Heron Therapeutics Corporate Update

OCT/2, 2019



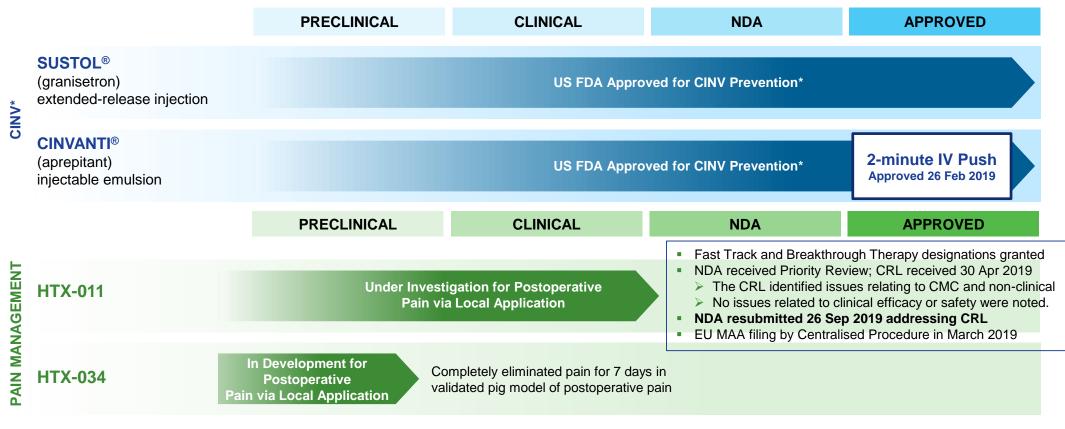
Forward-Looking Statements

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 2019 net product sales guidance for the CINV franchise; whether the FDA approves the NDA for HTX-011; the timing of the FDA's review process for HTX-011; the timing of the commercial launch of HTX-011; the timing of the CHMP's review process for HTX-011; whether the European Commission authorizes the MAA for HTX-011; the potential market opportunity for SUSTOL, CINVANTI and HTX-011; the timing and results of the studies in the HTX-011 and HTX-034 development programs; 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; and other risks and uncertainties identified in Heron'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 Has Shown Favorable Results on Postoperative Pain in Several High-Value Procedures

	Procedure	Annual Volume ('000s, US, 2015)				Overall % Local Anesthetic Use		
	riocedule		Inpatient	Outpatient (C-code)	ASC (C-Code)	Medicare	Non- Medicare**	Survey
	Knee arthroplasty	1,043	977	41	25	41%	59%	86%
	Hip arthroplasty	599	579	8	12	42%	58%	80%
Ortho Surgery	Shoulder arthroplasty	161	149	9	3	47%	53%	85%
Sargory	Rotator cuff repair	319	6	193	120	27%	73%	81%
	Spine procedures	1,459*	928	456	75	34%	66%	76%
	Bunionectomy & Phalangectomy	597	42	343	212	25%	75%	88%
	Hernia repair	1,064	212	731	121	26%	74%	82%
General	Cholecystectomy	987	323	600	64	10%	90%	83%
Surgery	Colon and small bowel resection	476	457	18	1	33%	67%	75%
Plastic Surgery	Abdominoplasty	130	23	95	12	16%	84%	75%
	Mammoplasty	292	32	208	52	16%	84%	79%
OB/GYN	C-Section	1,168	1158	10	0	2%	98%	58%

Completed studies

On-going studies



^{**} Non Medicare includes Commercial. Medicaid and Cash

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

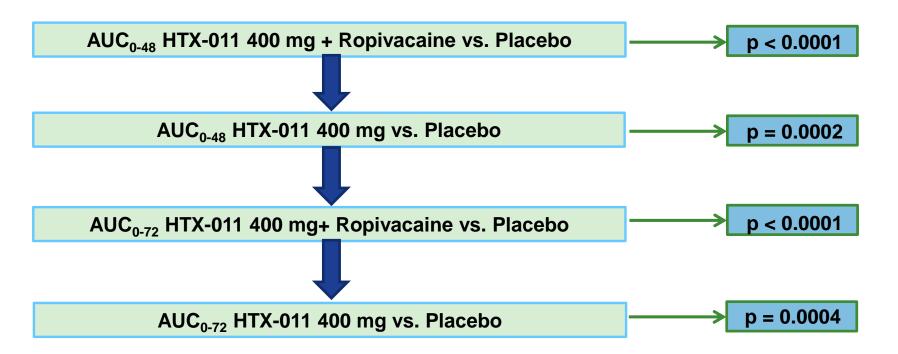
Study 209 Follow-on: HTX-011 + MMA in TKA* (Study 306)

*The multimodal analgesic (MMA) regimen used in this study was identical to the PILLAR Study of liposomal bupivacaine



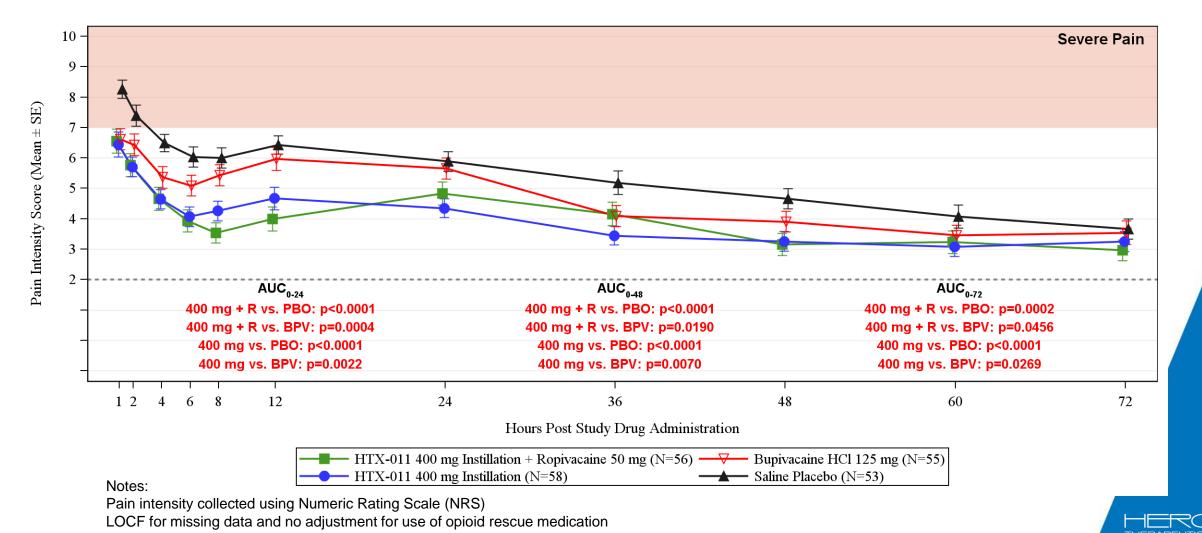
Study 209 TKA: Results Hierarchy

HTX-011 via instillation achieved primary and key secondary endpoints for reduction in pain intensity scores



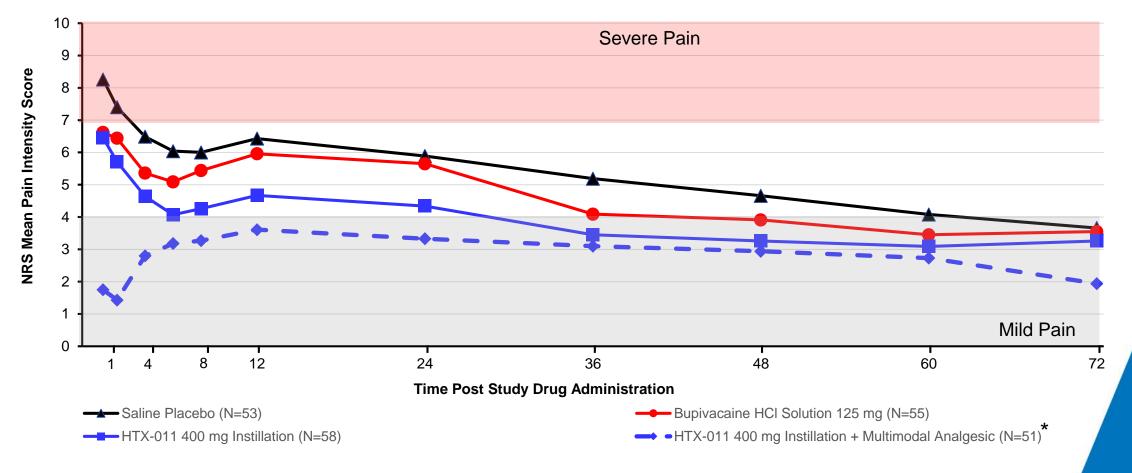


Study 209 TKA: HTX-011 Significantly Superior to Both Placebo and Bupivacaine Through 72 Hours Without Adjusting for Opioid Use





Study 209 Follow-on: HTX-011 + Generic Analgesics* Kept Pain in the Mild Range Through 72 Hours With 68% Less Opioid Than Bupivacaine



^{*} Multimodal analgesic (MMA) regimen for postoperative pain in Study 306 included oral acetaminophen 1000 mg every 8 hours (maximum 3000 mg/d) and oral celecoxib 200 mg every 12 hours until discharge, as described in Mont doi: 10.1016/j.arth.2017.07.024. Patients in Study 209 received no scheduled MMA and only received opioids for rescue



Cross-Study Comparison of Day 1 in Study 306 and Exparel PILLAR Study (Dysart 2019)

Cross-Study Comparison of 0 – 24 Hour Results in TKA Using Pillar-Based MMA and the Same Analysis ¹	Study 306 HTX-011 (N=51)
AUC0-24 VAS Pain ²	59.5
Opioid-Free	21.6%
Mean Opioid Consumption MME (SD)	10.6 (9.2)
Log-transformed Geometric Mean Opioid Consumption MME	0.54
Discharge Ready in 12 hours Based MPADSS ≥ 9	60.8%

PILLAR Study			
Exparel + Bupivacaine ¹ (N = 70)	Bupivacaine¹ (N = 69)		
98.5	121.6		
17.1%	1.4%		
45.5 (35.01)	56.8 (38.26)		
3.5	38.5		
42.9%	27.5%		

- 1. https://doi.org/10.1016/j.arth.2018.12.026.
- 2. Assumes LOCF as publication does not describe any correction for opioid use

Disclaimer

This is a cross-study comparison of Study 306 to the PILLAR Study of Exparel plus bupivacaine; these comparisons are not based on head-to-head clinical studies. The results from these two studies are not directly comparable and do not imply a clinical benefit of HTX-011 over Exparel.



Cross-Study Comparison of 48 Hour Results From Study 306 (Preliminary Results) and Exparel Pillar Study (Mont 2017)

Comparison of 48 Hr Results in TKA Using Pillar-Based MMA and the Same Analysis ¹	Study 306 HTX-011 (N=51)
Mean AUC12-48 VAS Pain	143.2
Opioid-Free	11.8%
Mean Opioid Consumption (MME)	19.6 (Median=16.7)
Log-transformed Geometric Mean Opioid Consumption MME	3.0
≤ 20 MME @ 48 hr	56.9%
> 20 and <u><</u> 220 MME @ 48hr	43.1%
> 220 MME @ 48 hr	0
DID NOT Receive a Discharge Prescription for Opioids	74.5%

PILLAR Study			
Exparel + Bupivacine ¹ (N = 70)	Bupivacaine ¹ (N = 69)		
180.8	209.3		
10%	0%		
Not Shown	Not Shown		
18.7	84.9		
18.6%	4.4%		
78.6%	87%		
2.9%	8.7%		
Not Shown	Not Shown		
1. Mont doi: 10.1016/j.arth.2017.07.024			

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comparisons are not based on head-to-head clinical studies. The results from these two studies are not
directly comparable and do not imply a clinical benefit of HTX-011 over Exparel.



Potential Reduction of Discharge Opioids Based on Study 306

 Currently, following TKA an average of 90 opioid pills are prescribed per patient at the time of discharge, with an additional 4 refills over the next year¹

Potential Impact on Discharge Opioids of Study 306 Extrapolated to the 1,043,000 TKA Surgeries Annually²

	Pills Prescribed
Current Practice Estimates With Initial Rx	93,870.000
Study 306 Results (25.5% only)	23,936,850
Potential Reduction with HTX-011 + MMA	69,933,150↓

^{1.} Truven Database – Commercial patients



Decisions Resources Group claims data 2018;

EPOCH 1:
Bunionectomy
Results
(Study 301)

EPOCH 1 Follow-on:
Opioid Elimination
Study in
Bunionectomy

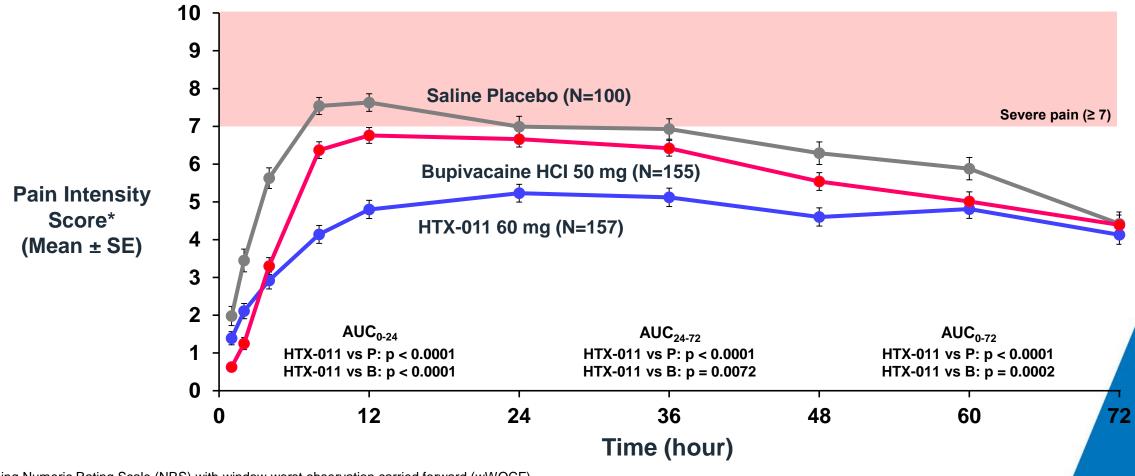


EPOCH 1 Bunionectomy: All Key Endpoints Favor HTX-011

Hierarchical hypothesis testing (P ≤ .05)NRS Pain Intensity (AUC₀₋₇₂) vs placebo p < 0.0001**Primary** 1st Key NRS Pain Intensity (AUC₀₋₇₂) vs bupivacaine HCl p = 0.0002Secondary 2nd Key Opioid Use (0-72 hours) vs placebo p < 0.0001Secondary 3rd Key Opioid Free (0-72 hours) vs bupivacaine HCl p = 0.0001Secondary 4th Key Opioid Use (0-72 hours) vs bupivacaine HCI \Rightarrow p = 0.0022 **Secondary**

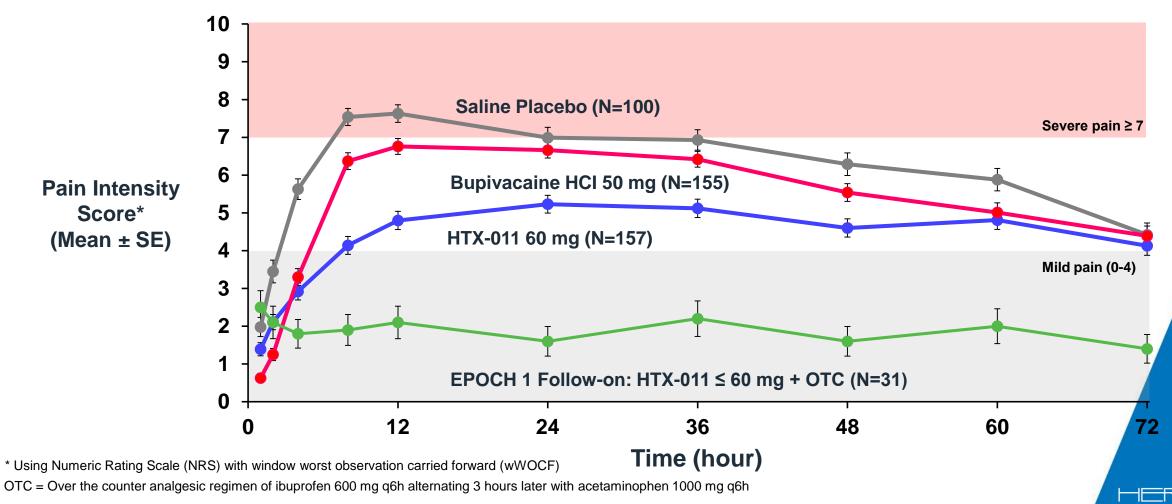


EPOCH 1 Bunionectomy: HTX-011 Significantly Reduced Pain Through 72-hours as Compared to Bupivacaine and Placebo



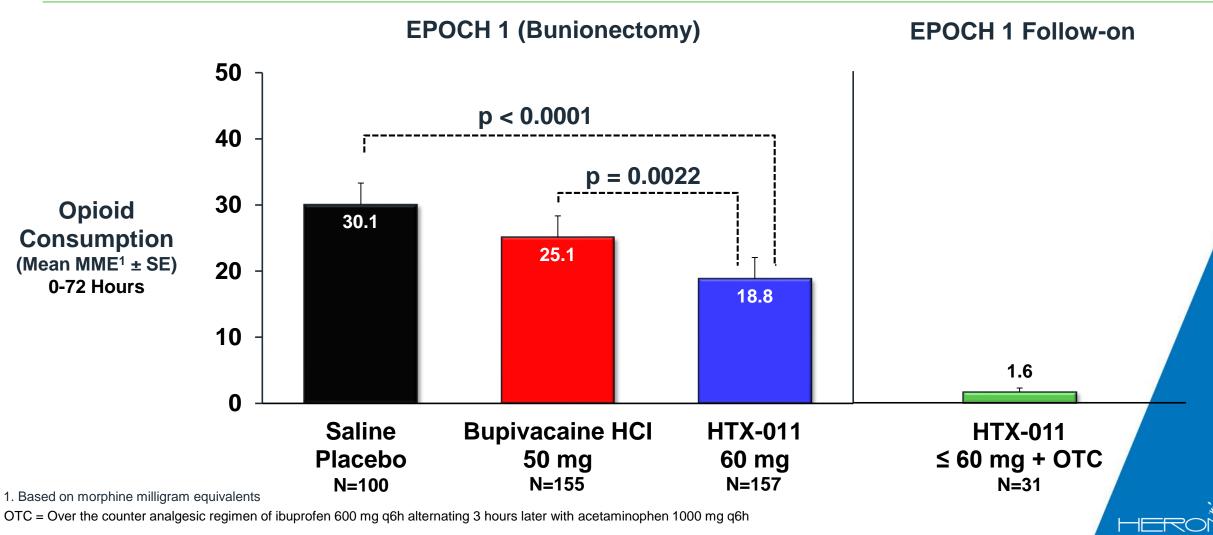
^{*} Using Numeric Rating Scale (NRS) with window worst observation carried forward (wWOCF)

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



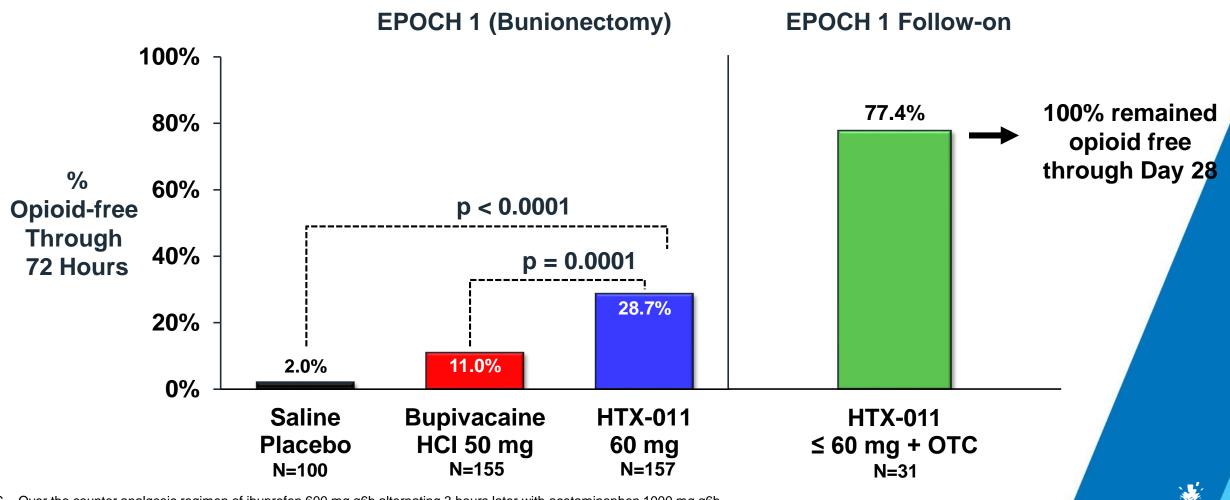
HTX-011 is an investigational new drug and not approved by the FDA

HTX-011 Significantly Reduced Total Opioid Consumption Through 72-hours as Compared to Bupivacaine and Placebo



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

HTX-011 Significantly Increased Proportion of Opioid-Free Patients Through 72-hours as Compared to Bupivacaine and Placebo



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

EPOCH 2:
Herniorrhaphy
Results
(Study 302)

EPOCH 2 Follow-on:
Opioid Elimination
Study in
Herniorrhaphy

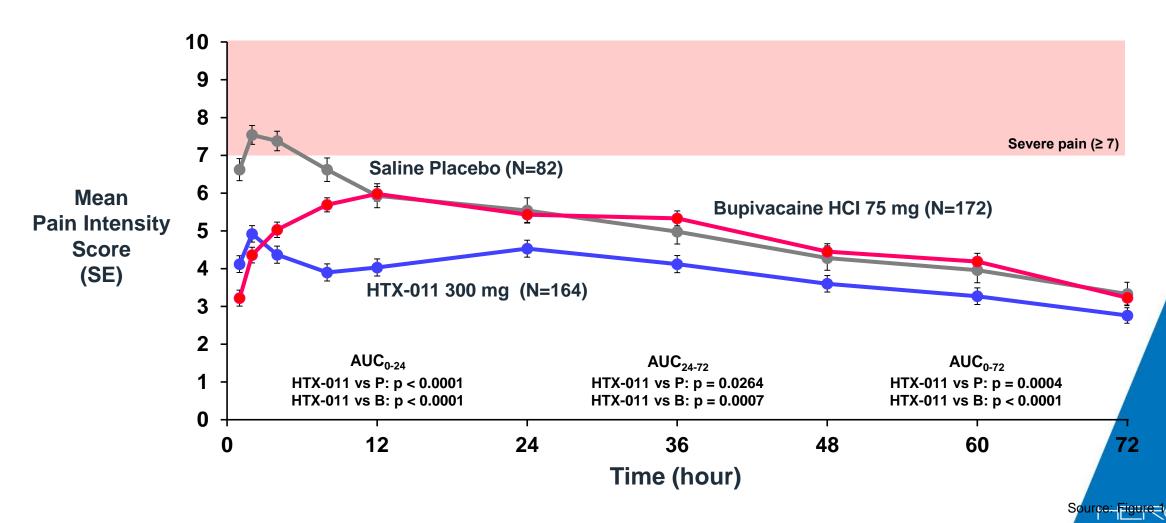


EPOCH 2 Herniorrhaphy: All Key Endpoints Favor HTX-011

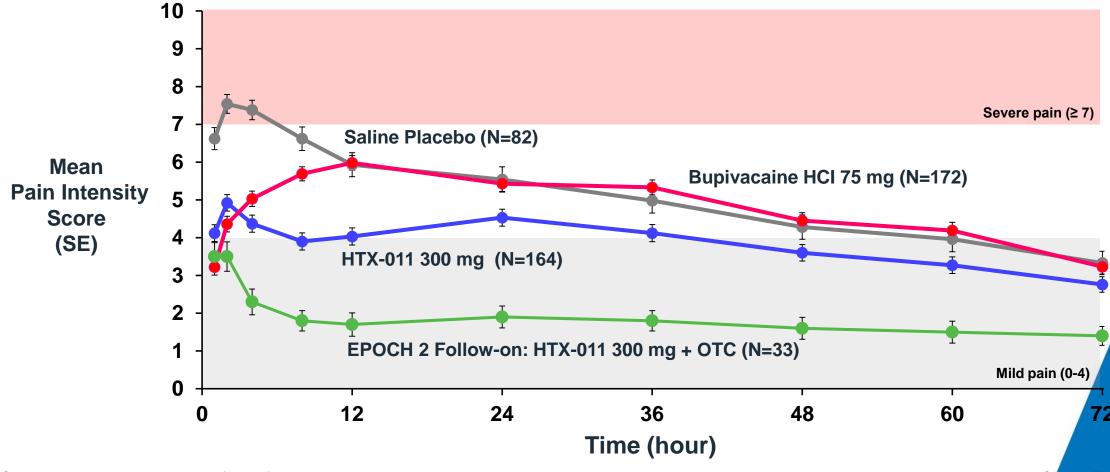
Hierarchical hypothesis testing (P ≤ .05)NRS Pain Intensity (AUC₀₋₇₂) vs placebo p = 0.0004**Primary** 1st Key NRS Pain Intensity (AUC₀₋₇₂) vs bupivacaine HCl p < 0.0001Secondary 2nd Key Opioid Use (0-72 hours) vs placebo p = 0.0001Secondary 3rd Key Opioid Free (0-72 hours) vs bupivacaine HCl p = 0.0486Secondary 4th Key Opioid Use (0-72 hours) vs bupivacaine HCI \Rightarrow p = 0.0240 **Secondary**

AUC: area under the curve; placebo: saline placebo

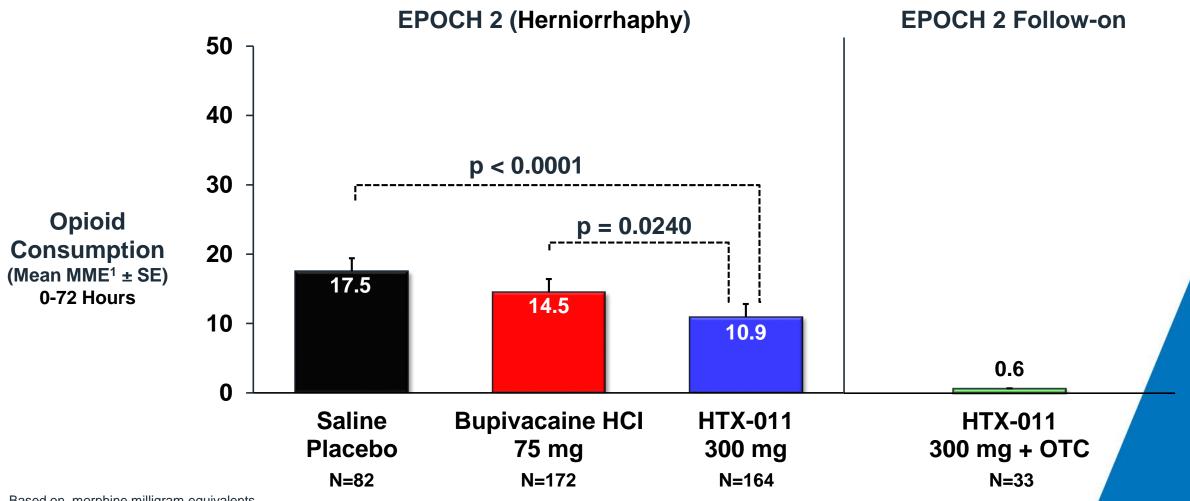
EPOCH 2 Herniorrhaphy: HTX-011 Significantly Reduced Pain Through 72-hours as Compared to Bupivacaine and Placebo



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



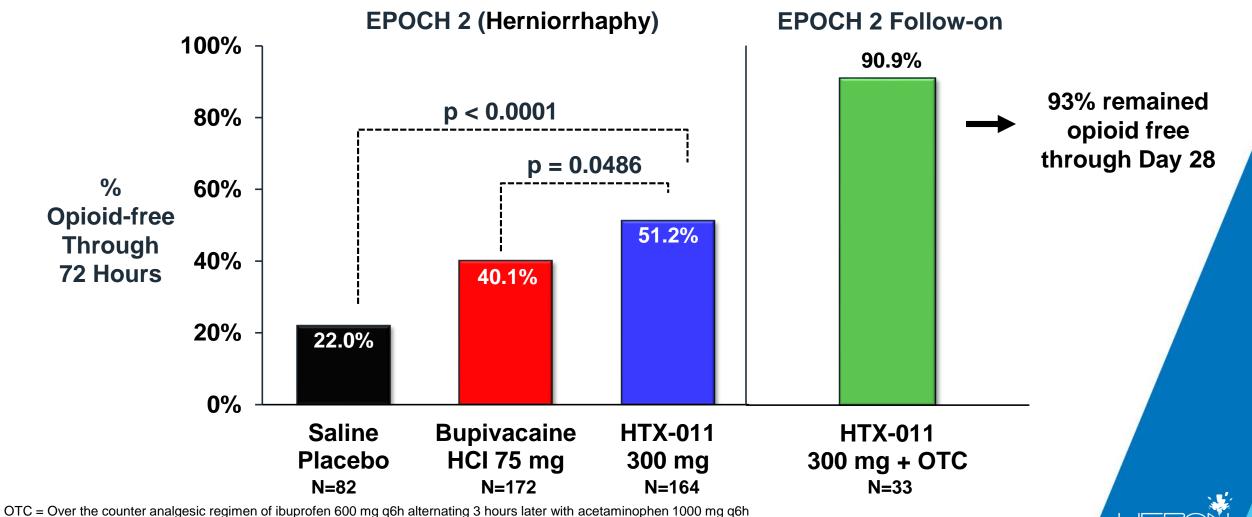
HTX-011 Significantly Reduced Total Opioid Consumption Through 72-hours as Compared to Bupivacaine and Placebo

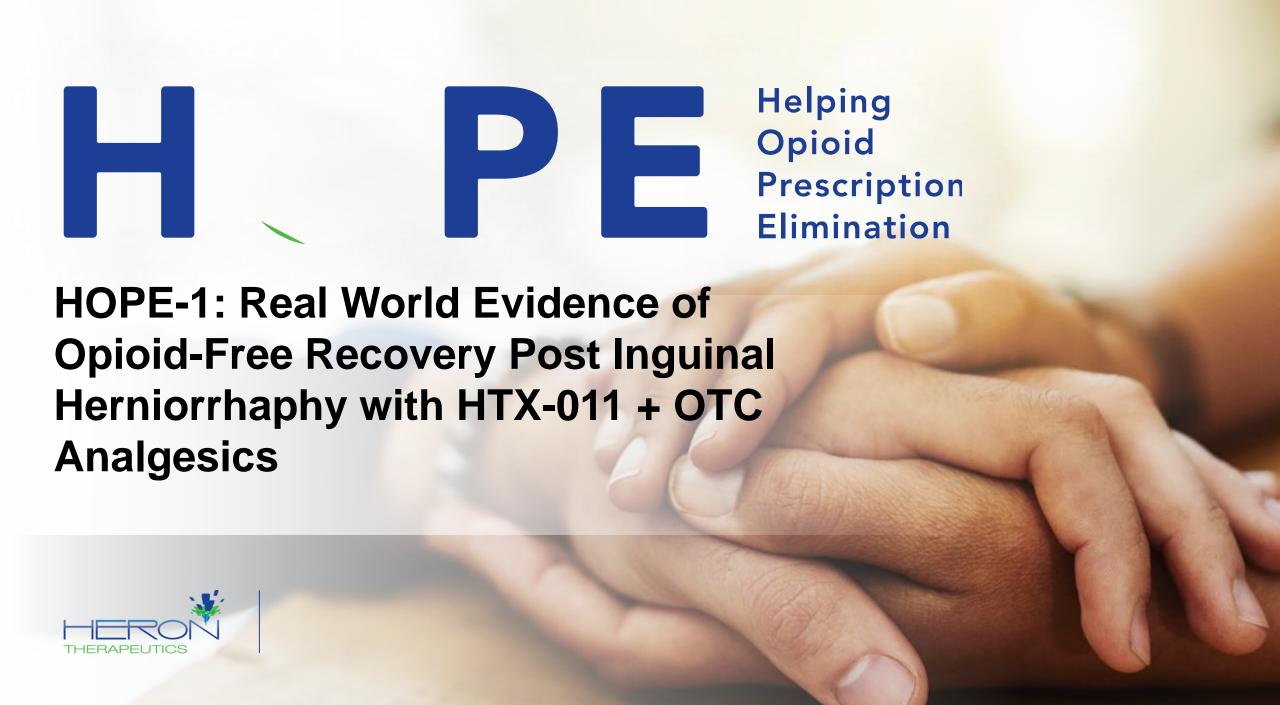


^{1.} Based on morphine milligram equivalents

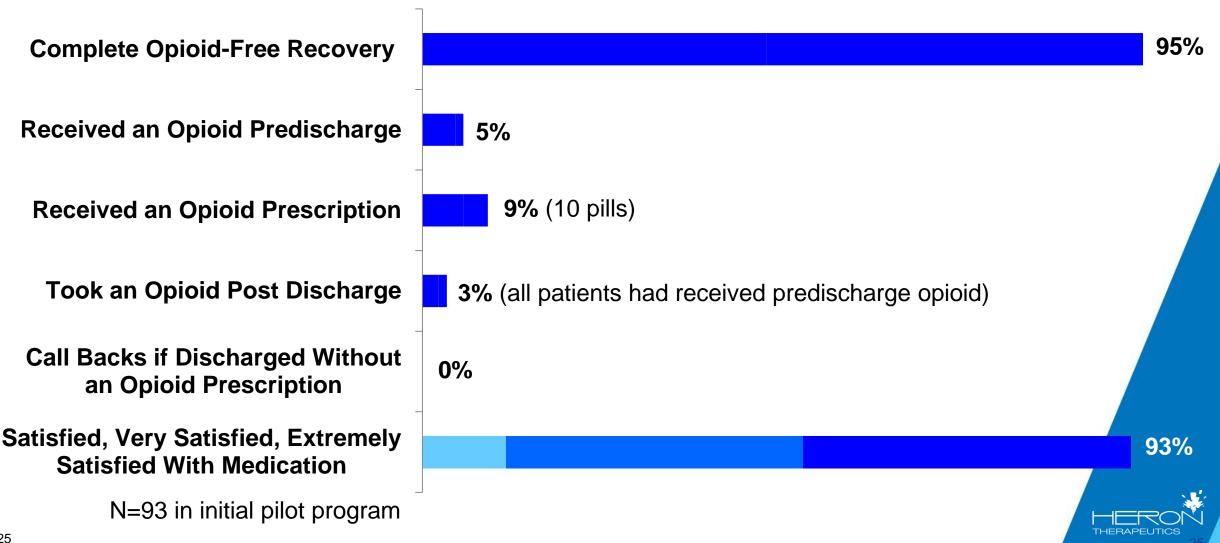
OTC = Over the counter analysesic regimen of ibuprofen 600 mg q6h alternating 3 hours later with acetaminophen 1000 mg q6h

HTX-011 Significantly Increased Proportion of Opioid-Free Patients Through 72-hours as Compared to Bupivacaine and Placebo





HOPE-1: Opioid-Free Recovery in 95% of Inguinal Herniorrhaphy Patients with HTX-011 + OTC Analgesics



Potential Reduction of Discharge Opioids Based on HOPE-1

 Currently, following inguinal hernia repair an average of 30 opioid pills are prescribed per patient of which an average of 9 pills are consumed¹

Potential Impact if HOPE-1 Extrapolated to the ~800,000² Inguinal Hernia Surgeries Annually

	Pills Prescribed	Pills Consumed	Pills Leftover
Current Practice Estimates	24,000,000	7,200,000	16,800,000
HOPE-1 Estimates	774,194	283,871	490,323
Potential Reduction with HTX-011 + OTC	23,225,806↓	6,916,129↓	16,309,677↓



^{1.} Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC)November 15, 2018

^{2.} Decisions Resources Group claims data 2017;

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
- Deaths (none on HTX-011; one on bupivacaine)

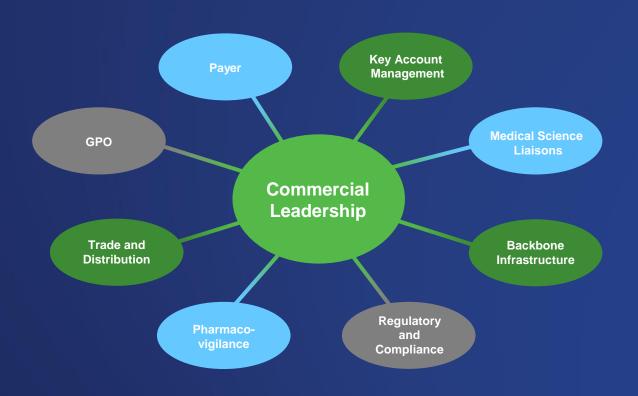






Established Platform With Experienced Teams in Place

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

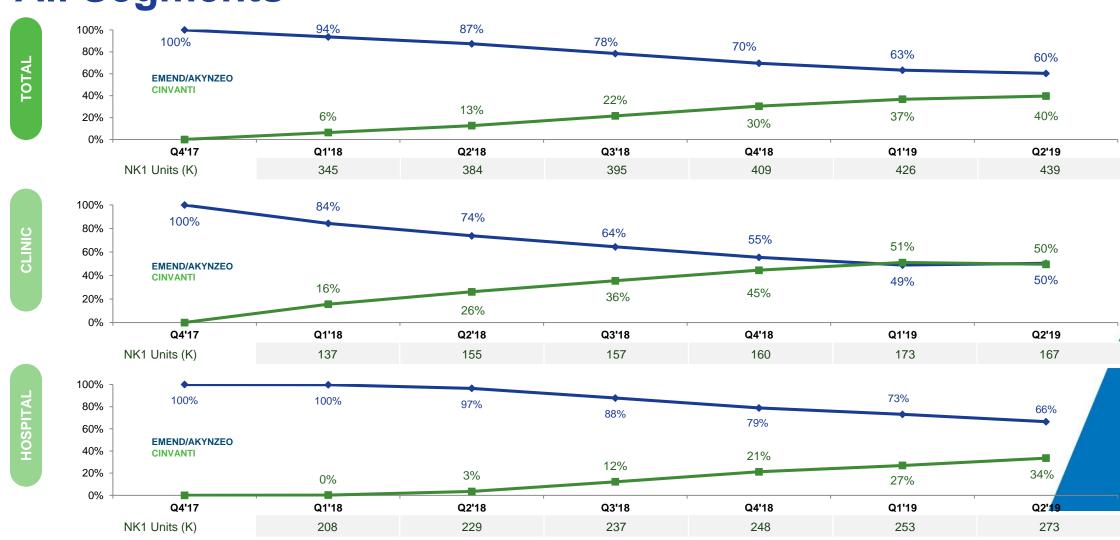


EXISTING PLATFORM ADVANTAGES

- 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 and3PL in place
- Safety monitoring structure in place
- Proven compliant execution
- Robust systems in place and pressure tested for blockbuster launch



CINVANTI Market Share is Climbing Steadily Across All Segments



Key CINVANTI Learnings to Support HTX-011 Launch

HTX-011

MOA, First and Only DALA

Broad Access Pricing

3-year pass through (C-Code)

Top 200 IDNs, 965 Hospitals and 340B

Selected GPOs / IDNs

Ambulatory Surgical Centers

Exparel, On-Q

Leverage ASCs and Outpatient for access and confidence

Reduce / Eliminate Risk with ASCs

Hospital driven / Multiple Surgical lines

KEY DRIVERS

DIFFERENTIATED PRODUCT

WAC

340B

FOCUS

CONTRACTING

ACCELERATE SALES

COMPETITION

REIMBURSEMENT

VALUE ADDED SERVICES

IMPLEMENTATION

CINVANTI

First and only polysorbate 80-free NK1 RA

Lower Acquisition Cost (-\$40)

3-year pass through (C-Code)

Top 200 IDNs, 340B

Selected GPOs / IDNs

Community Oncology

Merck

Leverage Community to create confidence

Reduce / Eliminate
Risk community setting

IDN driven pull through at affiliated hospitals



The Market is Large and Waiting for an Effective Non-opioid Solution

Theoretical and Target Market

~29M Annual US Surgical Procedures Requiring Postoperative Pain Management

~13.5M procedures

Initial Targets

Higher volume procedures across 4 major specialties

- ~5.9M Orthopedic
- ~4.2M General Surgery
- ~2.6M OB/GYN
- ~0.8M Plastic Surgery

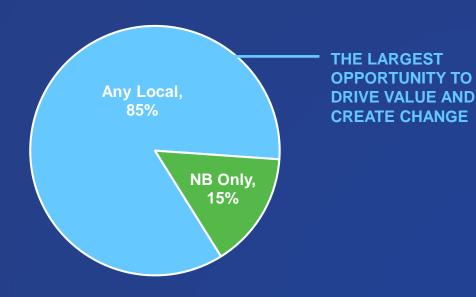
~15.5M procedures

Secondary Targets

Other procedures requiring postoperative pain management but not amongst initial targets for one or more of these reasons:

- Non-core specialties
- Relatively lower pain scores
- Lower volume per procedure

Local Anesthetic Route of Delivery *



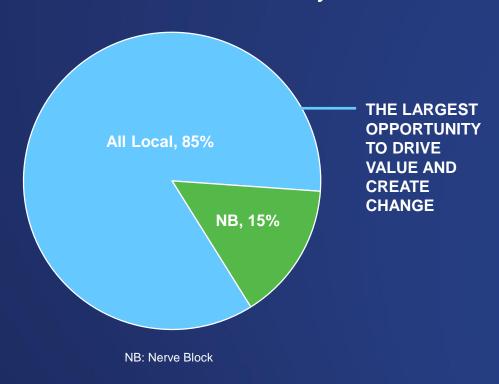
* Local Anesthetics are used in ~70% of procedures

NB: Nerve Block

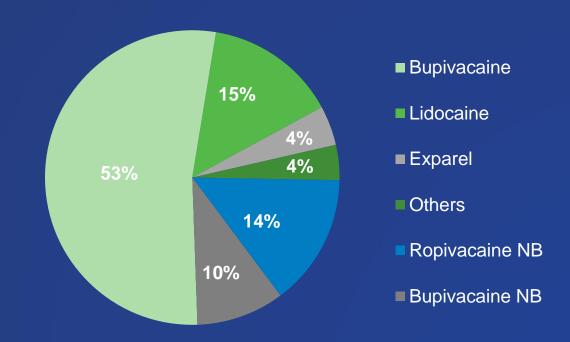


HTX-011 is Focused on the Largest Market Opportunity

Local Anesthetic Route of Delivery



Local Anesthetic Volume Share



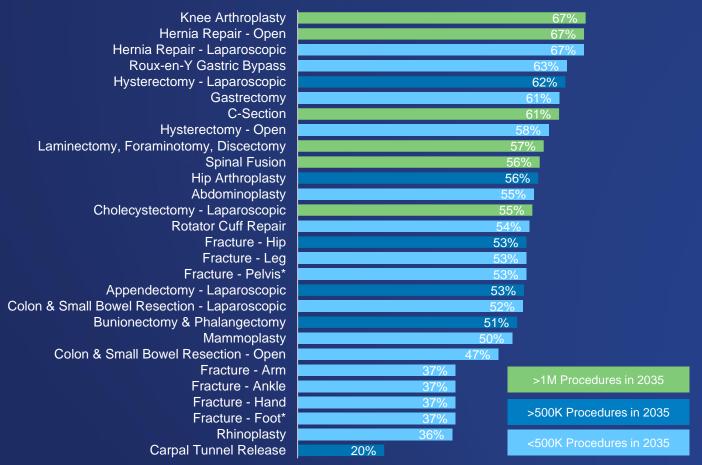
N = 22M Procedures





Physicians Indicated a Raw Preference Share of 56% for a Drug with HTX-011's Potential Attributes Across the Covered Procedures

Preference Share (%, Raw)



Overall Wt. Average Preference Share



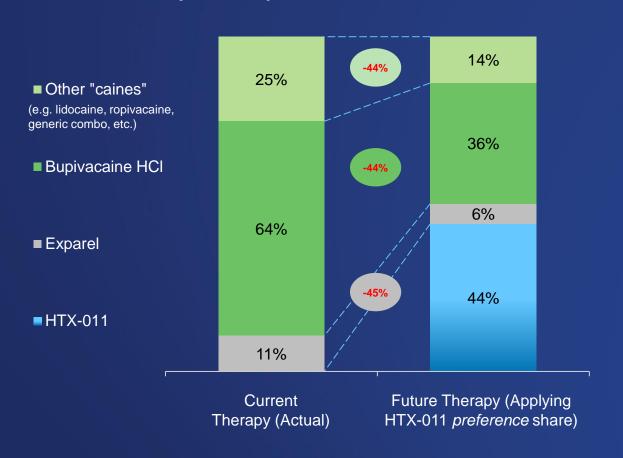
- Raw preference share for a drug with HTX-011's potential attributes from physicians: 56%
- The top procedures where physicians expected to use such a drug were knee arthroplasty and hernia repair
- Several procedures saw higher raw preference shares than prior market research, notably knee & hip arthroplasty, C-section, laparoscopic hysterectomy and spine procedures





A Drug with HTX-011's Potential Attributes Enjoyed a Physician Preference Share of 44%

Adjusted Physician Preference Share Distribution



- If approved, we believe HTX-011 is likely to initially convert share from Exparel, as well as the rest of the local anesthetics (bupivacaine & other "caines")
- There is an additional opportunity to convert physicians not using local anesthetics; physicians indicated a willingness to use such drug with characteristics similar to HTX-011 in ~30% of procedures where they are currently not using local anesthetics

Current therapy based on Claims data from 2017 for Exparel, other agents are based on 2018 Physician Survey

Data from analysis of physician static survey & conjoint - Sample includes n = 330 physicians



HTX-011 has Potential Strategic Advantages Across Each Setting of Care

Clearly differentiated strategy supported by building advocacy with pharmacy, surgeons, and anesthesiologists



Hospitals account for 91%, including top 200 IDNs (12.3M procedures)

52%Hospital
Inpatient
(7M procedures)

- Part of DRG payment
- Multiple SKUs lower average cost
- ~50% connected
 340B hospitals

39%
Hospital
Outpatient
(5.3M procedures)

- 3-year pass through (C-Code)
- 340B opportunity
- High value IDN and procedure focus

Ambulatory surgical centers account for 8% (1.1M procedures)

8%
Ambulatory Surgical
Centers (ASCs)
(1.1M procedures)

- ASP +6%
- Lower access barriers
- Targeted facilities
- Connected to top IDNs
- Targeted high value procedures

47% of the opportunity lends itself to favorable reimbursement and access

The remaining 1% of procedures are performed at private physician practices



340B Hospital Summary

- ~2258 hospitals (excluding children's & psych)
 - 8.4M outpatient surgeries/year
 - 4.4M inpatient surgeries/year
- Manufacturers required to provide 23.1% discount off ASP/WAC
- Discount does not impact ASP or best price calculations
- Products used in the OR that are considered part of the surgical package are not reimbursed, unless they have pass-through status
- Approximately 3 months after approval, HTX-011 will receive a C-Code providing pass-through status

340B Drug Reimbursement for Postoperative Pain

With C-Code	Without C-Code
ASP + 6%	Bundled Payment – No Direct Reimbursement



Heron is Well Positioned to Execute a Blockbuster Launch for HTX-011



Proven track record with hospital launch success



Existing robust platform and structure to support launch



Significant unmet need and market opportunity



Highly focused launch strategy to accelerate sales



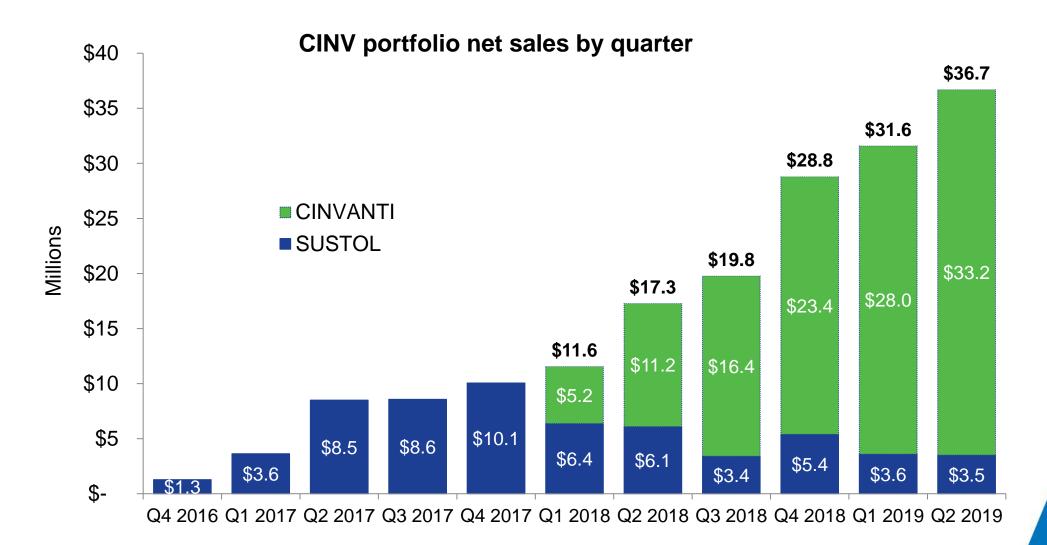
Unprecedented value proposition



CINV Commercial Products



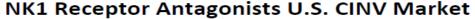
CINV Portfolio Continues to Grow With Over \$177M Since Inception

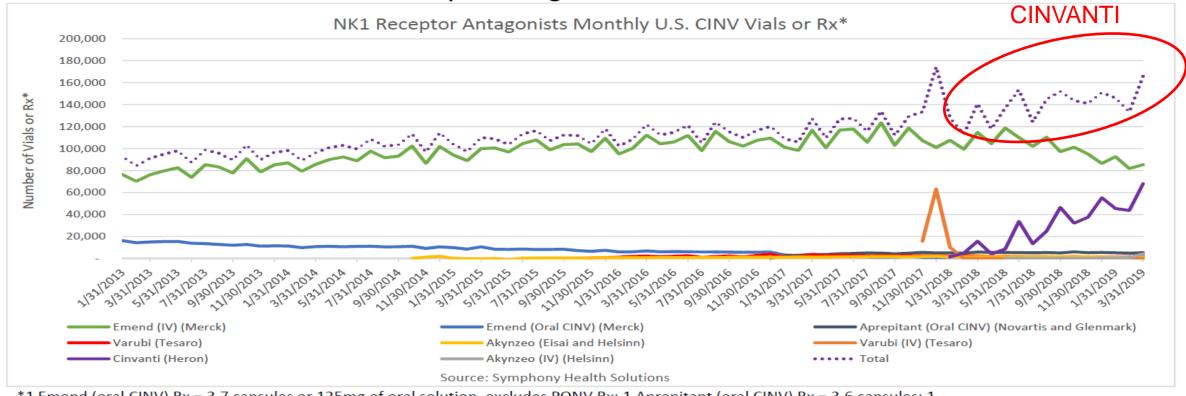




CINVANTI is Both Taking Share From Emend and Growing the NK1 Market

NK1 market has grown since introduction of





^{*1} Emend (oral CINV) Rx = 3.7 capsules or 125mg of oral solution, excludes PONV Rx; 1 Aprepitant (oral CINV) Rx = 3.6 capsules; 1 Varubi Rx = 2.4 tablets; 1 Akynzeo Rx = 1.3 capsules



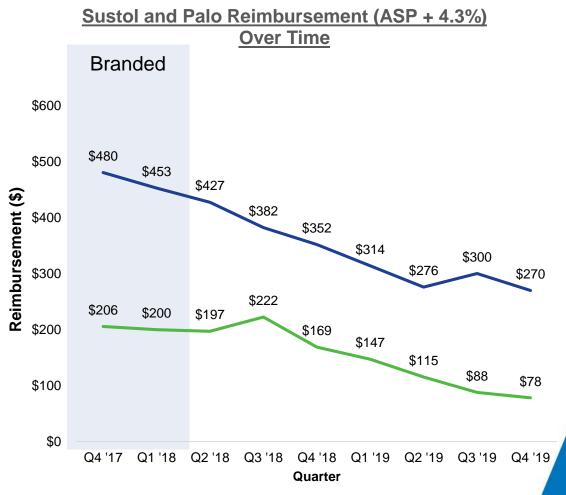
Strategy to Preserve CINVANTI Through Generic Arbitrage

- Leverage favorable 340B pass through status, ASP+ 6% through 2020
- IV push sNDA approved further differentiating CINVANTI from Emend and generics
- Long-term contracting
- CINVANTI has become an established brand across both clinics and hospital capturing 40% of the market in Q2 2019



ALOXI/Palonosetron Arbitrage Lasted Much Longer Than Projected, Resulting in an Accelerated Decline in Sustol ASP

- Even with multiple generics on the market, the price of palonosetron did not drop as quickly as in past arbitrage periods
- Slow decline in prices resulted in a very long arbitrage, which also resulted in an accelerated decline in the Sustol ASP
- The only way to rebuild value in the brand is to implement an innovative strategy:
 - Starting October 1, all discounting of Sustol was discontinued, which will result in lower sales
 - In approximately 5 quarters the ASP of Sustol will reset to approximately the WAC
 - Sustol will be re-launched with enhanced value for practices and Heron



2019 CINV Franchise Outlook



SUSTOL®: To recover from the protracted palonosetron arbitrage, Heron has implemented an innovative strategy to refresh the ASP

 This will result in greatly reduced sales for approximately 5 quarters, followed by a significant rebound in units and revenue



CINVANTI®

- Cinvanti continues to have the best overall profile compared to the other available NK₁ antagonists and is completely differentiated from generic fosaprepitant with the 2-min IV Push administration
- CINVANTI (aprepitant) injectable emulsion received unique J-Code J0185 effective January 1, 2019, so generic pricing does not effect Cinvanti reimbursement
- Generic fosaprepitant IV entered the market in September 2019
 - Due to significant sales in 340b hospitals, IV push label and other factors, we do not expect this arbitrage to have the same magnitude as the Aloxi arbitrage
 - Based on early price reductions within weeks of the first generic entry, the duration of the arbitrage should also be shorter than with Aloxi



CINV Franchise

2019 guidance: \$115M - \$120M



Financial Summary

Heron expects to end 2019 with more than \$190 million in cash, cash equivalents and short-term investments.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share data)	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
Net product sales	\$ 36,659	\$ 68,261
Operating expenses ¹	88,438	184,740
Other income, net	1,557	3,245
Net loss ¹	\$ (50,222)	\$ (113,234)
Net loss per share ²	\$ (0.63)	\$ (1.43)
Net cash used in operations	\$ (23,108)	\$ (72,132)

Condensed Balance Sheet Data (In thousands)	June 30, 2019
Cash, cash equivalents and short-term investments	\$ 276,005
Accounts receivable, net	\$ 66,821
Total assets	\$ 411,666
Total stockholders' equity	\$ 305,359

Common shares outstanding at June 30, 2019 totaled 79.8 million.



¹ Includes \$12.7 million and \$30.6 million of non-cash, stock-based compensation expense for the three and six months ended June 30, 2019, respectively. ² Based on 79.5 million and 79.0 million weighted-average common shares outstanding for the three and six months ended June 30, 2019, respectively.

Key Catalysts in Pain Management & CINV Franchises

HTX-011 & HTX-034 for Postoperative Pain	CINVANTI® and SUSTOL® for CINV
 CRL received 30 April 2019 identified issues relating to CMC and non-clinical No issues related to clinical efficacy or safety were noted NDA resubmitted 26 September 2019 addressing all the issues raised in the CRL – expect 6 month review 	 2019 net sales guidance for CINV franchise: \$115M - \$120M
HOPE Project launched across the US	
 Publication of Phase 3 and Phase 2b studies ✓ Phase 3 studies published in peer-reviewed journals ➢ EPOCH 1: Reg Anesth Pain Med. 2019;0:1–7. doi:10.1136/rapm-2019-100531 ➢ EPOCH 2: Hernia. doi: 10.1007/s10029-019-02023-6. 	
 Phase 2 with HTX-034 initiated in late 2019 	

