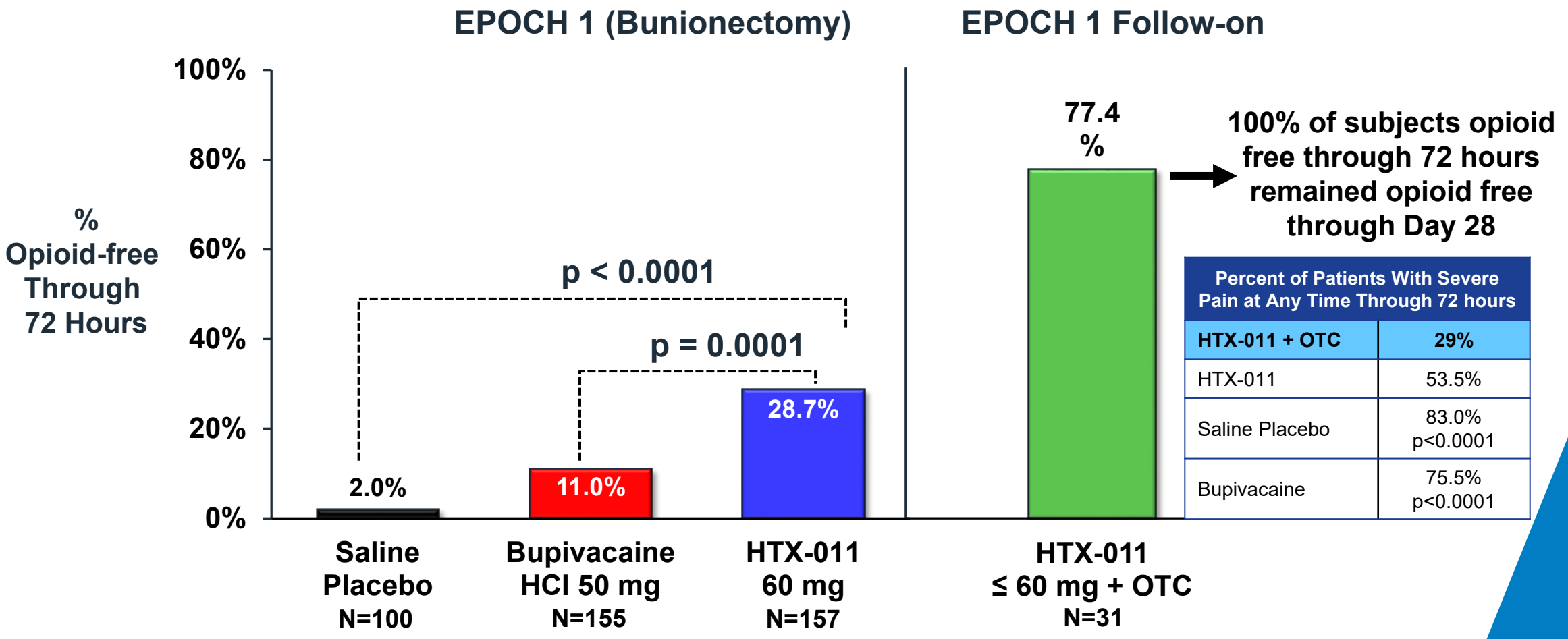
HTX-011 Significantly Reduced the Proportion of Patients Experiencing Severe Pain and Increased Proportion of Opioid-Free Patients



Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011 + OTC	**29%**
HTX-011	53.5%
Saline Placebo	83.0% p<0.0001
Bupivacaine	75.5% p<0.0001

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

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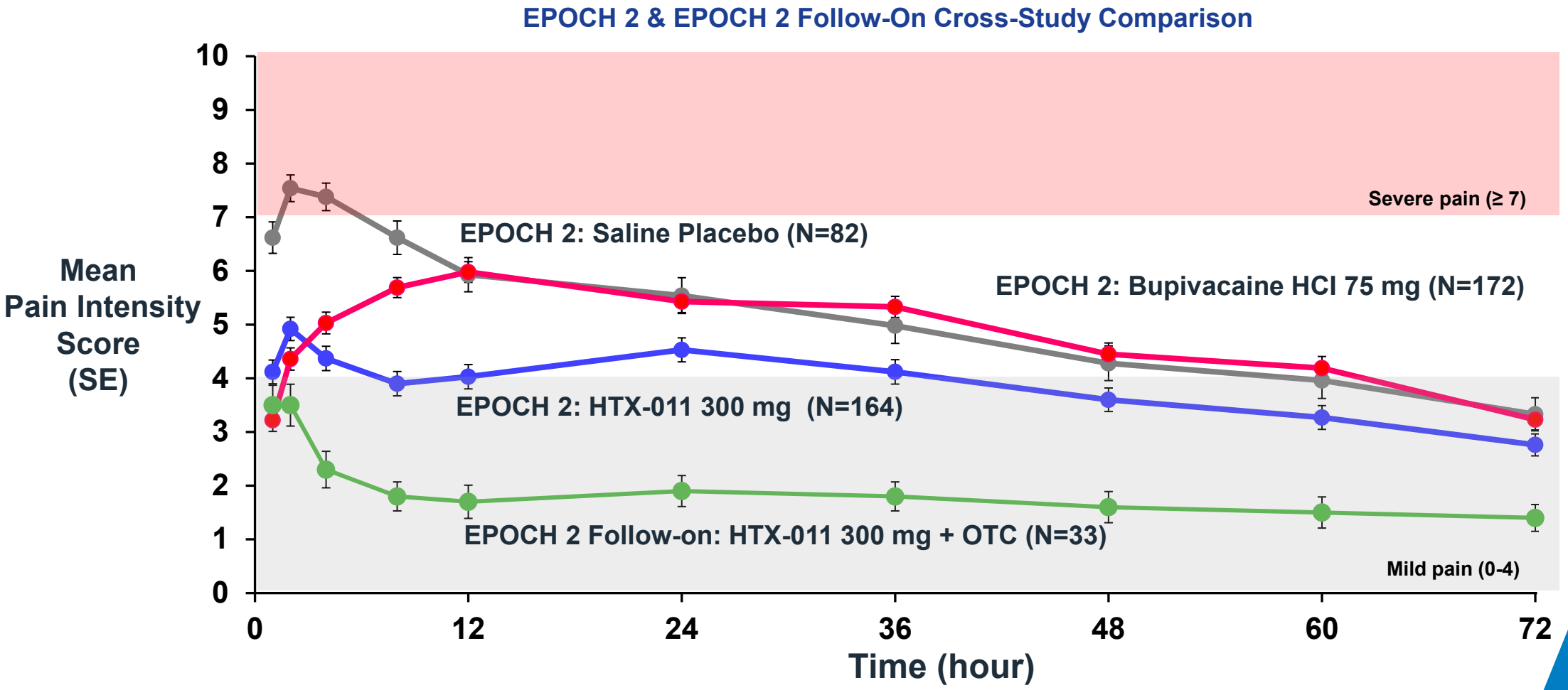
EPOCH 2 (Herniorrhaphy) and Follow-on Study

EPOCH 2 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours



OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

EPOCH 2: published online Hernia. doi: 10.1007/s10029-019-02023-6. EPOCH 2-Follow-on: Surgery. doi: 10.1016/j.surg.2020.06.036

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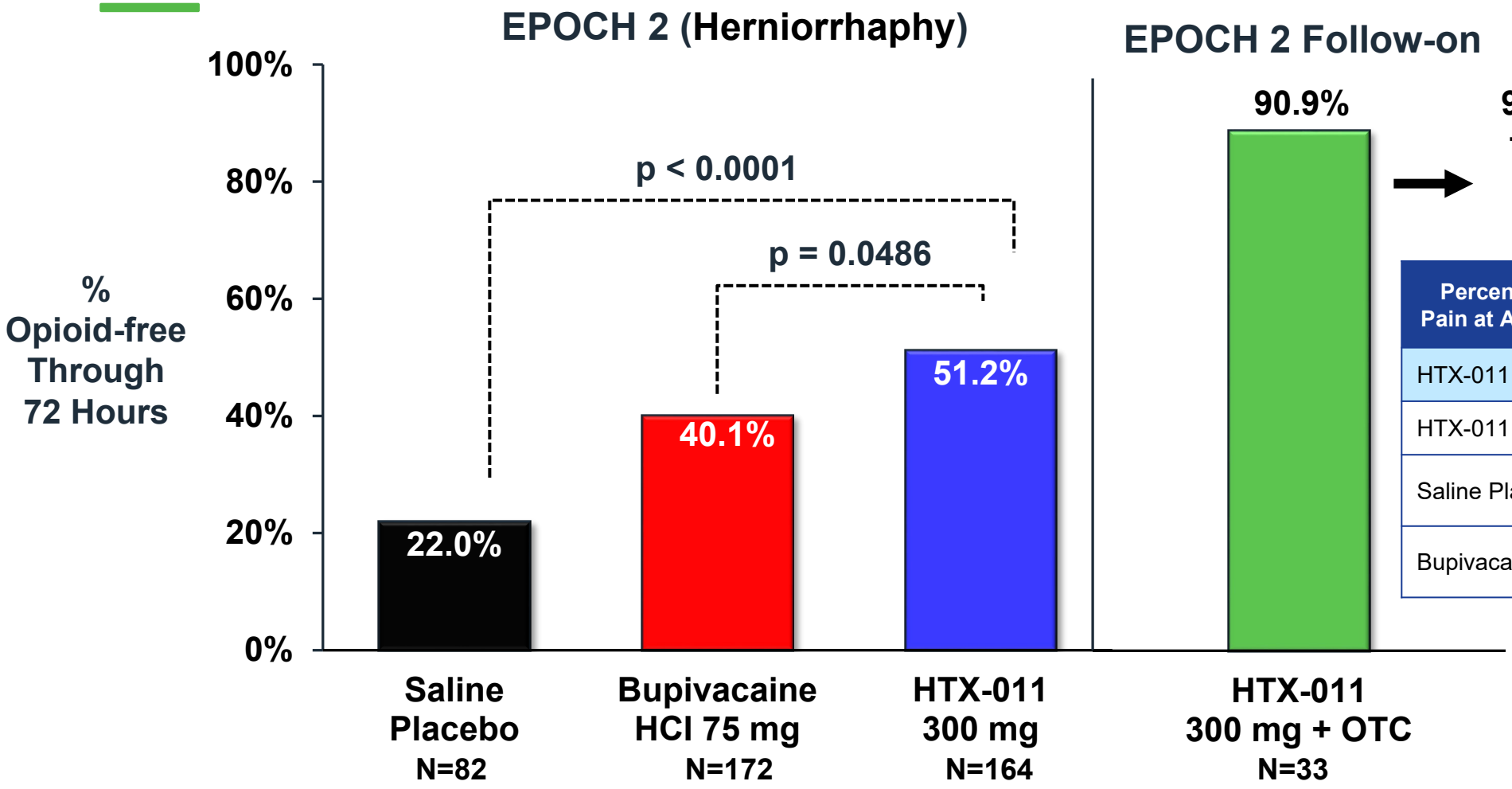
HTX-011 Significantly Reduced the Proportion of Patients Experiencing Severe Pain and Increased Proportion of Opioid-Free Patients



93% of subjects opioid free through 72 hours remained opioid free through Day 28

Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011 + OTC	15.2%
HTX-011	48.8%
Saline Placebo	81.7% p<0.0001
Bupivacaine	60.5% p=0.0372

OTC = Over the counter analgesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

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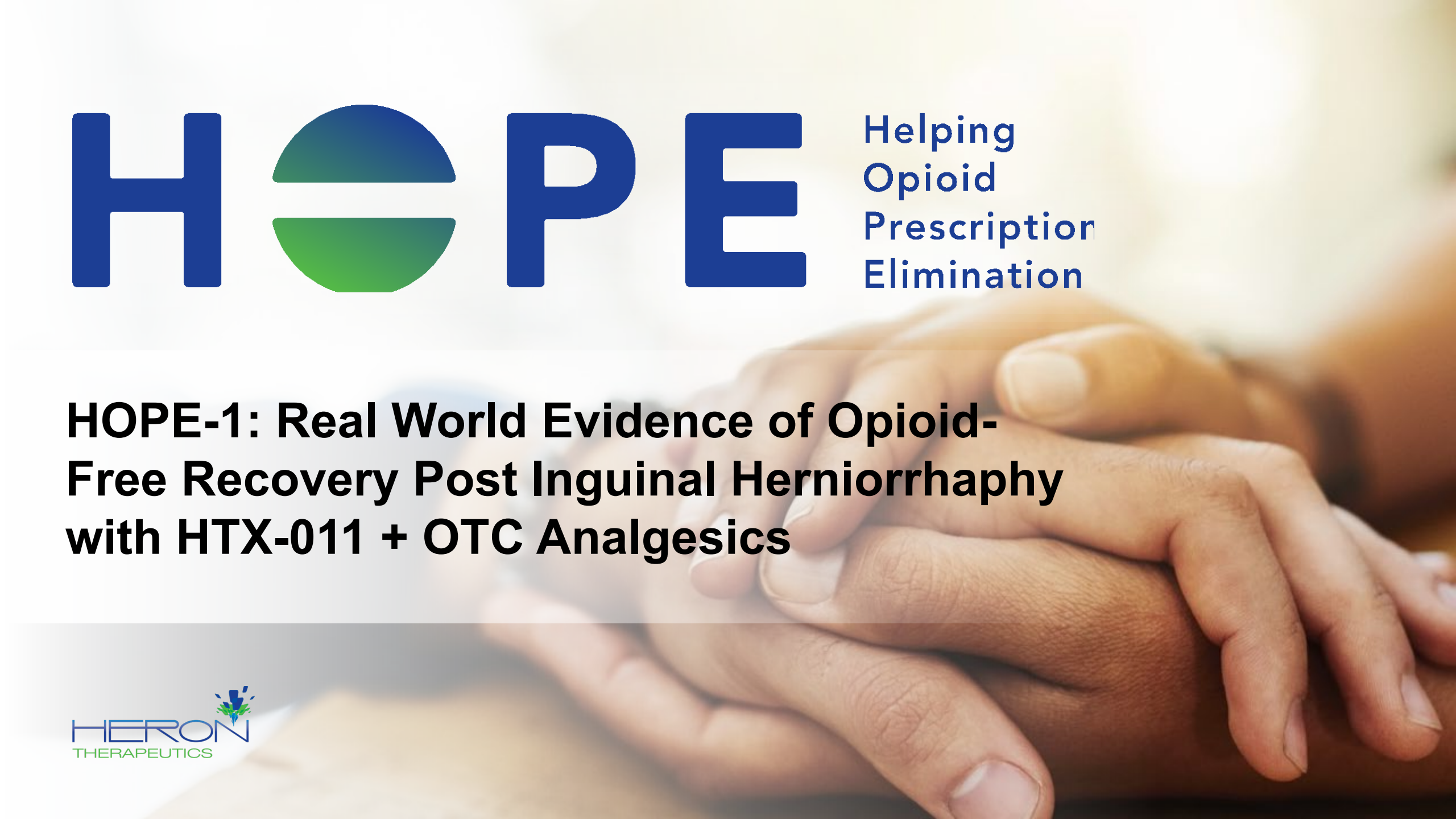

HOPE-1: Real World Evidence of Opioid-Free Recovery Post Inguinal Herniorrhaphy with HTX-011 + OTC Analgesics

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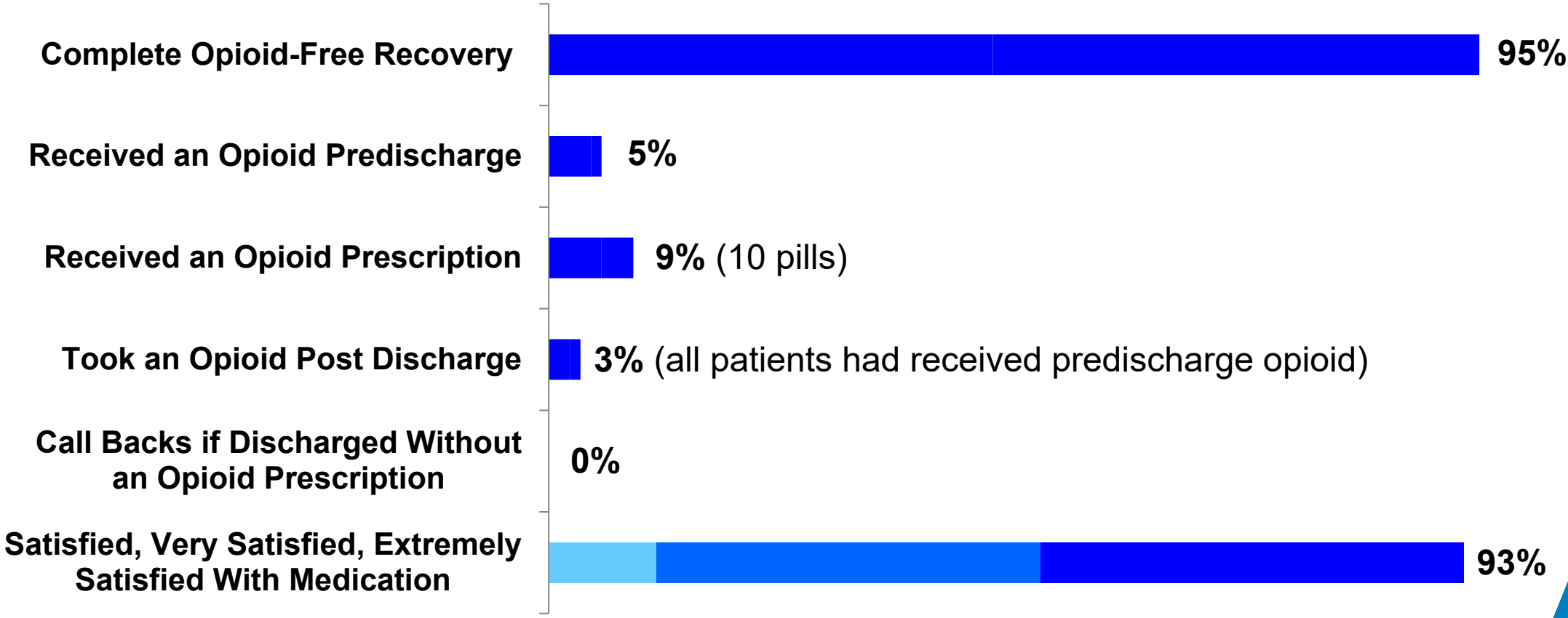
HOPE-1: Near Total Opioid-Free Recovery with HTX-011 + OTC



N=93 in initial pilot program
Presented at the American Society of Health-System Pharmacists (ASHP) Midyear 2019 Congress, December 8-12, 2019, Las Vegas, NV.

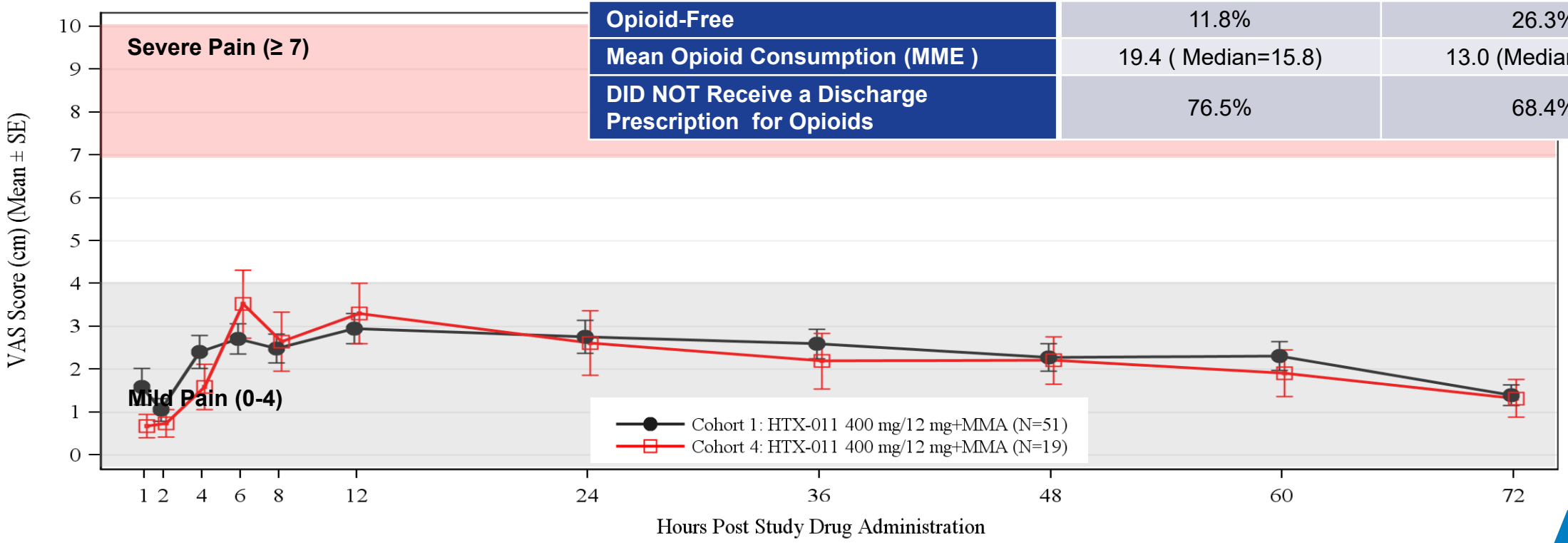
HTX-011 is an investigational new drug and not approved by the FDA

Not actual health care provider.

Study 306 Total Knee Arthroplasty (TKA)

Study 306 TKA: HTX-011 + Generic Non-Opioid Analgesics* Kept Pain in the Mild Range Through 72 Hours With Low Opioid Consumption and Up to 26% Opioid-Free

	Study 306	
	HTX-011 + APAP + celecoxib (Cohort 1, n=51)	HTX-011 + APAP + ibuprofen (Cohort 4, n=19)
Mean AUC12-48 VAS Pain	145.4	125.7
Opioid-Free	11.8%	26.3%
Mean Opioid Consumption (MME)	19.4 (Median=15.8)	13.0 (Median = 5.0)
DID NOT Receive a Discharge Prescription for Opioids	76.5%	68.4%



- Cohort 1 patients received oral acetaminophen 1000 mg every 8 hours (maximum 3000 mg/d) and oral celecoxib 200 mg every 12 hours for 72 hours. Mont doi: 10.1016/j.arth.2017.07.024
- Cohort 4 patients received over the counter analgesic regimen of acetaminophen 1000 mg q8h and ibuprofen 600 mg q6h for 72 hours

LOCF for missing pain data

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

HTX-011 Safety Summary

HTX-011 was generally well tolerated across all Phase 2 and Phase 3 studies with no clinically meaningful differences from placebo and bupivacaine 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
- No deaths on HTX-011 (one on bupivacaine)

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HTX-034 Development

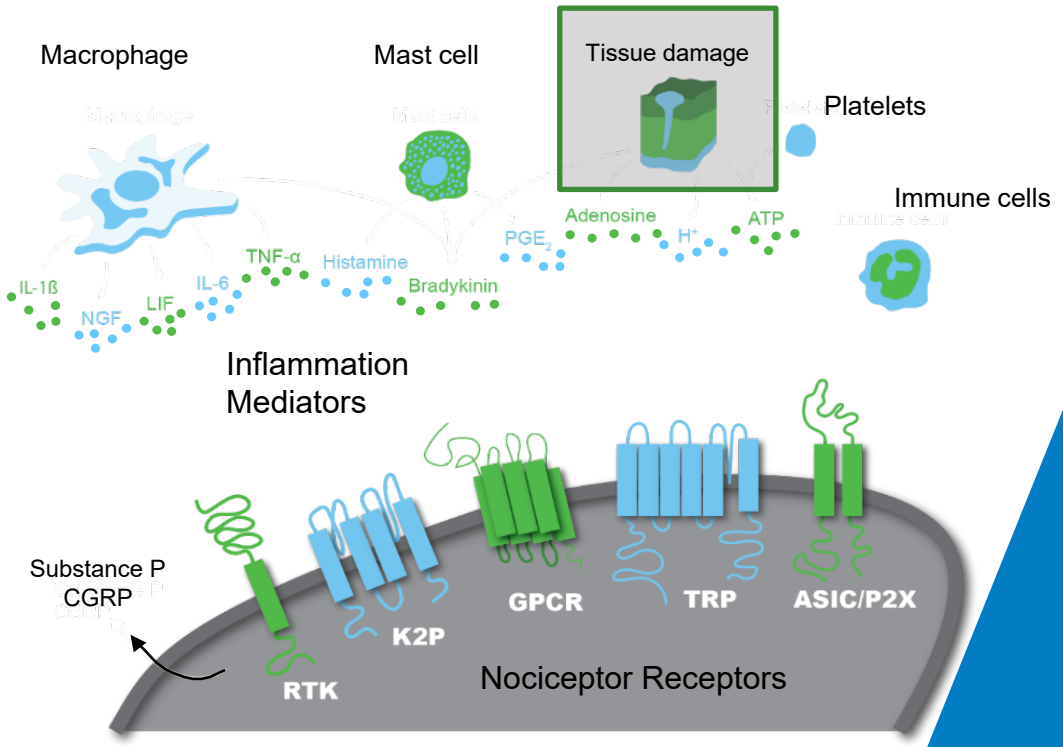
Next Generation Product for Postoperative Pain

In Addition to Changes in pH, Inflammation From Surgery Modifies Pain Pathways and Can Produce Hyperalgesia

Local tissue damage activates a variety of cells, which release inflammatory mediators[1,2]

HTX-034, an investigational non-opioid, is a fixed-dose combination, extended-release solution of the local anesthetic bupivacaine, the nonsteroidal anti-inflammatory drug meloxicam and aprepitant, an additional agent targeting the inflammatory process that further potentiates the activity of bupivacaine

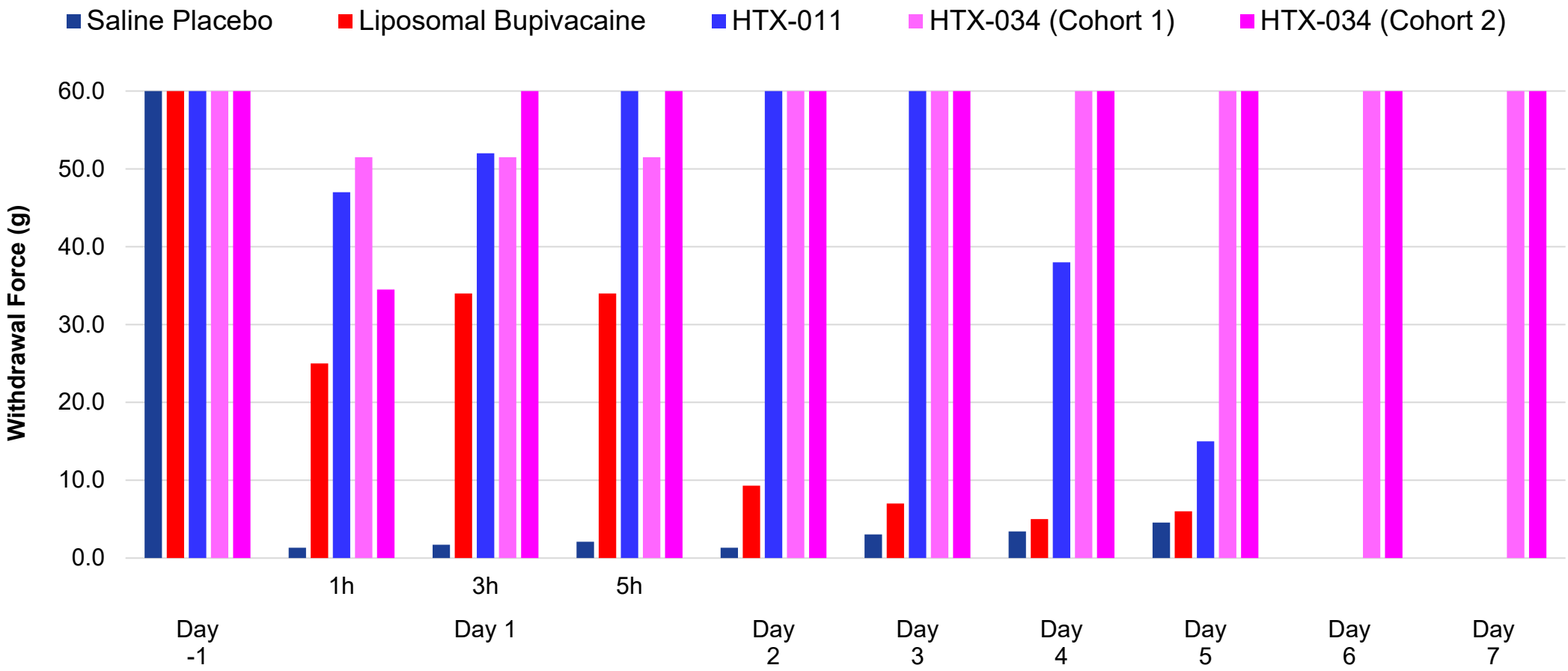
Peripheral mediators of inflammation



References: 1. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med*. 2004;140(6):441-451. **2.** Basbaum AI, Bautista DM, Scherrer G, Julius D. Cellular and molecular mechanisms of pain. *Cell*. 2009;139(2): 267-284.

HTX-034 is an investigational new drug and not approved by the FDA

HTX-034 Produces Complete Elimination of Pain Through 7 Days in Pig Postoperative Pain Model



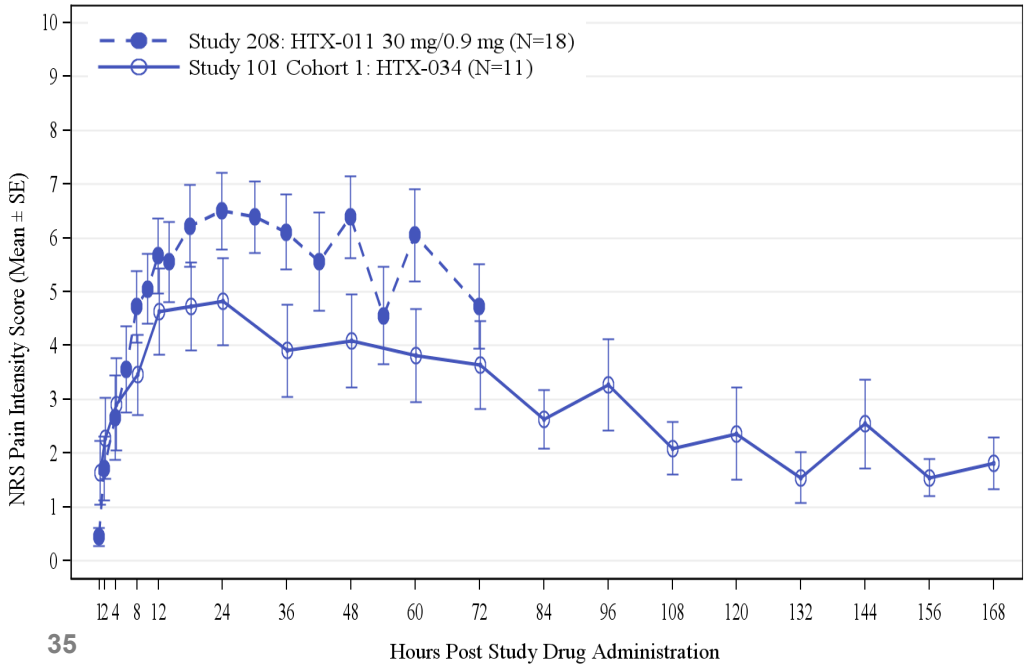
Data from multiple animal experiments using a validated postoperative pain model in pigs from Castle et al, 2013 EPJ

HTX-011 & HTX-034 are investigational new drugs and not approved by the FDA

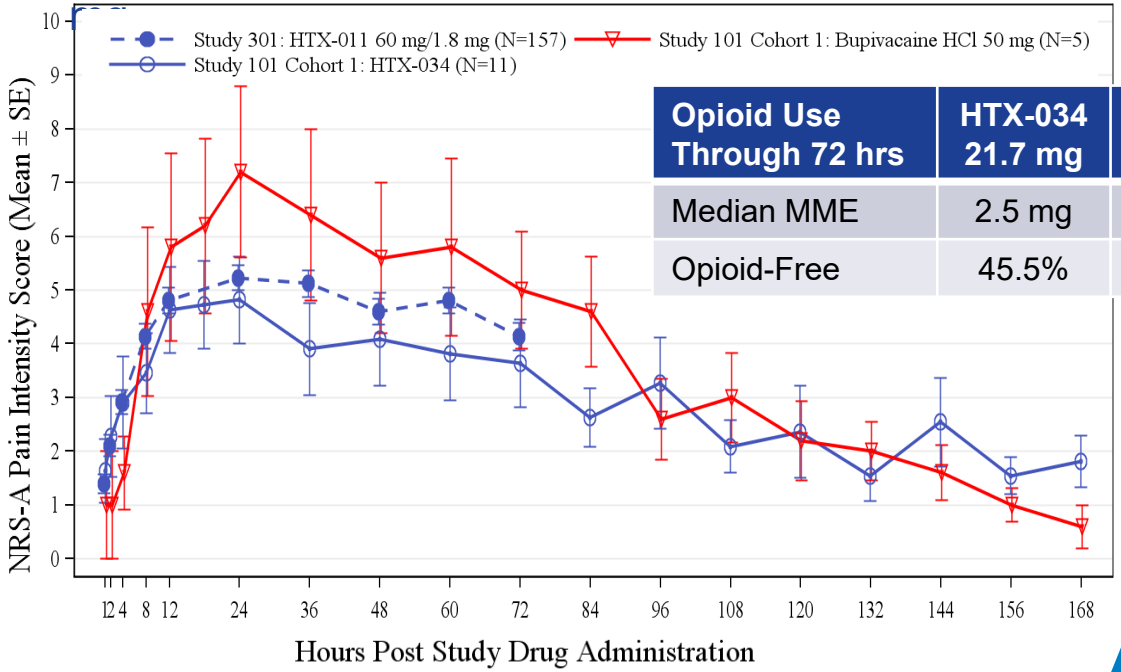
HTX-034 21.7 mg Produced Greater Pain Reduction and Lower Opioid Use than HTX-011 30 mg in Study 208 or HTX-011 60 mg in Study 301

- These cross-study comparisons confirm that addition of aprepitant in HTX-034 enhanced the activity of bupivacaine in the formulation
- 45.5% of patients receiving HTX-034 21.7 mg opioid-free through Day 15 without scheduled MMA
- **Phase 2 initiated in 1Q2021**

HTX-034 21.7 mg vs HTX-011 30 mg



HTX-034 21.7 mg vs Matched Bupivacaine and HTX-011 60



Opioid Use Through 72 hrs	HTX-034 21.7 mg	HTX-011 30 mg	HTX-011 60 mg
Median MME	2.5 mg	17 mg	12.5 mg
Opioid-Free	45.5%	16.7%	28.7%

HTX-034 Phase 1b Safety Summary

HTX-034 was well tolerated with no:

- Clinically meaningful differences in adverse events
- Serious adverse events
- Premature discontinuations due to adverse events
- Local anesthetic systemic toxicity (LAST)
- Wound healing related adverse events

HTX-019 for Postoperative Nausea and Vomiting (PONV)

HTX-019 is an investigational new drug for PONV and not approved by the FDA

PONV

- PONV is a large market ~20x the size of CINV
- HTX-019 has significant potential advantages over oral aprepitant and fosaprepitant
- IND active, BE to oral aprepitant demonstrated and 505(b)(2) NDA for PONV prevention planned for Q4 2021
- Several hundred million dollar a year potential market opportunity, taking the majority of the oral aprepitant market and use in high risk procedures

HTX-019 is an investigational new drug for PONV and not approved by the FDA

Aprepitant Efficacy – Large Differential in Vomiting Episodes Compared to Ondansetron*

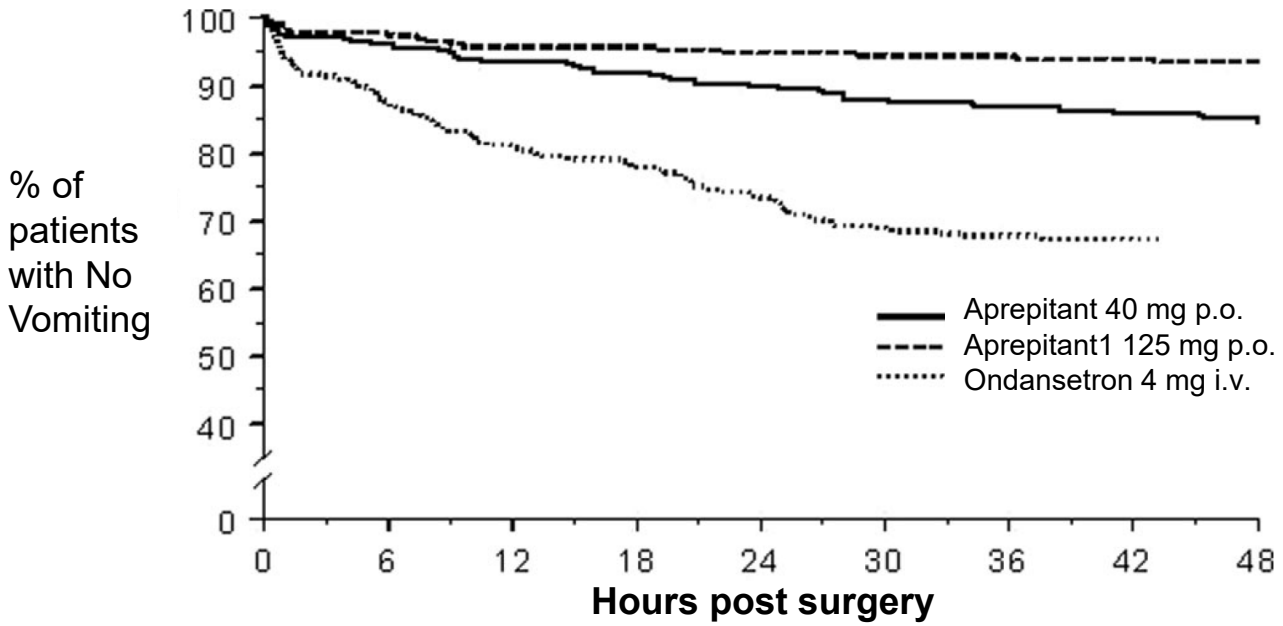


Figure 5. Kaplan-Meier curves for the time to first vomiting during the 48 h following surgery. The time to first vomiting was delayed by aprepitant; *P* 0.001 based on the log-rank test.

Aprepitant delayed the time to first vomiting episode compared with ondansetron.

*Published results from Gan TJ, et al. *Ambul Anesth*. 2007; 1082-89.

2020 Cochrane Meta-Analysis Concluded That Aprepitant is the Most Effective Drug for PONV*

Out-comes	Effects and confidence in the estimate of effects (network meta-analysis)											
	Aprepitant*		**Ramosetron***		**Granisetron***		**Dexamethasone***		**Ondansetron***		**Fosaprepi-tant***	**Droperidol***	
Vomiting (or dry retching) within 24 hours postoperatively													
Total studies: 282; total participants: 50,812; number of treatments: 65 (36 drug combinations, 28 single drugs, placebo)													
Place-bo (com-para-tor) 300 per 1000[a] (30%)	**RR 0.26** (0.18 to 0.38) Net-work esti-mate	222 few-er per 1000 (246 fewer to 186 fewer)	**RR 0.44** (0.32 to 0.59) Network estimate	168 fewer per 1000 (204 few-er to 123 fewer)	**RR 0.45** (0.38 to 0.54) Network estimate	165 fewer per 1000 (186 few-er to 138 fewer)	**RR 0.51** (0.44 to 0.57) Network estimate	147 fewer per 1000 (168 few-er to 471 fewer)	**RR 0.55** (0.51 to 0.60) Net-work esti-mate	135 few-er per 1000 (147 fewer to 120 fewer)	**RR 0.06** (0.02 to 0.21) Net-work esti-mate	282 fewer per 1000 (294 few-er to 237 few-er)	**RR 0.61** (0.54 to 0.69) Network estimate	117 few-er per 1000 (138 few-er to 93 fewer)
	⊕⊕⊕⊕ **High** Confidence in network estimate		⊕⊕⊕⊕ **High** Confidence in network estimate		⊕⊕⊕⊕ **High** Confidence in network estimate[1]		⊕⊕⊕⊕ **High** Confidence in network estimate[1]		⊕⊕⊕⊕ **High** Confidence in network esti-mate[1]		⊕⊕⊕⊖ **Moder-ate** Confidence in network esti-mate due to incoherence		⊕⊕⊖⊖ **Moderate** Confidence in net-work estimate due to publication bias and heterogeneity[1,2]	

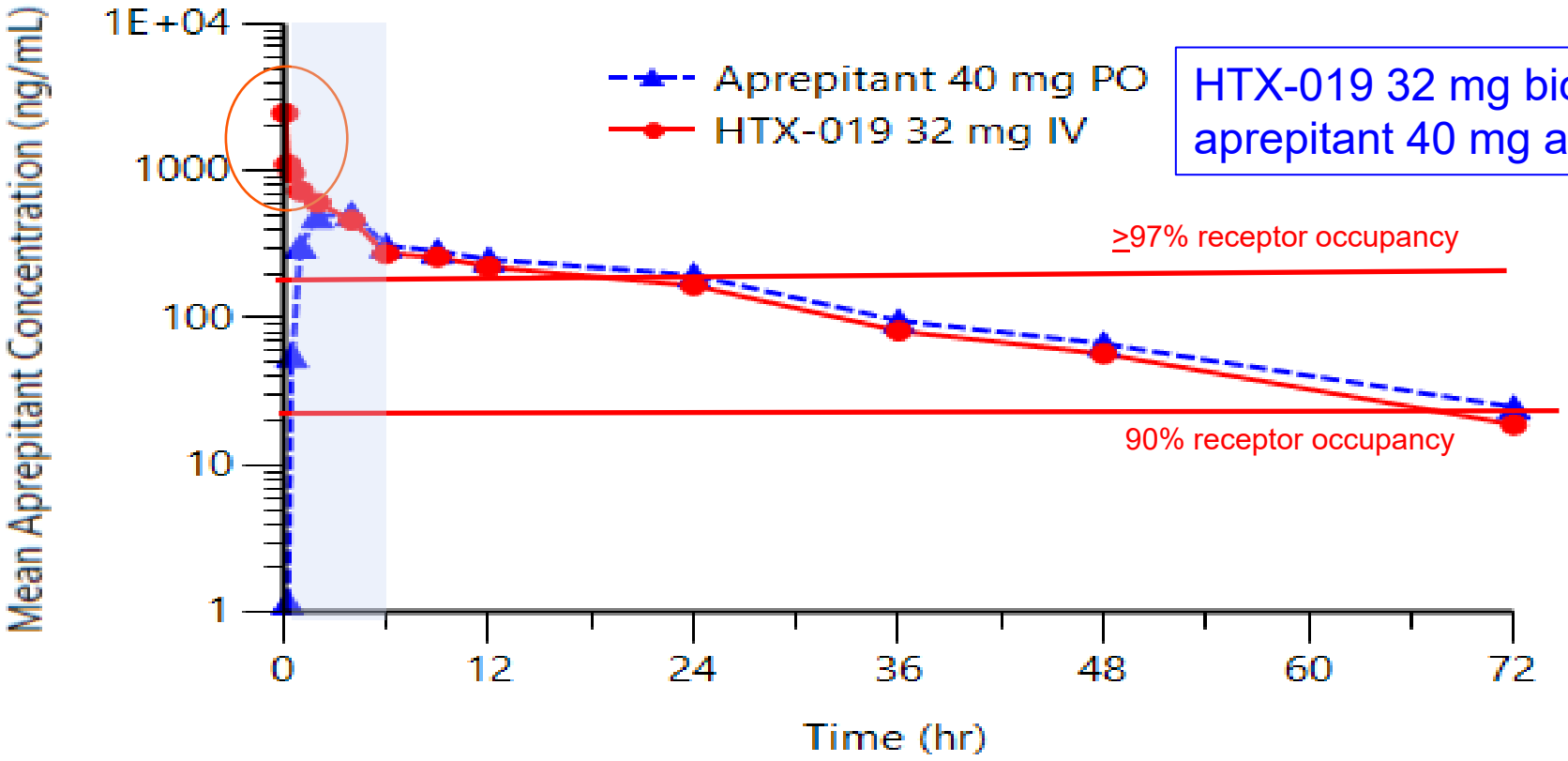
Approximately 100 fewer patients vomiting per 1000

*Weibel S, Rücker G, Eberhart LHJ, Pace NL, Hartl HM, Jordan OL, et al. *Cochrane Database of Systematic Reviews*. 2020

HERON THERAPEUTICS

100% Receptor Occupancy Should Occur Much Faster With HTX-019 IV Push Than Aprepitant Oral

Very high peak levels should quickly drive drug into the brain with 100% receptor occupancy during high risk period



HTX-019 32 mg bioequivalent to oral aprepitant 40 mg approved for PONV

HTX-019 is an investigational new drug for PONV and not approved by the FDA

41

PONV Market is >20X the size of the CINV Market

PONV ~53M Treatments vs. ~2.5M CINV Treatments

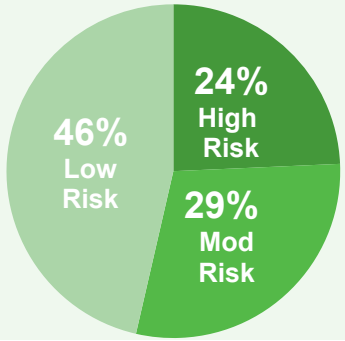
Patient Population & Market Size

Diagnostics

~26M

US Diagnostic Procedures at Risk of PONV in 2020

Patients by PONV Risk



Surgeries

~39M

US Surgical Procedures at Risk of PONV in 2020

- **Approximately 65M diagnostic and surgical procedures are at risk of resulting in PONV in the US**
- **More than half of these patients are at moderate to high risk of PONV**

Prophylaxis Patients

~35M

PONV Prophylaxis Patients in 2020

PONV Rescue Patients

~13M

PONV Rescue Patients in 2020

~5M

2nd Line Rescue in 2020

Source: *PONV quantitative survey DRG June 2020*

HERON THERAPEUTICS

42

Target ~ 14M Surgical Procedures Where PONV is High Clinical Concern

~39M Surgical Procedures that Could Result in PONV

Key Surgical Types where Postoperative Emesis could be Clinically Concerning

Abdominal (GI and OB)

As vomiting directly involves the gastrointestinal tract, emesis can directly injure surgical sites that involve this organ system

CV / CT

Retching and vomiting can lead to transient increases in blood pressure which can result in damage/disruption of arterial surgical sites

Cranial

Intracranial pressure increases during emesis, cranial surgeries, such as craniotomy, are at elevated risk of poor outcomes due to PONV

~14M

"High Clinical Concern" Procedures in 2020

(36% of all Surgical Procedures)

~5M Clinically Concerning Cases of PONV

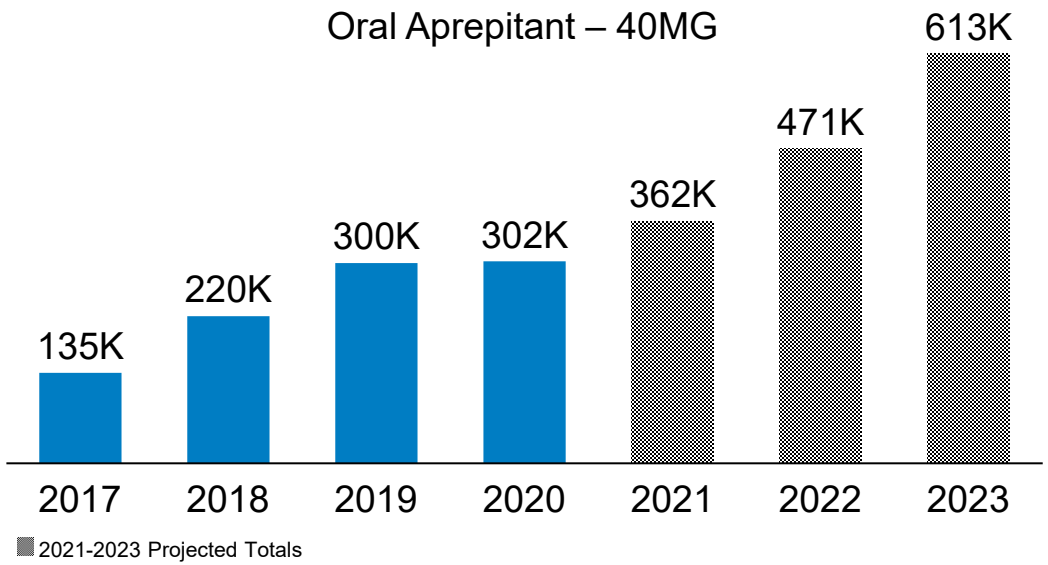
(35% of patients undergoing these procedures may develop PONV despite prophylaxis)

HCPs are more likely to take an aggressive approach managing PONV in cases where postoperative emesis could have a negative impact on the patient's clinical outcomes

Source: *PONV quantitative survey DRG June 2020*

HERON THERAPEUTICS

Oral Aprepitant is Already Rapidly Growing with No Promotion, Product Limitations and High Acquisition Cost



- Oral Aprepitant volume is growing rapidly at premium price despite no promotion
  - Q2'20 WAC ~ $88/capsule
  - Acquisition cost: $43 - $64 per capsule[1]
- **~ 1,100** current ordering accounts[2]

- **HTX-019 advantages vs. Oral Aprepitant**
  - Flexible 30-second IVP vs. oral administration
  - Onset of action – 5 minutes vs. 1 to 3 hours
  - Heron product promotion efforts
- **Strategic fit with HTX-011**
  - Same commercial organization
  - Same Hospital & ASC targets
  - Same surgeon, anesthesiology & pharmacy targets
- **More convenient formulations of NK-1 class are needed based on existing PONV guidelines**

Source: 1 Banner Health, 2 IQVIA DDD Non-Retail data Q4'20

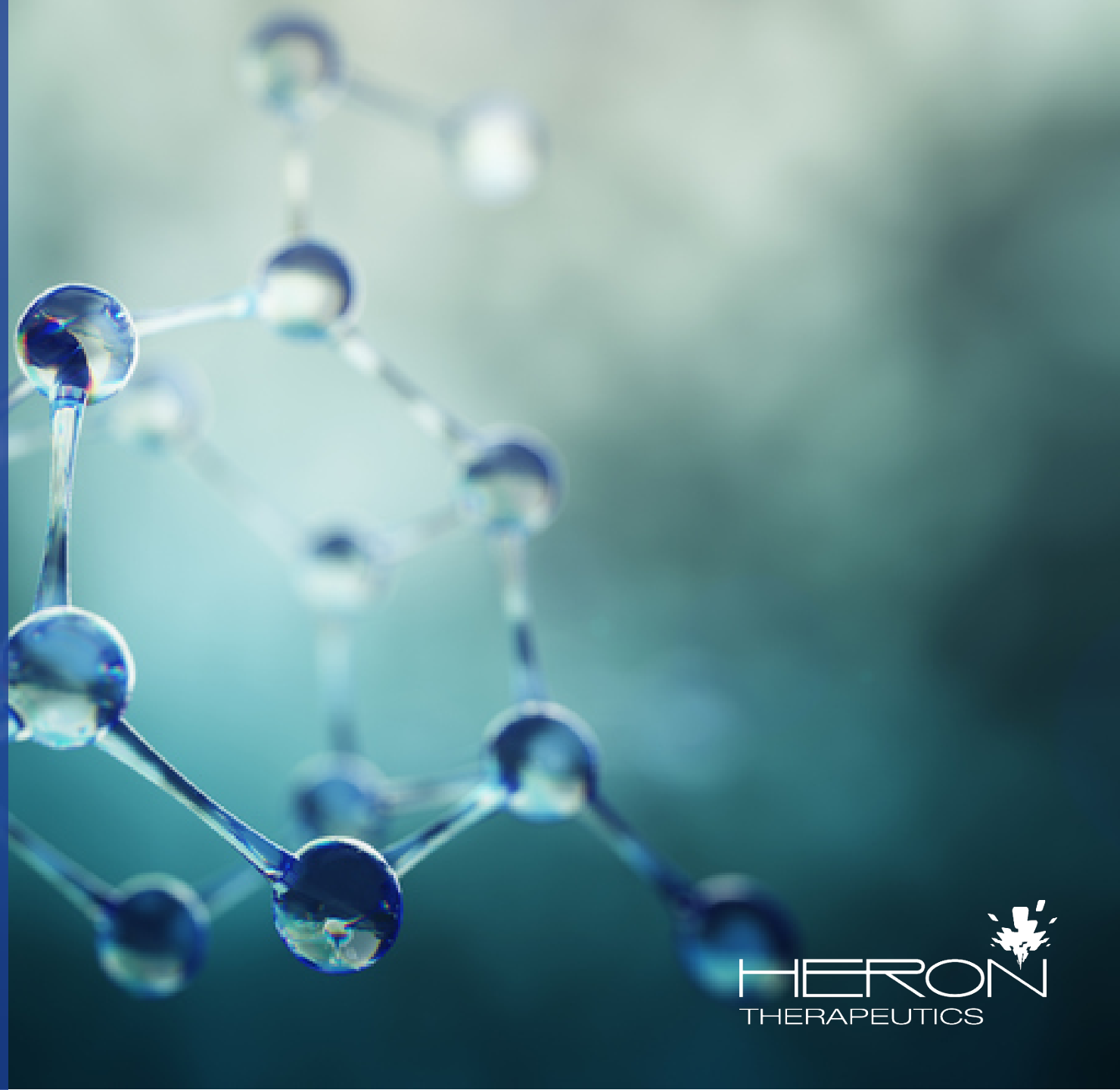
HTX-019 is an investigational new drug for PONV and not approved by the FDA

HTX-019 for PONV is Ideal Strategic Fit for Heron

- Large market ~ 14M target surgical procedures with significant unmet need for more convenient formulations of NK-1 class drugs
- Potential Significant Advantages of HTX-019
  - 30-second IV Push injection with immediate onset of action
  - Aprepitant is the most effective therapeutic agent for emesis
  - 505(b)(2) regulatory pathway for existing asset
  - Existing contract manufacturers
- Synergies with HTX-011 commercial organization
  - Same target accounts and target audiences
  - Capacity & access advantages of adding a 2nd product to promote
  - Minimal incremental investment will improve ROI

HTX-019 is an investigational new drug for PONV and not approved by the FDA

CINV Franchise Q1’21 Review



HERON THERAPEUTICS

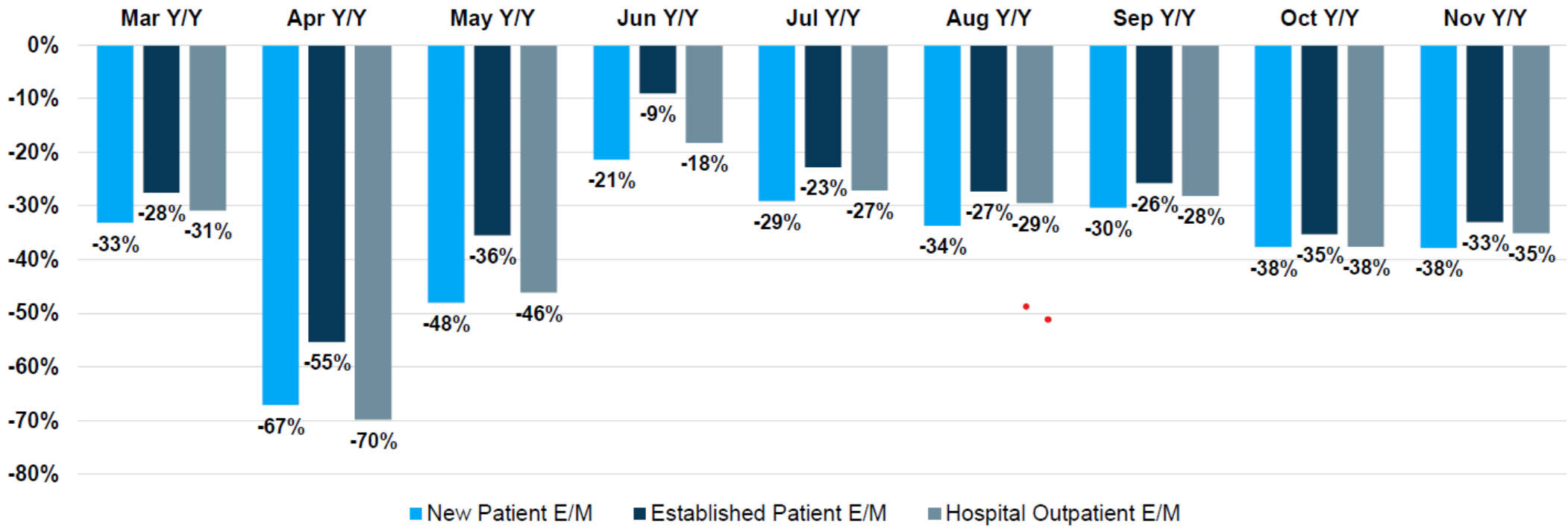
CINV Franchise 2021 Outlook

- Q1’21 sales trajectory was slower than expected due to:
  - reduction in the clinic anti-emetic market due to COVID-related reductions in cancer screening and patients visits
  - Continued aggressive competition from IV Akynzeo and final quarter of the IV EMEND arbitrage
- Recent wins in new and returning customers will support 10% - 20% growth in Q2’21 vs. prior quarter
  - Recently signed a long-term agreement with one of the largest buying groups to switch to CINVANTI
- CINV unit ramp-up will continue throughout 2021 and will be back-end loaded
  - Extensive COVID-19 vaccinations will increase new patient starts and re-open live customer access for sales force
- Virtually all HEC and majority of MEC regimens utilize 5HT3 + NK-1, thus the backlog of patients coming into treatment creates opportunities for both products
- **Maintaining 2021 full-year CINV Franchise net product sales guidance of $130M to $145M**

Barriers to Care Caused by COVID-19 Complications Have Resulted in Significant Reductions in Patient Visits

Relative Change in Billing Frequencies for Cancer-Related E/M Services

(March-November 2019 vs. March-November 2020)



The relative change in utilization was higher for new patient E/M than established patient E/M, which could reflect patient reluctance to visit providers due to COVID-19 concerns, as well as lowered rates of screening

Avalere Health and COA analysis of Inovalon Provider Clearinghouse data published online ahead of publication in the November issue of JCO Clinical Cancer Informatics. Supported, in part, by Amgen, BMS, Daiichi-Sankyo, Eisai, Janssen, Genentech & Pfizer
Note: Claims on average represent 5-7% of Medicare FFS nationally and include CMS-1450 claims from Institutional providers and CMS-1500 claims from Non-Institutional or Professional providers

E/M – Evaluation and management

HERON THERAPEUTICS

Review of Q1’21 CINV Market Dynamics

COVID-19 Impact on Clinics

- Year-over-year (March – Nov. 2020): cancer screening procedures declined **~ 25%** on average[1]
  - Mammogram, colon, lung & prostate

- Year-over-year (March – Nov. 2020): new & established patient visits declined **~ 35%** on average[1]

- Q1’21 weekly average anti-emetic units declined vs. Q4’20[2]
  - 5HT3 units declined **14%**
  - NK-1 units declined **3.7%**

CINV Competitive Factors

Two unexpected events occurred in Q1’21:

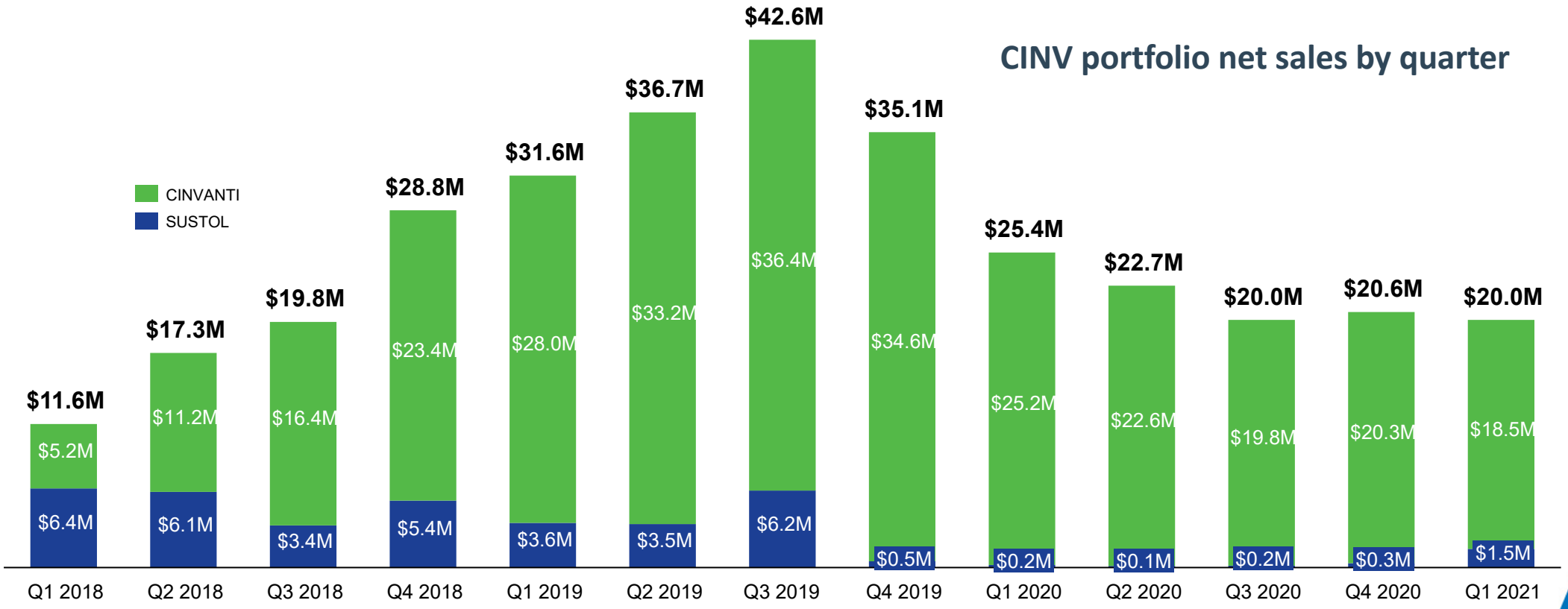
- IV Akynzeo ASP reimbursement of $696 in Q1’21 vs. $375 in Q3’20 allowed for greater contracting value[3]
  - Q2’21 ASP reimbursement drops to $641[3]
  - Unit volume past year: 22k – 27k per QTR[2]
- IV fosaprepitant arbitrage continued for another quarter with drop in acquisition costs for generic down to ~$30 compared to projected $40 leading to improved NCR with $63 ASP reimbursement in Q1’21[3]
  - Q2’21 ASP reimbursement drops to $51[3]

Sources [1]: Avalere Health & COA analysis of Inovalon Provider Clearinghouse data published online ahead of publication in the November issue of JCO
[2]: IMS DDD Weekly 3-26-2021 [3]: All ASP reimbursement based on CMS quarterly files

HERON THERAPEUTICS

Even with a 35% Decline in Patient Visits in Q4, Heron's CINV Portfolio Overall was Flat

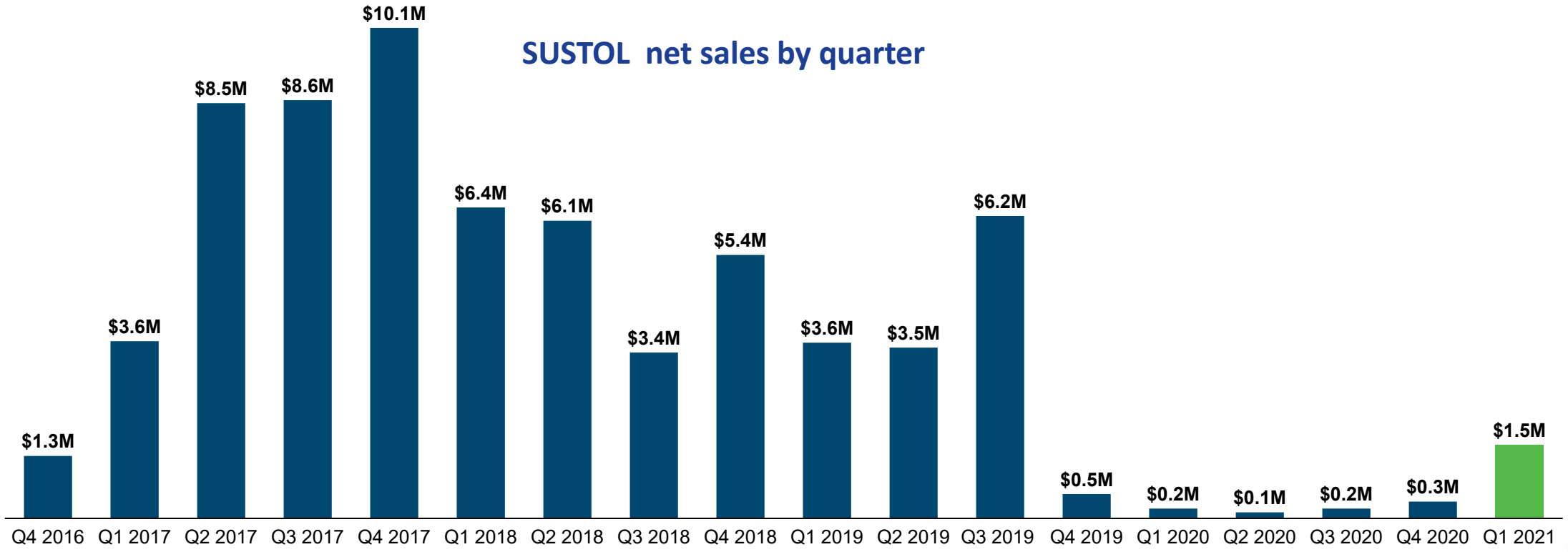
- CINVANTI units are expected to increase in Q2 and build throughout 2021
- SUSTOL sales began to rebound after reinstating promotion & contracting in Q1



Note: SUSTOL sales from Q4 2016- Q4 2017 of $32.05M not shown in graph

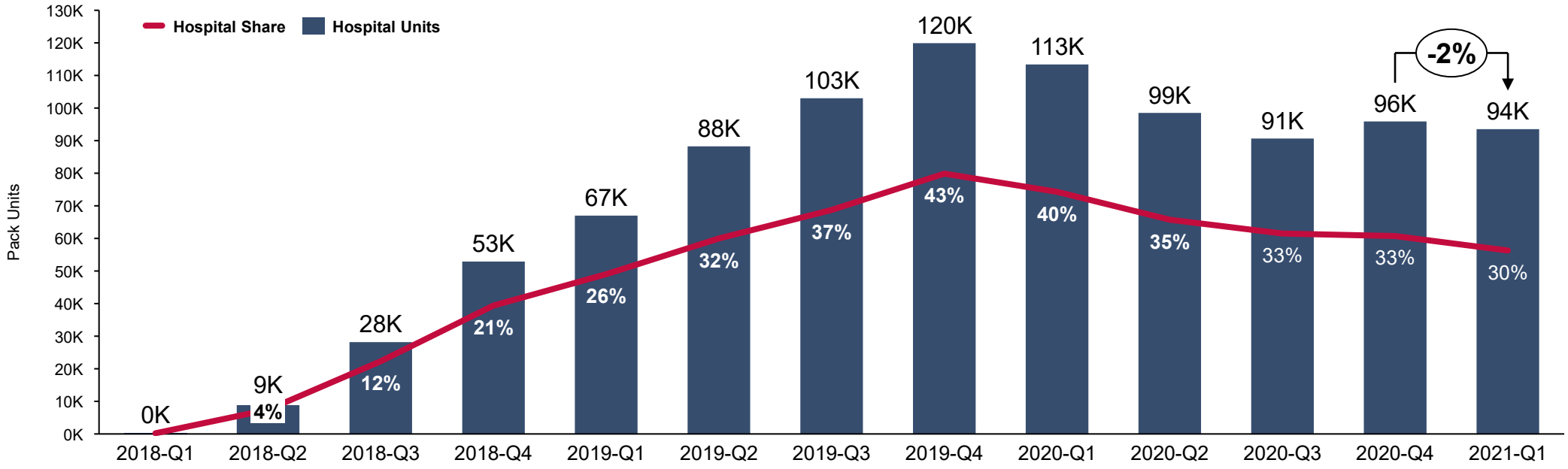
HERON THERAPEUTICS

SUSTOL Refresh Program Completed & Return to Growth in Q1



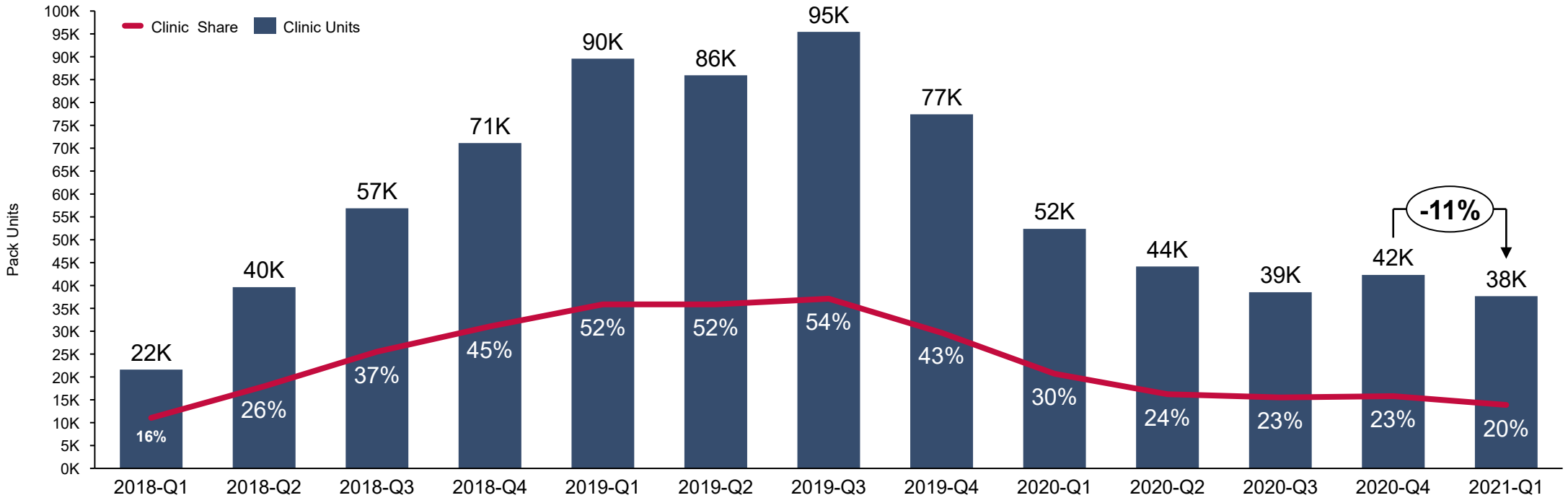
HERON THERAPEUTICS

CINVANTI – Hospital Units Generally Maintained During the Past Year Despite Significantly Lower Acquisition Cost of Generic Emend IV



SOURCE:867 4.21.21, : IMS DDD 4.2.21

CINVANTI – Clinic Units have Declined Due to the Emend IV Generic Arbitrage & Offer Significant Potential for Growth in 2021



SOURCE:867 4.21.21, : IMS DDD 4.2.21

Financial Summary

Heron expects that its cash, cash equivalents and short-term investments of $166.5 million as of March 31, 2021 will be sufficient to fund its operations into 2022.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended March 31, 2021
Net product sales	$ 20,018
Operating expenses[1]	72,132
Other income (expense)	(500)
Net loss[1]	$ (52,614)
Net loss per share[2]	$ (0.58)
Net cash used in operations	$ (41,938)

Condensed Balance Sheet Data (In thousands)	March 31, 2021
Cash, cash equivalents and short-term investments	$ 166,466
Accounts receivable, net	$ 38,525
Total assets	$ 310,932
Total stockholders' equity	$ 196,225

Common shares outstanding as of March 31, 2021 totaled 91.4 million.

[1] Includes $11.5 million of non-cash, stock-based compensation expense for the three months ended March 31, 2021.
[2] Based on 91.4 million weighted-average common shares outstanding for the three months ended March 31, 2021.

HERON THERAPEUTICS

Key Catalysts in Pain Management, CINV and PONV Franchises

Acute Care Product Portfolio		Oncology Care Product Portfolio
HTX-011 & HTX-034 for Postoperative Pain	**HTX-019 for PONV**	**CINVANTI ® and SUSTOL® for CINV**
• HTX-011 NDA PDUFA goal date of 05/12/2021 ➢ Label negotiations underway with the FDA	• 505(b)(2) NDA for PONV planned for 4Q2021 • Potential approval in 2H2022	• 2021 net sales guidance for CINV franchise: $130M - $145M
• Promising HTX-034 Phase 1b bunionectomy results • Phase 2 started 1Q; data in 2021		

HTX-011, HTX-034 and HTX-019 are investigational new drugs and not approved by the FDA