UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 11, 2021

Heron Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-33221**	**94-2875566**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

4242 Campus Point Court, Suite 200, San Diego, CA	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code (858) 251-4400

N/A

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	**HRTX**	**The Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On January 11, 2021, Heron Therapeutics, Inc. (the "Company") issued a press release announcing, among other things, certain of its financial results for the three and twelve months ended December 31, 2020 (the "Press Release"). A copy of the Press Release is furnished herewith as Exhibit 99.1.

This Item 2.02 and the Press Release attached hereto as Exhibit 99.1 are being furnished to the Securities and Exchange Commission.

Item 7.01 Regulation FD Disclosure.

Press Release.

On January 11, 2021, the Company issued the Press Release providing, among other things, a general update on corporate progress, as described in the Press Release.

Corporate Presentation.

A copy of presentation materials describing the business of the Company, all or a part of which may be used by the Company in investor or scientific presentations from time to time, is furnished herewith as Exhibit 99.2 (the "Corporate Presentation"). The Corporate Presentation has also been posted on the Company's website at *www.herontx.com*. The Company does not undertake any obligation to update the Corporate Presentation.

This Item 7.01, the Press Release and the Corporate Presentation are being furnished to the Securities and Exchange Commission.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated January 11, 2021
99.2	Corporate Presentation, dated January 11, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Heron Therapeutics, Inc.

Date: January 11, 2021

/s/ David Szekeres
David Szekeres
Executive Vice President, Chief Operating Officer

Heron Therapeutics Highlights Progress in Pain Management and CINV Franchises and Announces New Development Program

- Preliminary Full-Year 2020 Net Product Sales for CINV Franchise of Approximately $88.3 Million, versus Guidance of $85 Million -

- Full-Year 2021 Net Product Sales Guidance for CINV Franchise of $130 Million to $145 Million -

- New Drug Application for HTX-011 for Postoperative Pain Management is Under Review in the US with a May 12, 2021 PDUFA Date -

- Preliminary Results From Phase 1b Bunionectomy Study with HTX-034 Shows Pain Reduction Through 96 Hours with 45.5% of Patients Opioid-Free Through Day 15 -

- Preliminary Results from Phase 1 Study of Low Dose HTX-019 IV Injection Demonstrated Bioequivalence to Approved Oral Aprepitant 40 mg Dose for Prevention of Postoperative Nausea and Vomiting -

SAN DIEGO, Jan. 11, 2021 /PRNewswire/ -- Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs, today highlights progress in its pain management and chemotherapy-induced nausea and vomiting (CINV) franchises and announces a new development program for postoperative nausea and vomiting (PONV).

Recent Corporate Progress

Pain Management Franchise

- **New Drug Application Resubmission for HTX-011 Under Review:** The New Drug Application (NDA) resubmission for HTX-011, an investigational agent for the management of postoperative pain, submitted November 12, 2020 to the U.S. Food and Drug Administration (FDA), continues under review. The FDA set a Prescription Drug User Fee Act (PDUFA) goal date of May 12, 2021.

- **Low Dose HTX-034 Produced Greater Pain Reduction to Bupivacaine, the Current Standard-of-Care, Through 96 hours in Bunionectomy Study:** In the Phase 1b portion of this Phase 1b/2 double-blind, randomized, active-controlled dose-escalation study in 33 patients undergoing bunionectomy, the reduction in pain intensity observed with the lowest dose of HTX-034 evaluated (containing 21.7 mg of bupivacaine plus

meloxicam and aprepitant) was greater than the bupivacaine 50 mg solution group through 96 hours.

- In addition, 45.5% of HTX-034 patients remained opioid-free through Day 15 with median opioid consumption of 2.5 milligram morphine equivalents (same as one 5 mg oxycodone pill) through 72-hours, a 71% reduction compared to bupivacaine solution.
- The expanded Phase 2 portion of the study for HTX-034 will begin this quarter.

CINV Franchise

- **Fourth-Quarter 2020 Net Product Sales:** Preliminary fourth-quarter 2020 net product sales for the CINV franchise were approximately $20.3 million. This included net product sales of approximately $20.0 million for CINVANTI® (aprepitant) injectable emulsion and approximately $0.3 million for SUSTOL® (granisetron) extended-release injection, compared to $34.6 million and $0.5 million, respectively, for the same periods in 2019. Heron believes the most significant impact of the generic arbitrage is over and expects to grow CINVANTI market share in 2021 and beyond.

- **Full-Year 2020 Net Product Sales:** Preliminary full-year 2020 net product sales for the CINV franchise were approximately $88.3 million versus guidance of $85 million. This included net product sales of approximately $87.6 million for CINVANTI and approximately $0.7 million for SUSTOL, compared to $132.2 million and $13.8 million, respectively, for the same periods in 2019. On October 1, 2019, the Company discontinued all discounting of SUSTOL, which resulted in significantly lower SUSTOL net product sales. Heron expects SUSTOL to return to growth in 2021 and beyond.

- **Full-Year 2021 Net Product Sales Guidance:** Heron expects full-year 2021 net product sales for the CINV franchise of $130 million to $145 million.

PONV Franchise

- **HTX-019 Achieved Bioequivalence to Approved Oral Aprepitant 40 mg Dose for Prevention of PONV:** A new IND for HTX-019 (aprepitant injectable emulsion) for PONV was approved by the FDA in late September of 2020. In the Phase 1 bioequivalence study, HTX-019 32 mg as a 30-second intravenous (IV) injection was bioequivalent to oral aprepitant 40 mg, which is approved for the prevention of PONV. An NDA for HTX-019 is planned in late 2021 for prevention of PONV in adults.

Corporate Update

- **Year-End 2020 Cash Balance:** Heron ended 2020 with approximately $208.5 million in cash, cash equivalents and short-term investments.

"We have made important advances in 2020 in both our pain management and CINV franchises, highlighted by receiving an EU marketing authorization for ZYNRELEF™ (also known as HTX-011), the rapid resubmission to the FDA of the NDA for HTX-011, very promising clinical data with HTX-034, and maintaining stronger than expected net product sales for CINVANTI. We are also excited to announce the development of HTX-019 for PONV, a market that is approximately 20-times larger than CINV, with an expected NDA submission late this year," said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. "2021 should be a transformational year for Heron with significant growth in our CINV products with net product sales guidance of $130 million - $145 million and the anticipated launch of HTX-011, if approved by the FDA."

About HTX-011 for Postoperative Pain (ZYNRELEF in the European Union and European Economic Area)

HTX-011, an investigational non-opioid analgesic, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. The U.S. FDA granted Breakthrough Therapy designation to HTX-011 and the NDA received Priority Review designation. A complete response letter (CRL) was received from the FDA regarding the NDA for HTX-011 in June 2020 relating to non-clinical information. No clinical safety or efficacy issues and no chemistry, manufacturing and controls (CMC) issues were identified. Heron resubmitted an NDA to the FDA for HTX-011 in November 2020 and the FDA set a PDUFA goal date of May 12, 2021. Heron is working to respond to a list of questions received from Health Canada in July 2020. In September 2020, the European Commission (EC) granted a marketing authorization for ZYNRELEF (also known as HTX-011) for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. The EC's centralized marketing authorization is valid for the 27 countries that are members of the European Union, and the other countries in the European Economic Area, including the United Kingdom.

About HTX-034 for Postoperative Pain

HTX-034, an investigational non-opioid analgesic, is a triple-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam and aprepitant, an additional agent that further potentiates the activity of bupivacaine. HTX-034 is formulated in the same proprietary polymer as HTX-011. By combining two different mechanisms that each enhance the activity of the local anesthetic bupivacaine, HTX-034 is designed to provide superior and prolonged analgesia. Local administration of HTX-034 in a validated preclinical postoperative pain model resulted in sustained analgesia for 7 days.

About CINVANTI (Aprepitant) Injectable Emulsion
CINVANTI, 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 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 is an IV formulation of aprepitant, a substance P/neurokinin-1 (NK_1) receptor antagonist (RA). CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 RA to significantly reduce nausea and vomiting in both the acute phase (0–24 hours after chemotherapy) and the delayed phase (24–120 hours after chemotherapy). The FDA-approved dosing administration included in the United States prescribing information for CINVANTI is a 30-minute IV infusion or a 2-minute IV injection.

CINVANTI is under investigation for the treatment of COVID-19 as a daily 2-minute IV injection when added to the current standard of care.

Please see full prescribing information at www.CINVANTI.com.

About HTX-019 for Postoperative Nausea and Vomiting

HTX-019 is an IV injectable emulsion formulation designed to directly deliver aprepitant, the active ingredient in EMEND® capsules, which is the only NK_1 RA to be approved in the United States for the prevention of PONV in adults. The FDA-approved dosing for oral EMEND is 40 mg capsules within 3 hours prior to induction of anesthesia for surgery. In a Phase 1 clinical trial, HTX-019 32 mg as a 30-second IV injection was demonstrated to be bioequivalent to oral aprepitant 40 mg.

About SUSTOL (Granisetron) Extended-Release Injection

SUSTOL 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. SUSTOL is an extended-release, injectable 5-HT_3 RA that utilizes Heron's Biochronomer® drug delivery technology to maintain therapeutic levels of granisetron for ≥5 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL's efficacy and safety in more than 2,000 patients with cancer. SUSTOL's efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0–24 hours after chemotherapy) and delayed phase (24–120 hours after chemotherapy).

Please see full prescribing information at www.SUSTOL.com.

About Heron Therapeutics, Inc.

Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer. For more information, visit www.herontx.com.

Forward-looking Statements

This news release contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers that forward-looking statements are based on management's expectations and assumptions as of the date of this news release and

are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, those associated with: adjustments to the preliminary fourth-quarter 2020 and full-year 2020 net product sales for the CINV franchise in connection with completion of financial closing procedures and an audit for the 2020 fiscal year; risks associated with the full-year 2021 net product sales guidance for the CINV franchise; whether the FDA approves the NDA for HTX-011; 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 the HTX-034 and PONV 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; 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 U.S. Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and Heron takes no obligation to update or revise these statements except as may be required by law.

Investor Relations and Media Contact:
David Szekeres
EVP, Chief Operating Officer
Heron Therapeutics, Inc.
dszekeres@herontx.com
858-251-4447

Exhibit 99.2

Heron Therapeutics Update

January 11, 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: adjustments to the preliminary fourth-quarter 2020 and full-year 2020 net product sales for the CINV franchise in connection with the completion of the financial closing procedures and an audit for the 2020 fiscal year; 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; the timing of the commercial launch of HTX-011 in the U.S.; 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 PONV 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.

Corporate Updates

Strong Financial Positioning

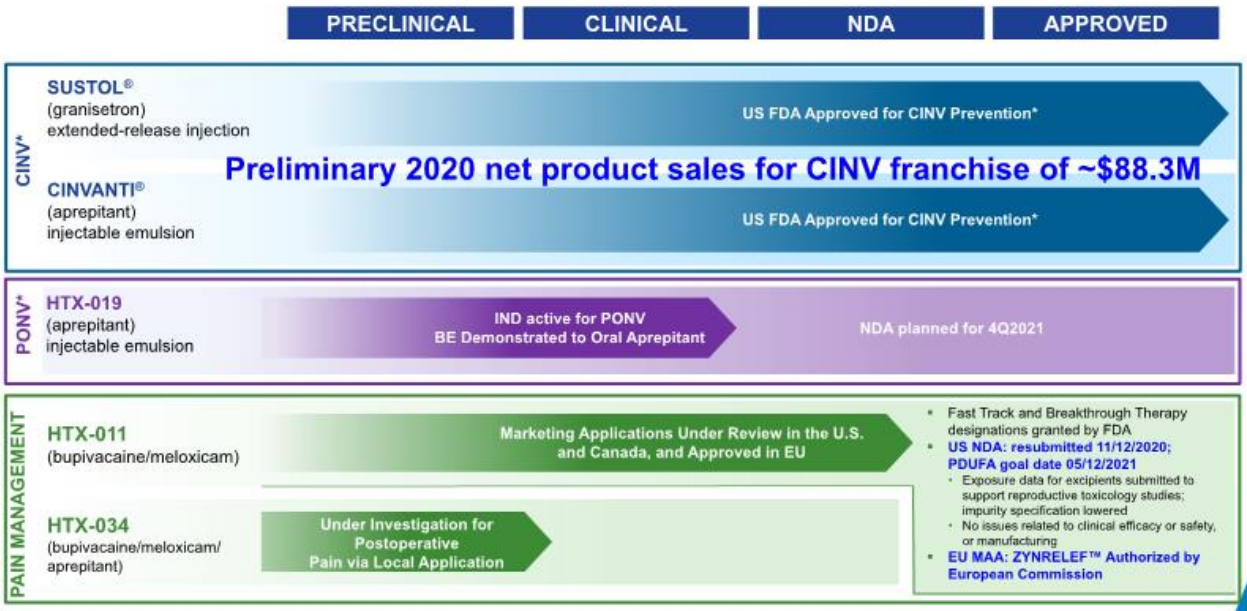
- ✓ Preliminary Q4 2020 net product sales for CINV franchise of ~$20.3 Million
- ✓ Preliminary full-year 2020 net product sales for CINV franchise of ~$88.3 Million
  - Versus Guidance of $85 Million
- ✓ Full-year 2021 net product sales guidance for CINV franchise of $130-$145 Million
- ✓ Preliminary 2020 year-end cash balance of ~$208.5 Million

Clinical/Regulatory Updates

- ✓ **HTX-011** – New Drug Application for postoperative pain management is under review in the US
  - May 12, 2021 PDUFA Date
- ✓ **HTX-034** – Preliminary results from Phase 1b bunionectomy study shows pain reduction through 96 hours with 45.5% of patients opioid-free through day 15
- ✓ **HTX-019** – Preliminary results from Phase 1 study of low dose IV injection demonstrated bioequivalence to approved oral aprepitant 40 mg dose for prevention of postoperative nausea and vomiting

Investment Areas

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

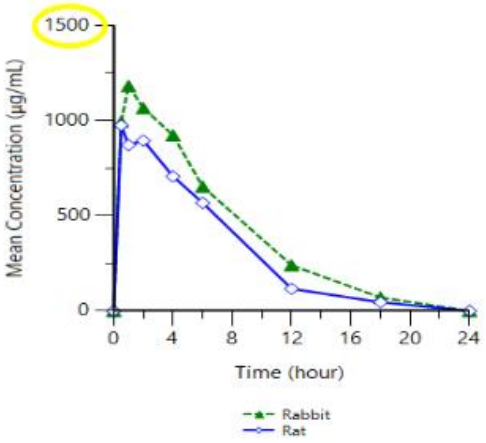
NDA Resubmitted Based on Guidance at Type A Meeting

- 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 CRL issue addressed by lowering impurity specification for final drug product to FDA agreed upon level
- **FDA has acknowledged Class 2 resubmission with 6-month review clock: PDUFA goal date of 05/12/2021**

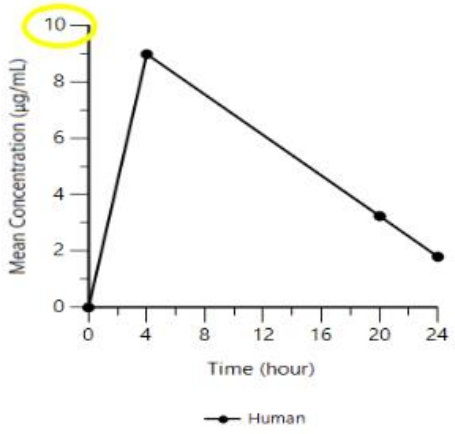
DMSO: Animal Pharmacokinetics (PK) vs Human Plasma Levels in TKA Study

DMSO Cmax in toxicology animals 106- to 129-fold higher than humans

Animal PK NOAEL Dose Level



Human PK (HTX-011 400 mg)

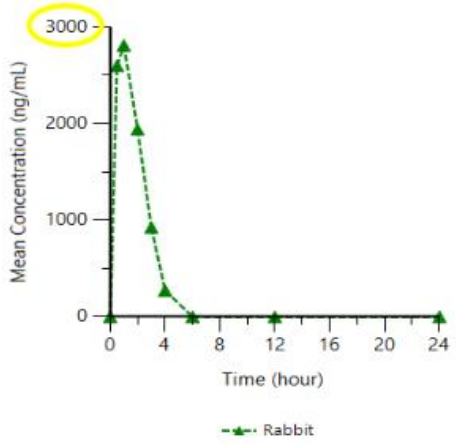


Note: Mean Plasma Concentration Time Profiles of DMSO in Pregnant Rats and Rabbits (1,000 mg/kg/day DMSO via Oral Administration) and in Humans (HTX-011 400 mg/12 mg via Installation into the Surgical Site)

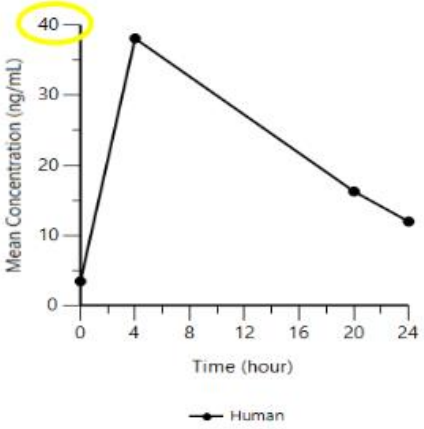
Maleic Acid: Animal Pharmacokinetics vs Human Plasma Levels in TKA Study

Maleic Acid Cmax in toxicology animals >50-fold higher than humans

Rabbit PK NOAEL Dose Level



Human PK (HTX-011 400 mg)

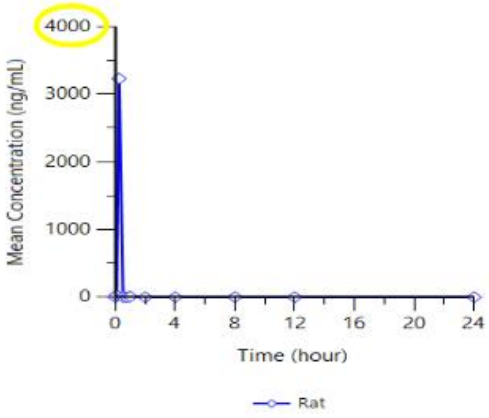


Note: Mean Plasma Concentration Time Profiles of Maleic Acid in Pregnant (20 mg/kg/day Maleic Acid via Oral Administration) and in Humans (HTX-011 400 mg/12 mg via Installation into the Surgical Site)

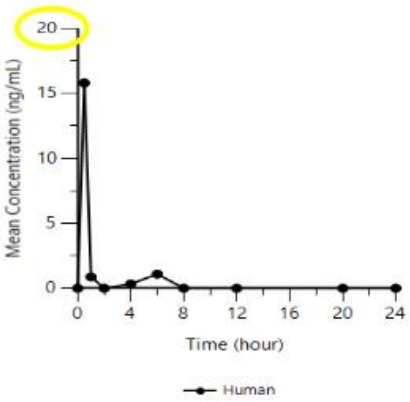
Triacetin: Animal Pharmacokinetics vs Human Plasma Levels in TKA Study

Triacetin Cmax in toxicology animals >200-fold higher than humans

Rat PK NOAEL Dose Level



Human PK (HTX-011 400 mg)



Note: Mean Plasma Concentration Time Profiles of Triacetin in Rats (1,000 mg/kg Triacetin via Oral Administration) and in Humans (HTX-011 400 mg/12 mg via Installation into the Surgical Site)

HTX-011 Commercialization

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

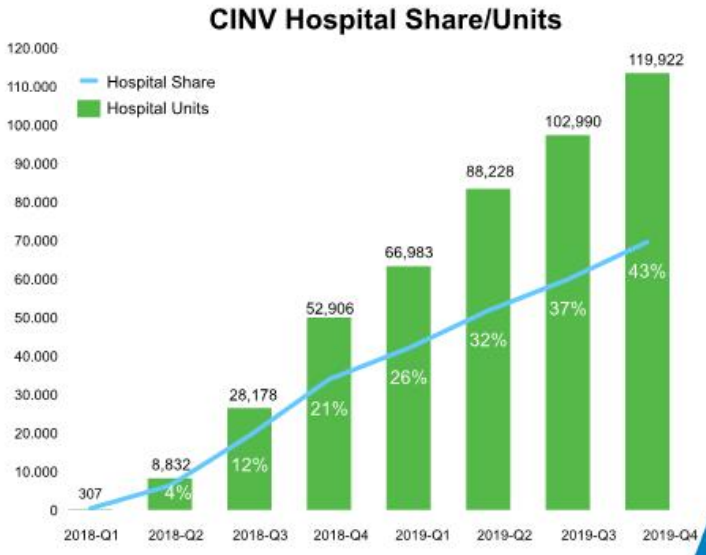
- Strong KOL relationships
- Successful hospital and pain management launch experience
- IDN/hospital/ASC expertise and relationships
- Reimbursement infrastructure in place
- GPO contracts in place
- Full-line wholesaler agreements and 3PL in place
- Safety monitoring structure in place
- Proven compliant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

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.



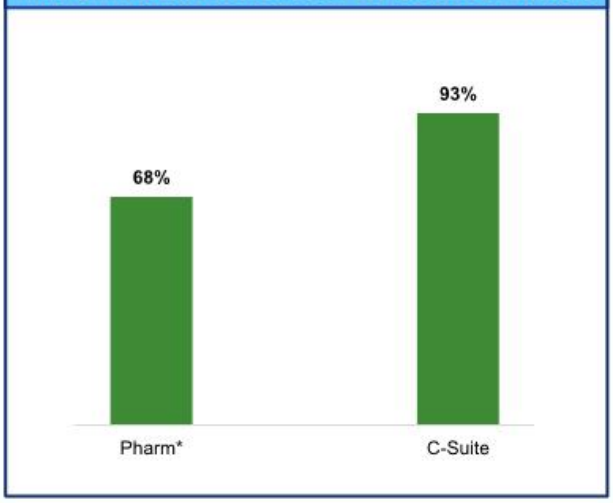
Source: IMS DDD12.25.20, 867 1.5.21

HTX-011 Is 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 LA
  - Reduction in Severe Pain
  - Elimination of Opioid Discharge Prescriptions
  - 72 Hour Duration

HTX-011 Aided Awareness P&T Decision Makers

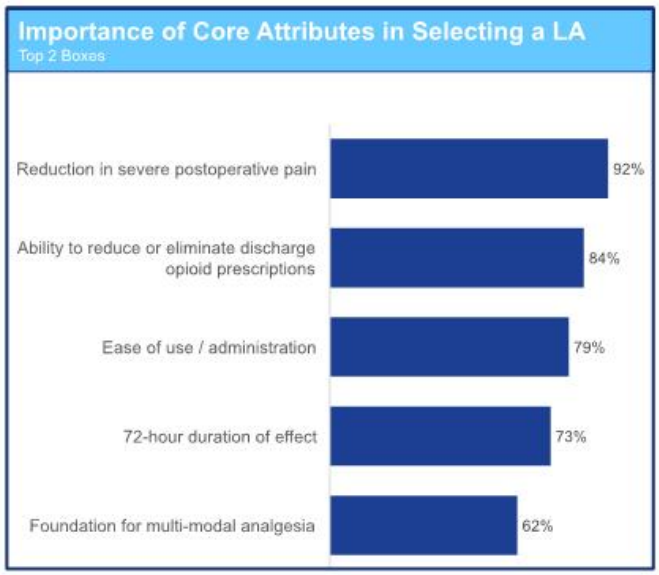


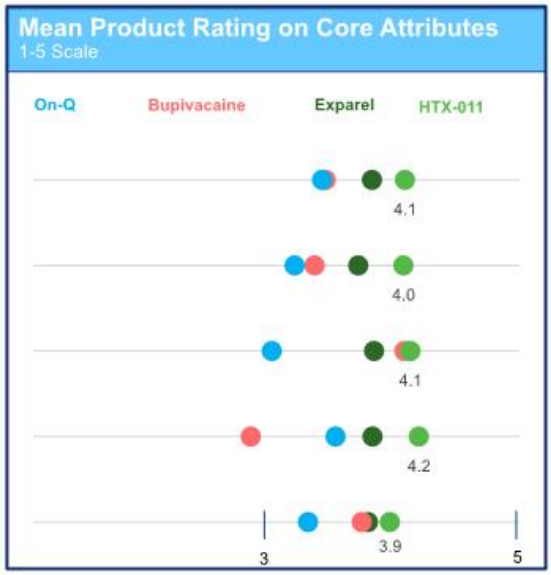
Source: Company-sponsored ATU Study July 2020 – Survey of 386 surgeons, anesthesiologists, pharmacists, NP/Pas of potential use of an approved product with the attributes for which we are developing HTX-011

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

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





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

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

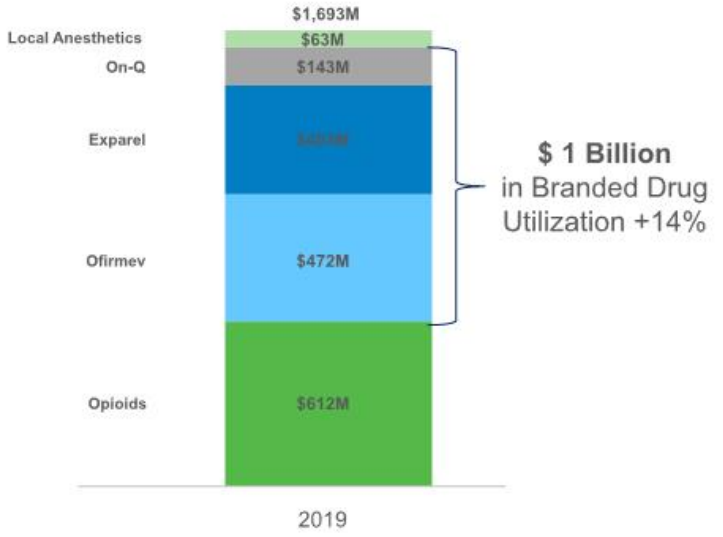
Large Body of Peer-Reviewed Data for Launch

- Published Peer-Reviewed Manuscripts
  - EPOCH 1 (301), *Regional Anesthesia & Pain Medicine*
  - EPOCH 2 (302), *Hernia*
  - Hernia Follow-on (215), *Surgery*
  - EPOC TKA (209), *Journal of Arthroplasty*
  - Mechanism of Action, *Regional Anesthesia & Pain Medicine*
  - Truven HEOR (Opioid Naïve Users), *Journal of Managed Care & Specialty Pharmacy*
- Accepted for publication:
  - Bunion (218), *J. Am Podiatric Med Assoc* (JAPMA)
  - Truven HEOR, *JMCP* (*Persistent Opioid Users*)
- 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.

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

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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HTX-011 Competitive Position Across Settings of Care

14 MILLION Target Procedures

Hospital Inpatient 47% (6.6M procedures)

- Bundled in DRG
- 56% (3.7M) of inpatient procedures are done in 340B hospitals

Hospital Outpatient 43% (6.0M procedures)

- 16% (1.0M) have Medicare reimbursement (3-year pass-through)
- 57% (3.4M) eligible for 340B discount
- Multiple SKUs – lower average costs

Ambulatory Surgical Centers 9% (1.3M procedures)

- 17% (0.2M) eligible for Medicare reimbursement at ASP + 6%
- Multiple SKUs – lower average costs

OVERALL TOTAL

- HTX-011 has lower acquisition cost benefit over bundled branded products
- Only HTX-011 will have HOPD reimbursement – 3-year pass-through
- Only HTX-011 will offer 340B pricing

52% of the opportunity lends itself to favorable reimbursement and access

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

New CMS OPPS* Rules

- CMS will eliminate the Inpatient Procedure Only (IPO) list over 3 years starting in CY 2021
  - In CY 2021 266 musculoskeletal-related procedures will be 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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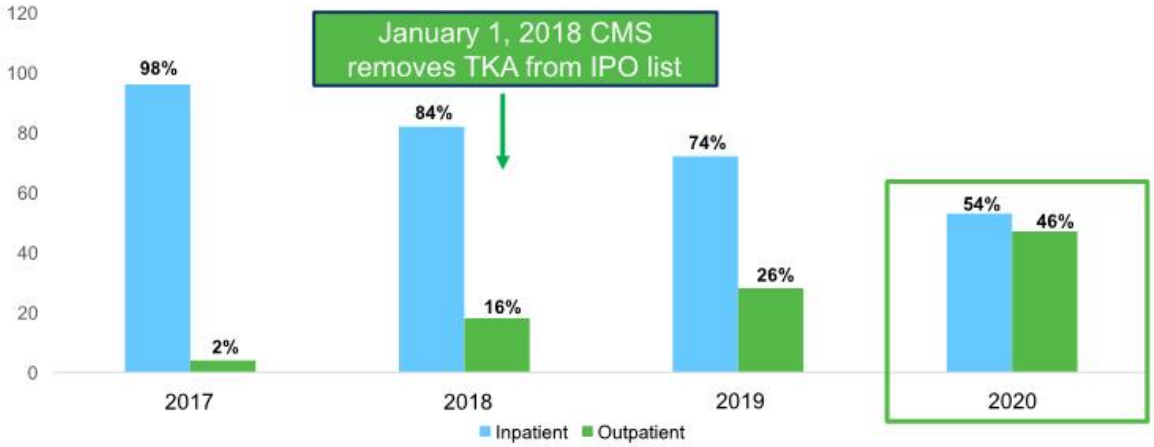
Impact of Previous CMS Rule Change on TKA

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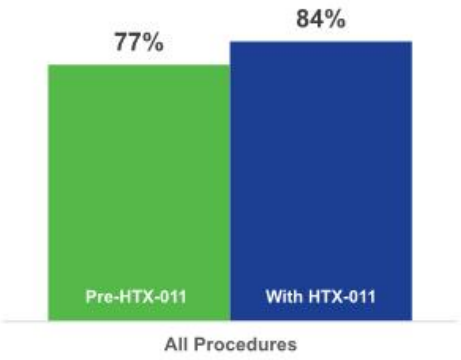
Physicians and Pharmacists Surveyed Believe HTX-011 Will Grow the Local Anesthetics Market

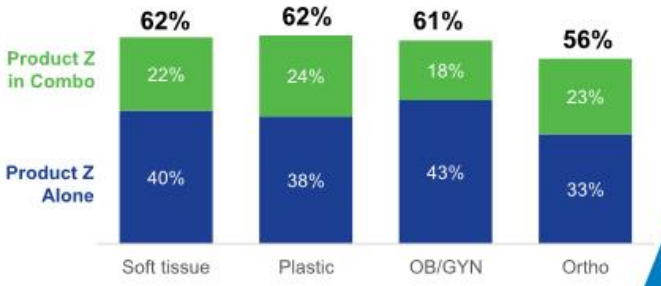
With the option of using Product Z available, respondents preferred using a local anesthetic 7% more of the time across their procedures

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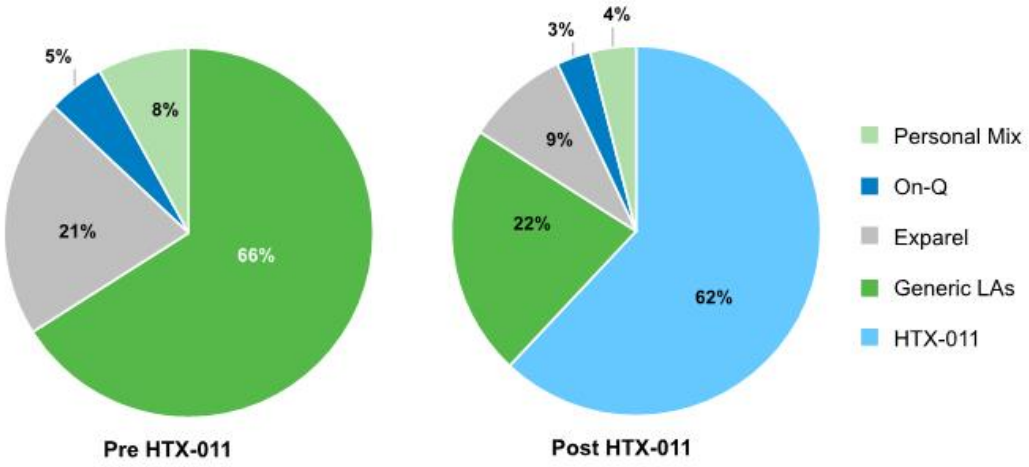
General Surgeons: HTX-011 Expected to Take Share from Other Treatment Options, With the Most Significant Being from Generic LAs

Anticipated Local Anesthetic Use - Soft Tissue Procedures



Pre HTX-011 **Post HTX-011**

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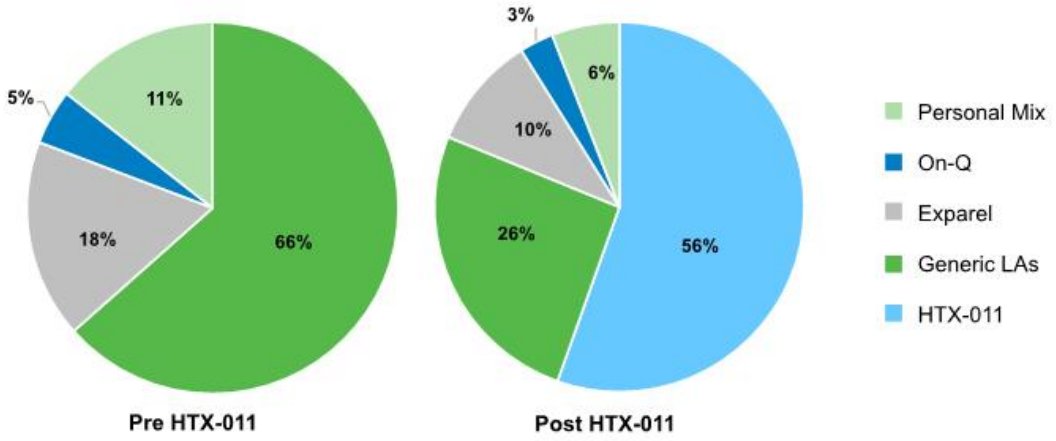
Orthopedic Surgeons: HTX-011 Expected to Take Share from Other Treatment Options, With the Most Significant Being from Generic LAs

Anticipated Local Anesthetic Use - Orthopedic Procedures



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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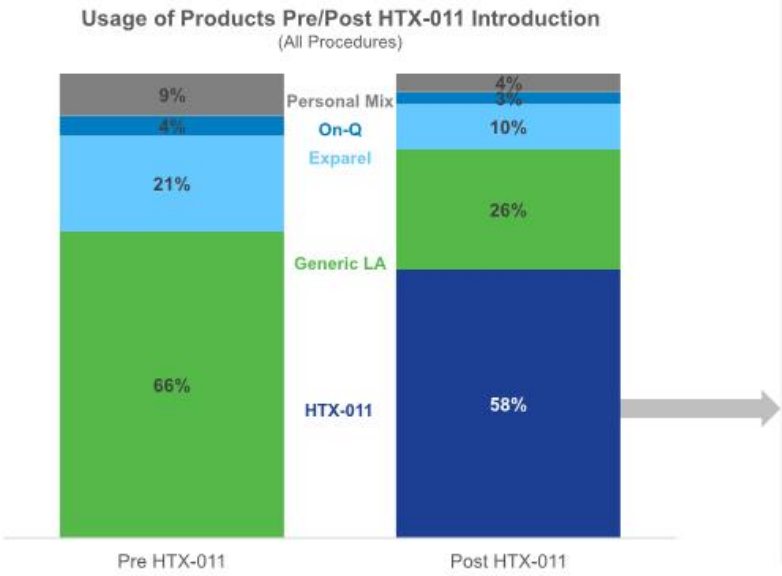
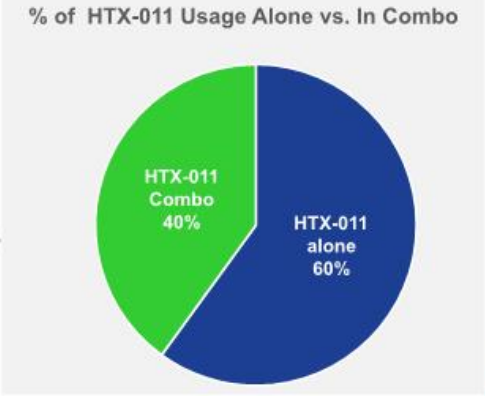
Across All Customers Surveyed, HTX-011 is Expected to Take Share from Both Exparel and Generic LAs



While generic LA usage appears to decline by 40 percentage points, 40% of HTX-011 preference includes use in combination with another local anesthetic – the majority of which will be generic LAs.



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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Highly Focused Launch Approach: 3 Primary Hospital Targets Using $570M in Branded Pain Drugs

	Hospitals	340B %	Target Procedures		Branded Utilization	
Hospital Targets	**1,305**	54%	**8.3M**	66%	**$573.9M**	76%
Target 1 340B + Branded	**486**	*100%*	**3.2M**	*38%*	**$259.2M**	*45%*
Target 2 Non-340B + Branded	**450**	*0%*	**2.4M**	*29%*	**$250.1M**	*44%*
Target 3 Large-Procedure Volume	**369**	*50%*	**2.7M**	*33%*	**$64.6M**	*11%*

	ASCs	Target Procedures		Brand Utilization	
ASCs Targets	**559**	**615K**	47%	**$16.9M**	24%

Source: Symphony Drug Market – 2017-2019 / LexisNexis Procedure Data August 2019 YTD and DRG Claims Data 2018

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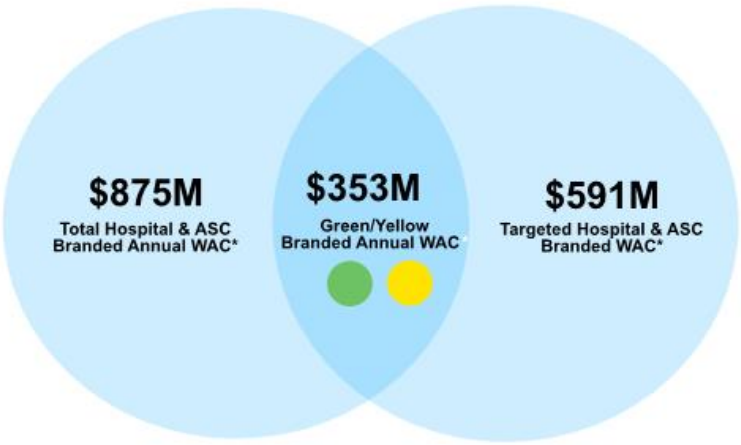
Profiled and Prioritized Fastest Moving Launch Accounts



0-3 Months
When will the account order post commercial availability of HTX-011

4-8 Months
When will the account order post commercial availability of HTX-011

	#	340B %	Target Procedures	Branded Utilization
Hospitals	722	49%	4.6M	$337M
ASC	445		466K	$16M

Source: Symphony Drug Market – 2017-2019 / LexisNexis Procedure Data August 2019 YTD
* Excludes ON-Q

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HTX-011 Ease of Use and Implementation

- **Needle-free application**
  - Eliminates the need for up to 120 injections (as in total knee arthroplasty)[1] and the time needed for aspiration and application
  - Avoids risks of inadvertent venous punctures and eliminates accidental needle sticks with local anesthetics[2]
- **No specialized training or certification required to administer[2]**
- **2 SKUs for different surgery requirements**
  - Reducing cost per procedure
  - Minimizing waste
- **Room temperature storage**
- **Kits fit standard OR medication carts (eg. Pyxis™) and include all components**

400 mg bupivacaine
12 mg meloxicam
14-mL

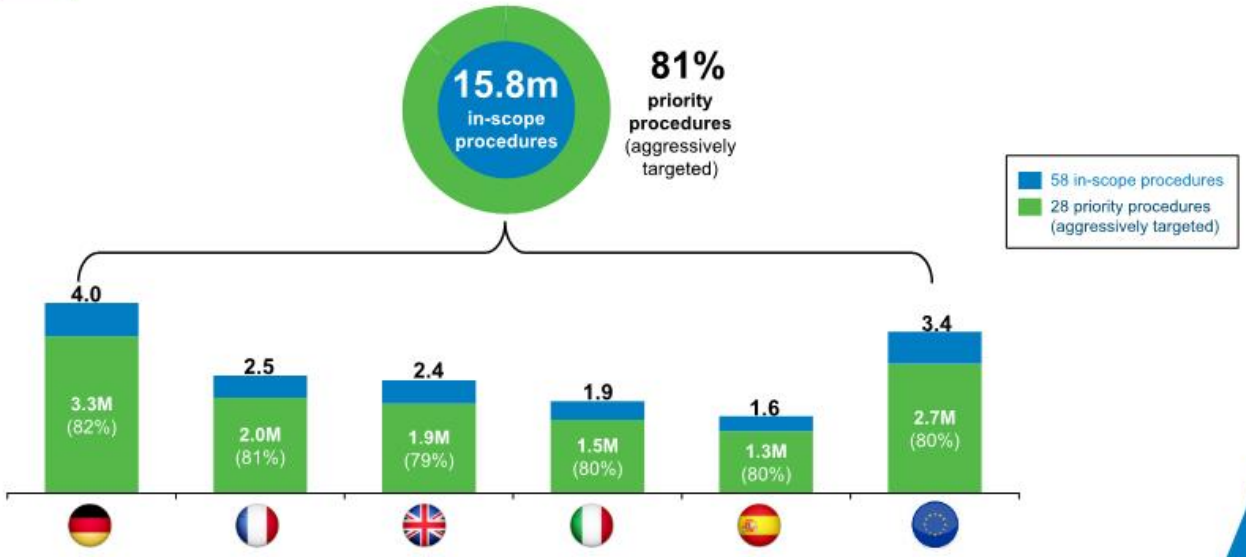
200 mg bupivacaine
6 mg meloxicam
7-mL

SKU: stock keeping unit. [a]Kit components include single-dose glass vial, Luer lock syringe(s), vented vial spike, Luer lock applicator(s), and tip cap(s).

Source: 1. Mont MA, Beaver WB, Dysart SH, et al. J Arthroplasty. 2018;33(1):90-96. **2.** ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2020. **3.** ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2020.

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

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 the European Union for the treatment of somatic postoperative pain from small - to medium-sized surgical wounds in adults

Resource Savings and Better Pain Management are Key Value Messages in EU5, as is Opioid Reduction, Particularly in the UK

EU5

Potential alleviation of **staff and bed constraints** is a **key value driver** for **Zynrelef**

1

Extended duration is a key strength to ~80% of HCPs and payers across the EU5. Demonstrating **earlier discharge**, reduction in **length of stay** and **cost of care** is highly compelling for payers[1]

ZYNRELEF's ability to **better manage severe pain** versus the standard of care is a **highly positive** value message for HCPs

2

Adequate treatment options for **severe pain** is seen as a key unmet need in Europe and for ~70% of physicians this is a **key strength** of ZYNRELEF

Messaging around **reduction in opioid use resonates highly in the UK**, where there is an opioid crisis, and is an issue of **growing importance in Europe**

3

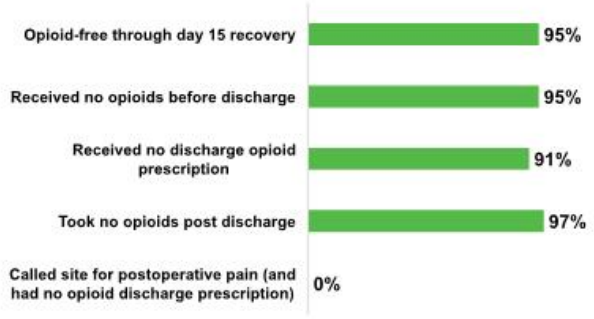
In the **UK**, the majority of physicians feel there already is an opioid **crisis** and ~70% of HCPs and ~90% of payers see opioid-free as a strength of ZYNRELEF

In the wider EU5, risks of opioids are perceived to be lower due to strict **controls** and **regulations**, however, there is a **growing recognition due to rapidly increasing opioid consumption**

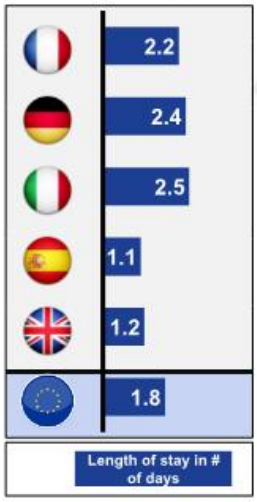
Notes: 1) Aside from length of stay and cost of care, resource utilization savings can also be achieved through reducing re-admissions, less staff time and effort required to manage postoperative pain (e.g. reducing the need to adjust the titration of IV opioids every few hours, pressure on limited staff to manage pain for the entire recovery ward) and lowering total drug spend

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**

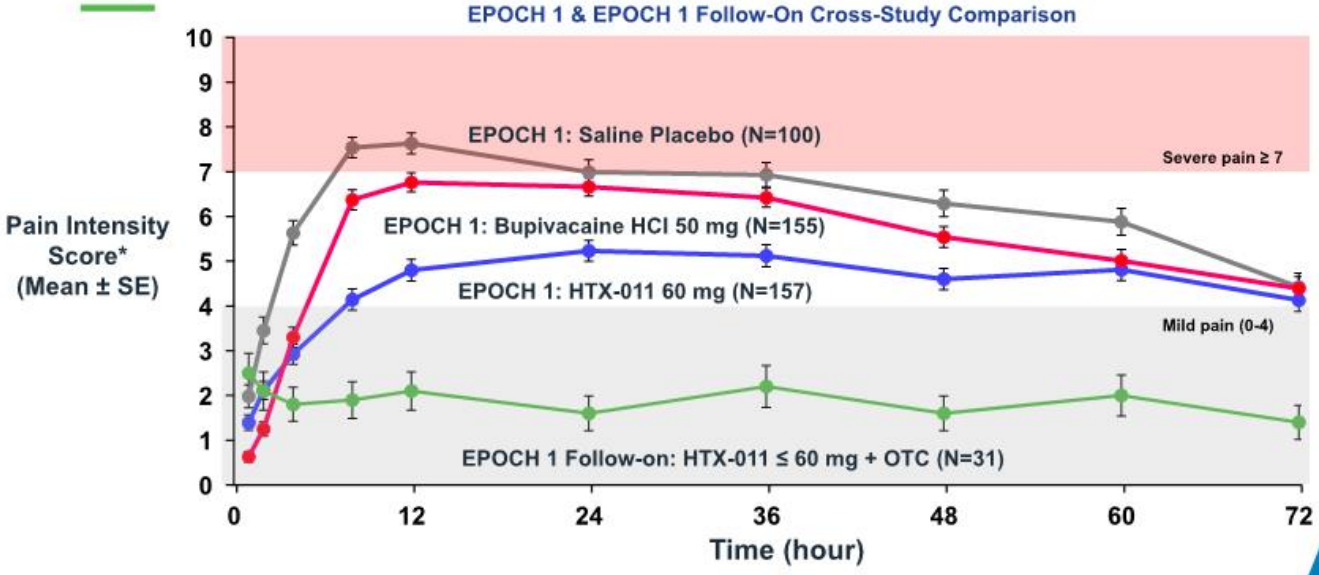
Notes: 1) Open inguinal hernia repair patients were treated with ZYNRELEF and a scheduled non-opioid oral over-the-counter (OTC) analgesic regimen (N = 93). 2) Two cohorts of patients were studied under Alternating or Concurrent multimodal analgesia (MMA) regimens. Alternating regimen (N=46): OTC regimen 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 ≥5 (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

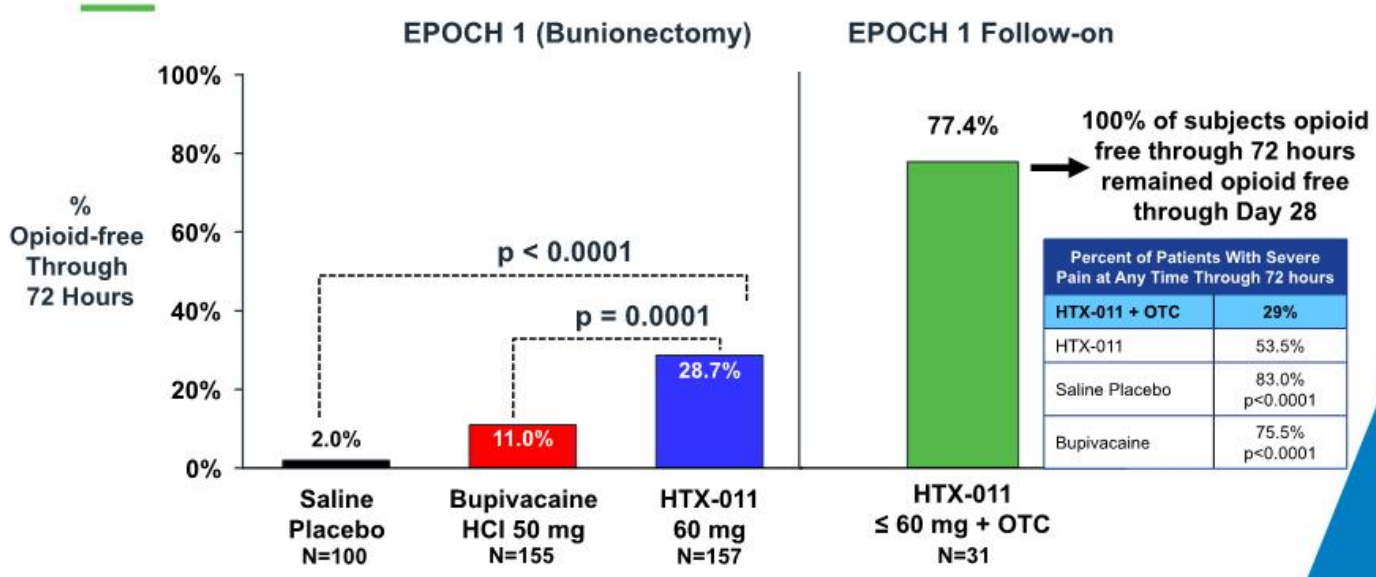
EPOCH 1 Follow-on: HTX-011 + OTC Acetaminophen and Ibuprofen Kept Pain in the Mild Range Through 72 Hours



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)

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

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



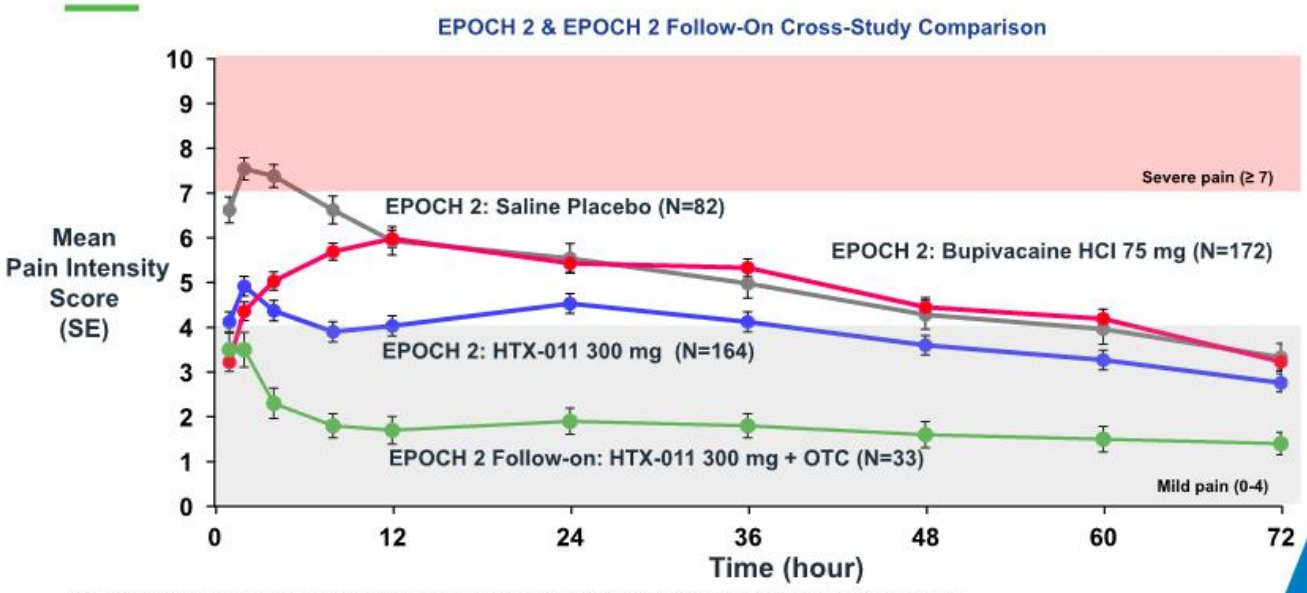
Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011 + OTC	29%
HTX-011	53.5%
Saline Placebo	83.0% p<0.0001
Bupivacaine	75.5% p<0.0001

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

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

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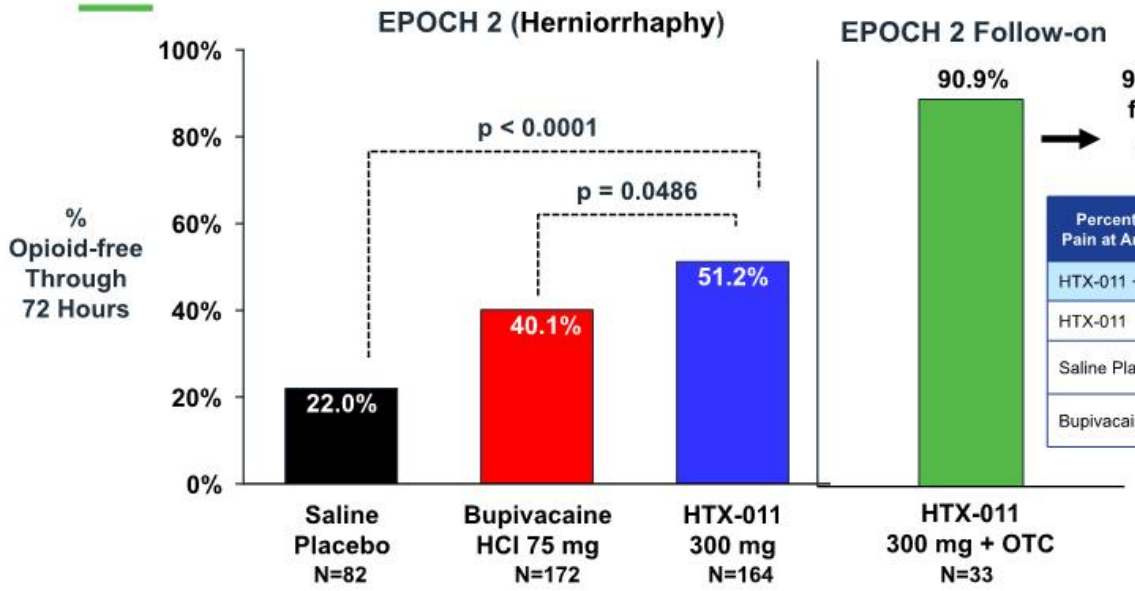
HTX-011 Significantly Reduced the Proportion of Patients Experiencing Severe Pain and Increased Proportion of Opioid-Free Patients

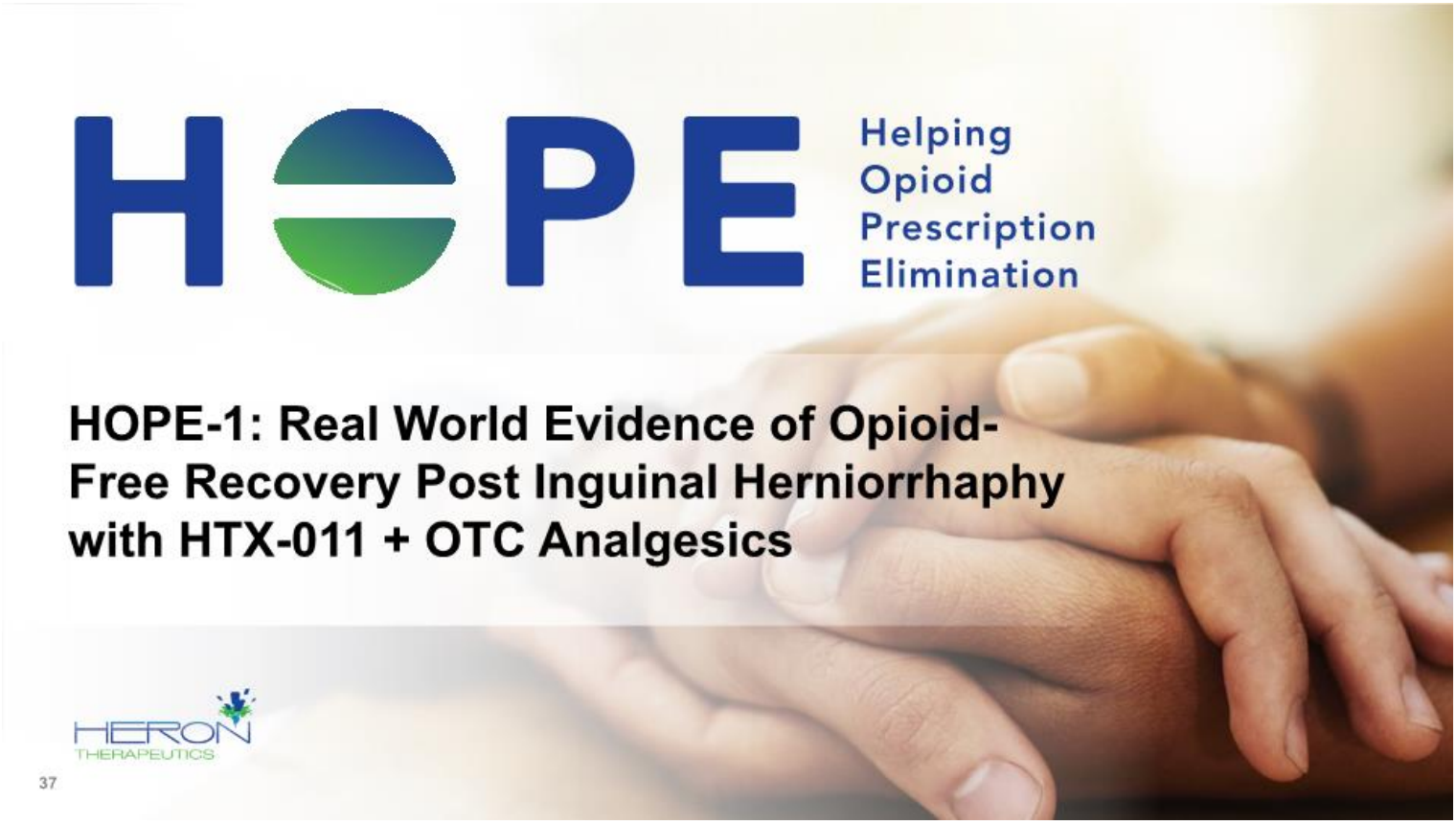


93% of subjects opioid free through 72 hours remained opioid free through Day 28

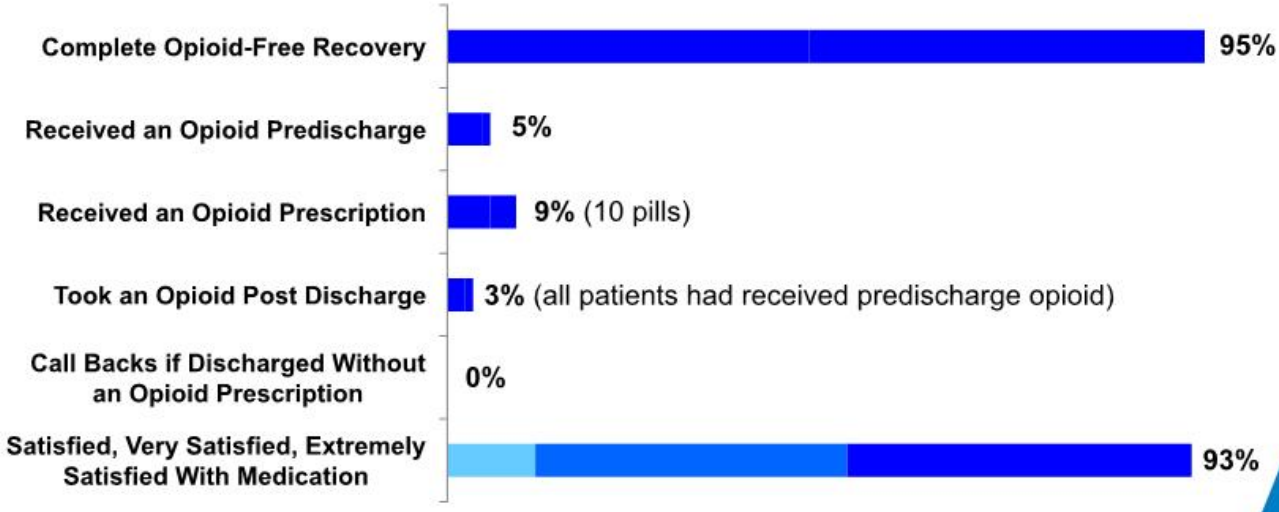
Percent of Patients With Severe Pain at Any Time Through 72 hours	
HTX-011 + OTC	15.2%
HTX-011	48.8%
Saline Placebo	81.7% p<0.0001
Bupivacaine	60.5% p=0.0372

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

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


HOPE
Helping
Opioid
Prescription
Elimination
HOPE-1: Real World Evidence of Opioid-Free Recovery Post Inguinal Herniorrhaphy with HTX-011 + OTC Analgesics
HERON
THERAPEUTICS
37

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

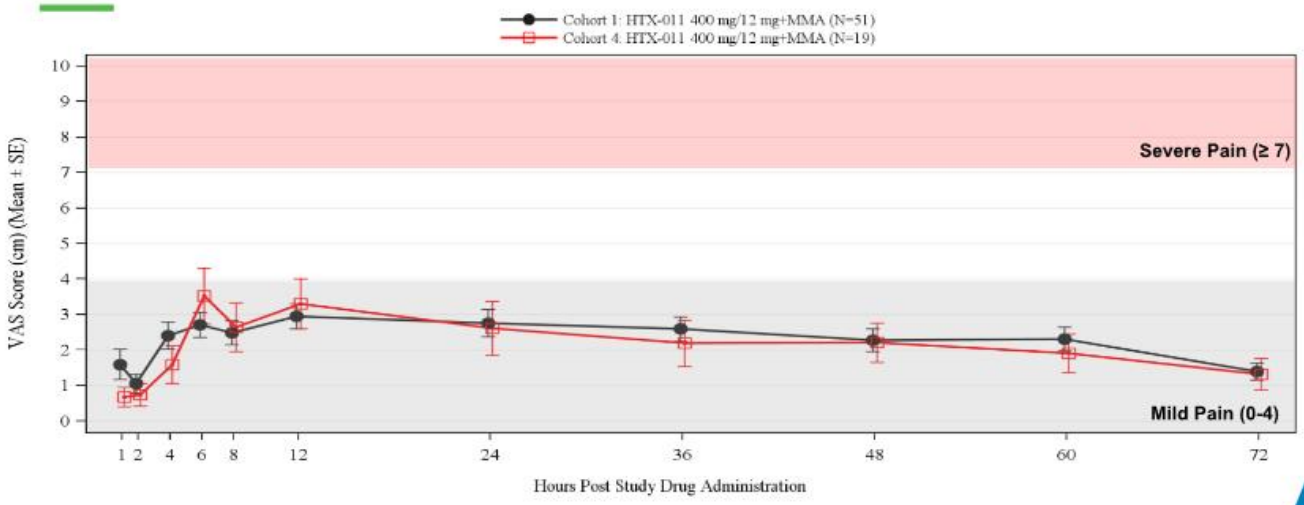


N=93 in initial pilot program
Presented at the American Society of Health-System Pharmacists (ASHP) Midyear 2019 Congress, December 8-12, 2019, Las Vegas, NV.

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

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



- **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

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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		PILLAR Study	
	HTX-011 + APAP + celecoxib (Cohort 1, n=51)	HTX-011 + APAP + ibuprofen (Cohort 4, n=19)	Exparel + Bupivacaine[1] (N = 70)	Bupivacaine[1] (N = 69)
AUC0-24 VAS Pain[2]	59.8	62.1	98.5	121.6
Opioid-Free	21.6%	47.4%	17.1%	1.4%
Mean Opioid Consumption MME (SD)	10.6 (9.25)	5.9 (7.95)	45.5 (35.01)	56.8 (38.26)
Log-transformed Geometric Mean Opioid Consumption MME	0.54	0.01	3.5	38.5
Discharge Ready in 24 hours Based MPADSS ≥ 9	68.6%	73.7%	Not shown	Not shown

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 do not imply a clinical benefit of HTX-011 over Exparel

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

Comparison of 48 Hr Results in TKA Using Pillar-Based MMA and the Same Analysis[1]	Study 306		PILLAR Study	
	HTX-011 + APAP + celecoxib (Cohort 1, n=51)	HTX-011 + APAP + ibuprofen (Cohort 4, n=19)	Exparel + Bupivacine[1] (N = 70)	Bupivacaine[1] (N = 69)
Mean AUC12-48 VAS Pain	145.4	125.7	180.8	209.3
Opioid-Free	11.8%	26.3%	10%	0%
Mean Opioid Consumption (MME)	19.4 (Median=15.8)	13.0 (Median = 5.0)	Not Shown	Not Shown
Log-transformed Geometric Mean Opioid Consumption MME	3.0	0.3	18.7	84.9
≤ 20 MME @ 48 hr	58.8%	73.7%	18.6%	4.4%
> 20 and ≤ 220 MME @ 48hr	41.2%	26.3%	78.6%	87%
> 220 MME @ 48 hr	0	0	2.9%	8.7%
DID NOT Receive a Discharge Prescription for Opioids	76.5%	68.4%	Not Shown	Not Shown

1. Mont doi: 10.1016/j.arth.2017.07.024

Disclaimer

This is a cross-study comparison of Study 306 to the PILLAR Study of Exparel plus bupivacaine; these comparisons do not imply a clinical benefit of HTX-011 over Exparel

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)

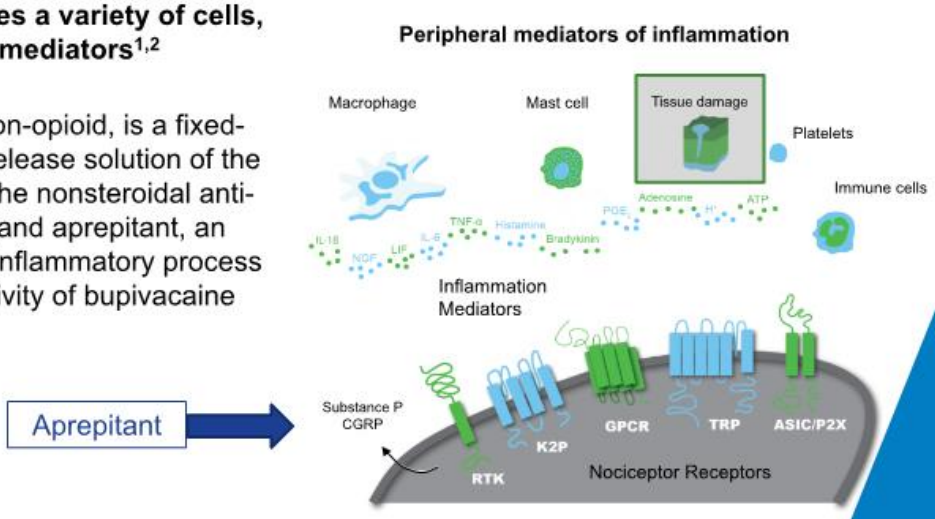
HTX-034 Development

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]

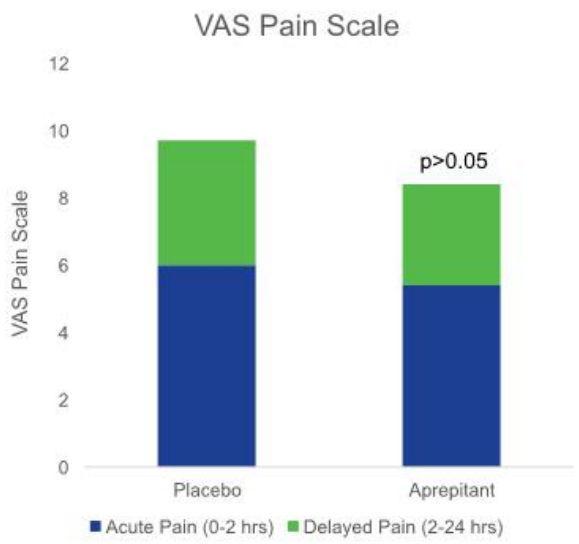
HTX-034, an investigational non-opioid, is a fixed-dose combination, extended-release solution of the local anesthetic bupivacaine, the nonsteroidal anti-inflammatory drug meloxicam and aprepitant, an additional agent targeting the inflammatory process that further potentiates the activity of bupivacaine

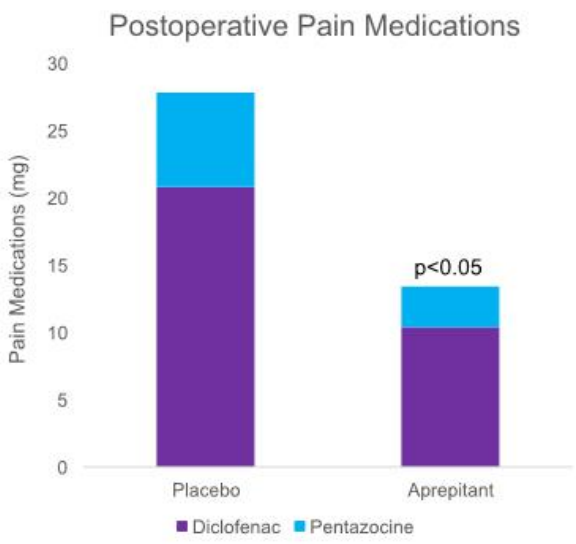


References: 1. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med.* 2004;140(6):441-451. **2.** Basbaum AI, Bautista DM, Scherrer G, Julius D. Cellular and molecular mechanisms of pain. *Cell.* 2009;139(2): 267-284.

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

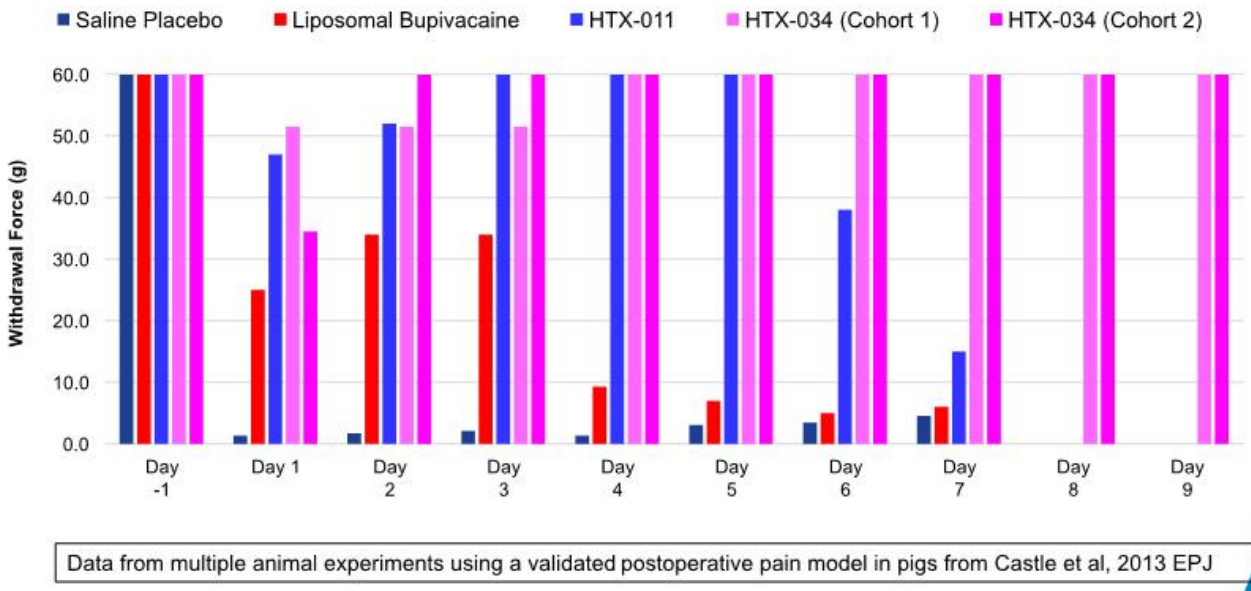
Aprepitant Has Been Shown to Significantly Reduce Postoperative Pain Medications and Lower Pain After Laparoscopic Gynecological Procedures*





*Published results from Kakuta N, et al. J Med Invest 58:246-251;2011 (n=64)

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



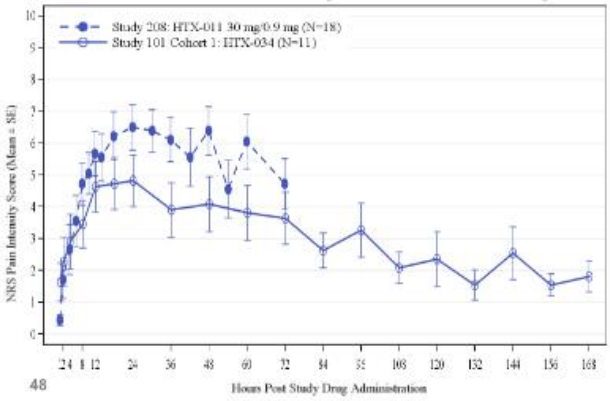
Data from multiple animal experiments using a validated postoperative pain model in pigs from Castle et al, 2013 EPJ

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

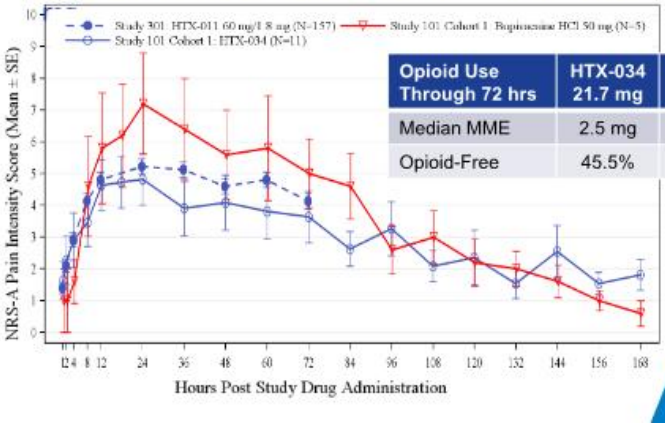
HTX-034 21.7 mg Produced Greater Pain Reduction and Lower Opioid Use than HTX-011 30 mg in Study 208 or HTX-011 60 mg in Study 301

- 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 will begin 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*

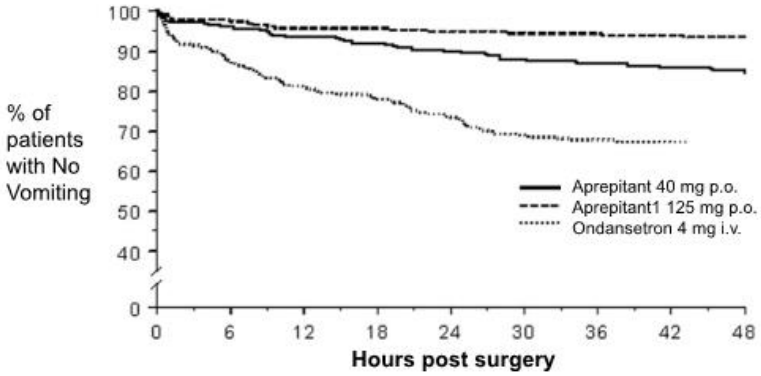


Figure 5. Kaplan-Meier curves for the time to first vomiting during the 48 h following surgery. The time to first vomiting was delayed by aprepitant; *P* 0.001 based on the log-rank test.

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*

Outcomes	Effects and confidence in the estimate of effects (network meta-analysis)															
	Aprepitant*		Ramosetron*		Granisetron*		Dexamethasone*		Ondansetron*		Fosaprepitant*		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)																
Placebo (comparator) 300 per 1000[a] (30%)	**RR 0.26** (0.18 to 0.38) Network estimate	222 fewer per 1000 (246 fewer to 186 fewer)	**RR 0.44** (0.32 to 0.59) Network estimate	168 fewer per 1000 (204 fewer to 123 fewer)	**RR 0.45** (0.38 to 0.54) Network estimate	165 fewer per 1000 (186 fewer to 138 fewer)	**RR 0.51** (0.44 to 0.57) Network estimate	147 fewer per 1000 (168 fewer to 471 fewer)	**RR 0.55** (0.51 to 0.60) Network estimate	135 fewer per 1000 (147 fewer to 120 fewer)	**RR 0.06** (0.02 to 0.21) Network estimate	282 fewer per 1000 (294 fewer to 237 fewer)	**RR 0.61** (0.54 to 0.69) Network estimate	117 fewer per 1000 (138 fewer 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 estimate[1]		⊕⊕⊕⊖ **Moderate** Confidence in network estimate due to incoherence		⊕⊕⊕⊖ **Moderate** Confidence in network 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

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

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

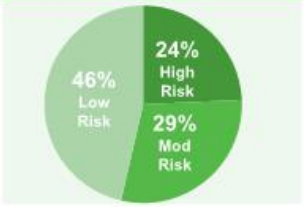
Patient Population & Market Size

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*

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)	CV / CT	Cranial
As vomiting directly involves the gastrointestinal tract, emesis can directly injure surgical sites that involve this organ system	Retching and vomiting can lead to transient increases in blood pressure which can result in damage/disruption of arterial surgical sites	Intracranial pressure increases during emesis, cranial surgeries, such as craniotomy, are at elevated risk of poor outcomes due to PONV

~14M

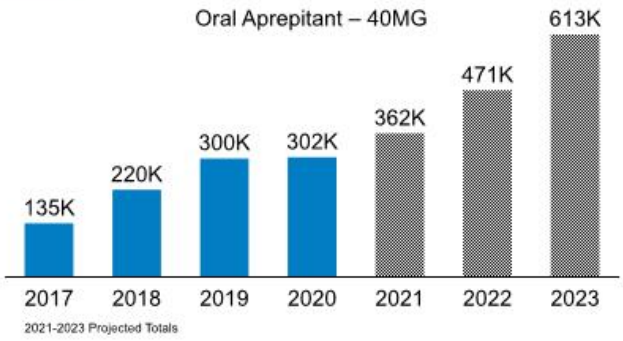
"High Clinical Concern" Procedures in 2020
(36% of all Surgical Procedures)

~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*

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 Commercial Products

2020 CINV Franchise Outlook

CINVANTI®

- Cinvanti continues to have the best overall profile compared to the other available NK_1 antagonists and is completely differentiated from generic fosaprepitant with the 2-min IV Push administration
- Generic fosaprepitant entered the market in September 2019 and let to reduced sales of CINVANTI in 2020; however, we believe the impact of the arbitrage is substantially over, with customers returning to CINVANTI beginning in 1Q2021

SUSTOL®

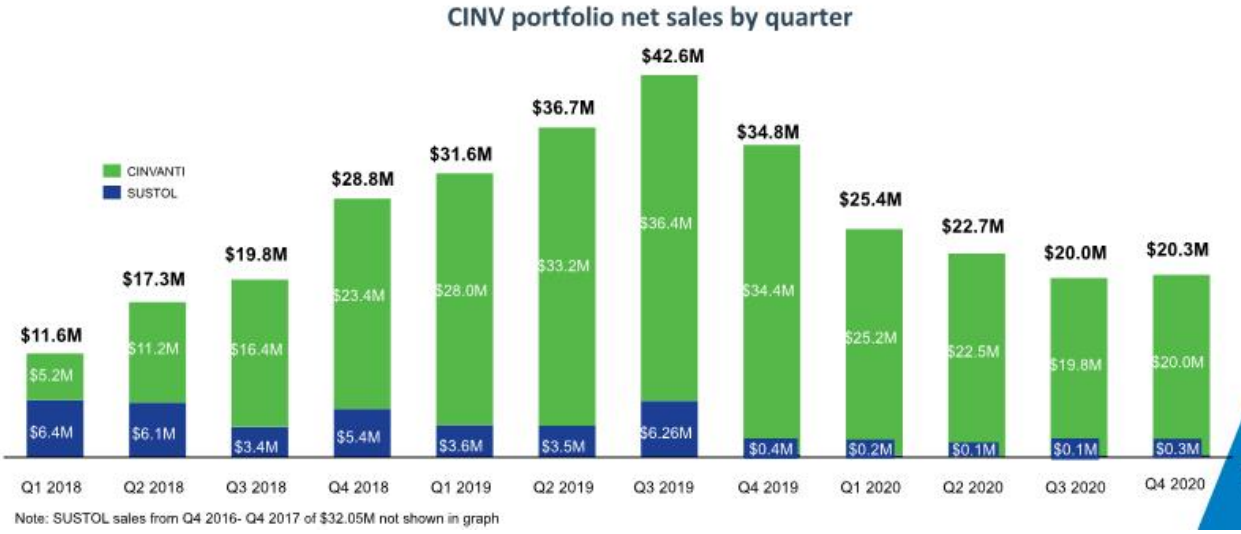
- The Aloxi arbitrage is over and Heron has implemented an innovative strategy to refresh the value of SUSTOL
- The ASP for SUSTOL was reset January 2021, which should allow for increased sales

CINV Franchise

- **Preliminary 2020 net product sales for CINV franchise of ~$88.3M compared to guidance of $85M, which was increased from $70M - $80M**
- **2021 net sales guidance for CINV franchise: $130M - $145M**

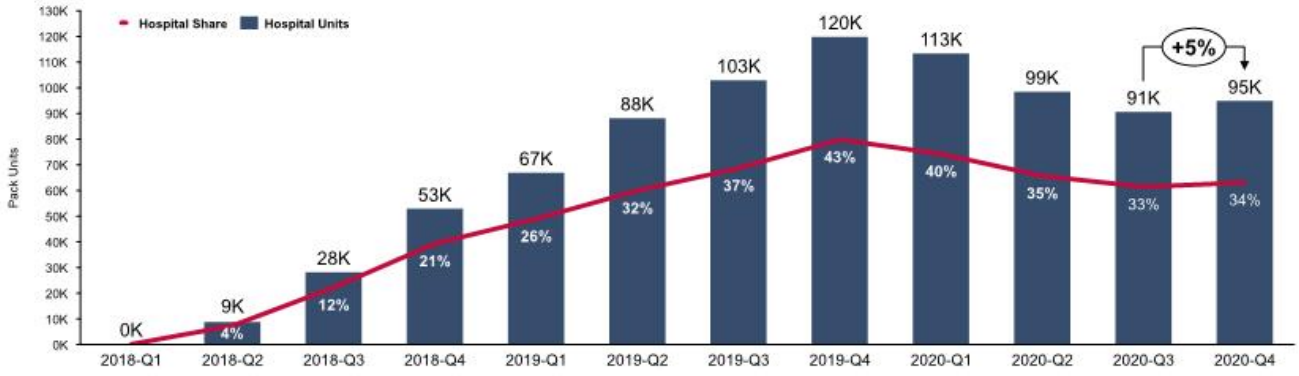
Heron's CINV Portfolio Has Generated Over $340M Since Inception, CINV Franchise Sales Will Return to Growth in 2021 & Beyond

- Launch of generic Emend IV in September 2019 resulted in declining CINVANTI sales
- Clinic-based practices are much faster to take advantage of the arbitrage, but are expected to return to CINVANTI post-arbitrage in early 2021
- SUSTOL sales continue to be low due to the Refresh Program and should rebound in 1Q2021



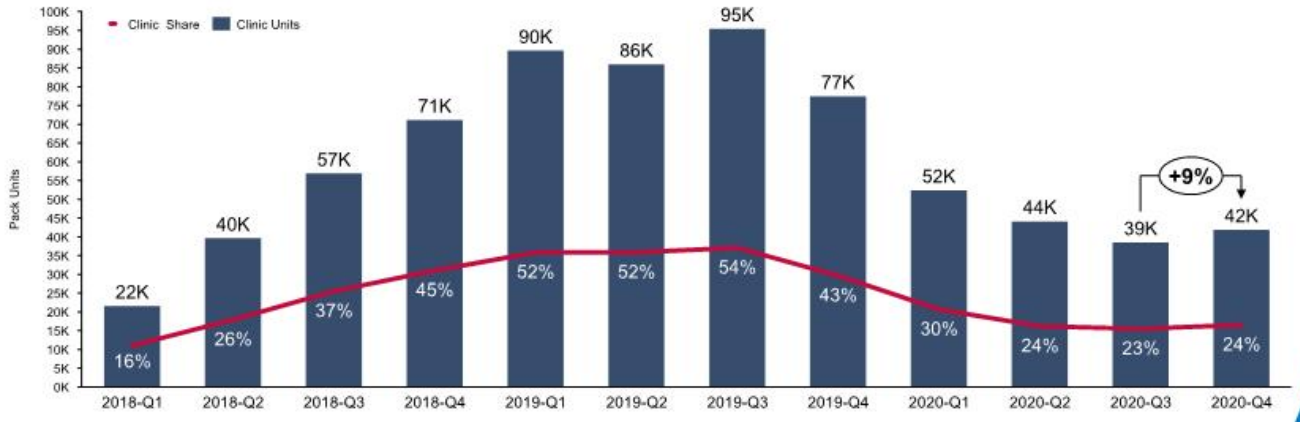
Note: SUSTOL sales from Q4 2016- Q4 2017 of $32.05M not shown in graph

CINVANTI – Hospital Share/Units Were Down in 1Q20 Through 3Q20 Due to the Emend IV Generic Arbitrage, but Began to Rebound in 4Q



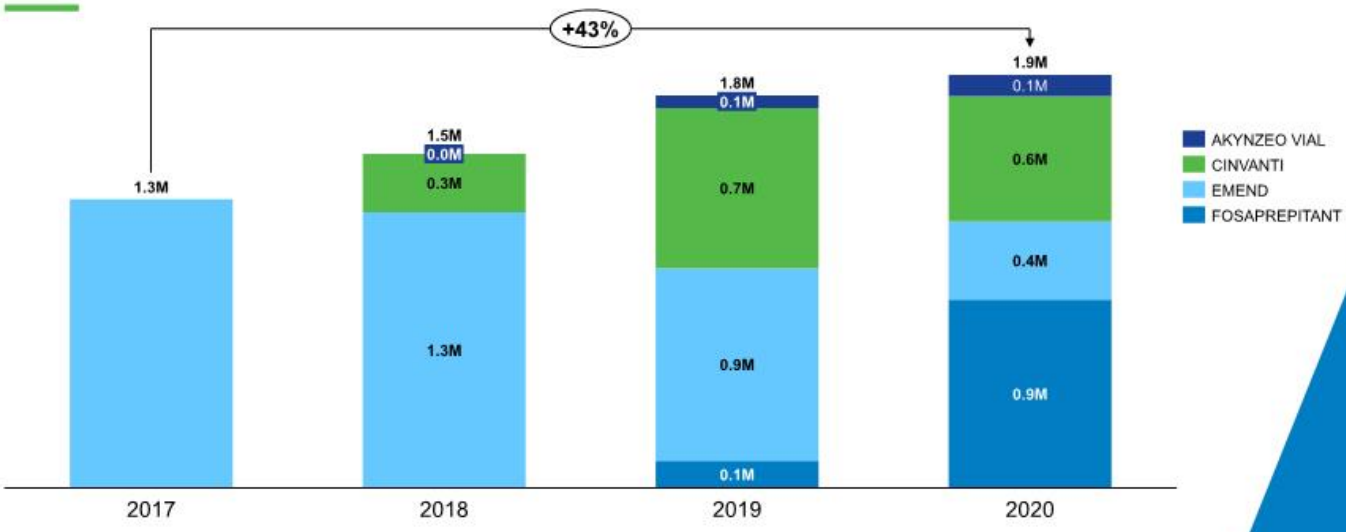
Source:867 1.5.21, : IMS DDD Q4'20 though 12.25.20 with final week projected

CINVANTI – Clinic Share/Units Declined in 1Q20 Through 3Q20 Due to the Emend IV Generic Arbitrage, but Began to Rebound in 4Q



Source:867 1.5.21, IMS DDD Q4'20 though 12.25.20 with final week projected

The NK1 Market Has Grown 43% Since the Launch of CINVANTI



63 **Source:** IMS DDD Q4'20 though 12.25.20 with final week projected

Financial Summary

Heron ended 2020 with cash, cash equivalents and short-term investments of ~$208.5 million.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended September 30, 2020	Nine Months Ended September 30, 2020
Net product sales	$ 19,965	$ 68,033
Operating expenses[1]	78,349	234,900
Other income, net	156	1,870
Net loss[1]	$ (58,228)	$ (164,997)
Net loss per share[2]	$ (0.64)	$ (1.82)
Net cash used in operations	$ (42,054)	$ (132,266)

Condensed Balance Sheet Data (In thousands)	September 30, 2020
Cash, cash equivalents and short-term investments	$ 258,146
Accounts receivable, net	$ 33,654
Total assets	$ 390,023
Total stockholders' equity	$ 277,147

Common shares outstanding as of September 30, 2020 totaled 90.9 million.

[1] Includes $11.1 million and $34.2 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2020, respectively.
[2] Based on 90.8 million and 90.7 million weighted-average common shares outstanding for the three and nine months ended September 30, 2020, respectively.

Key Catalysts in Pain Management & CINV Franchises

HTX-011 & HTX-034 for Postoperative Pain	CINVANTI ® and SUSTOL® for CINV	HTX-019 for PONV

• **CRL received 26 June 2020**
  • **NDA resubmitted; PDUFA goal date of 05/12/2021**
• **EU Centralised Procedure**
  • **European Commission Authorization received**
  • **UK Authorization received**
• **Canadian NDS**
  • **Responses to questions in process**
	• **2020 net product sales of ~$88.3M compared to guidance of $85M for CINV franchise (raised from $70M - $80M)**	• Bioequivalence of HTX-019 32 mg to oral aprepitant 40 mg achieved in Phase 1 study
		• 5050(b)(2) NDA for PONV planned for 4Q2021

• Promising HTX-034 Phase 1b bunionectomy results • **Phase 2 will start 1Q**	• **2021 net sales guidance for CINV franchise: $130M - $145M**	• Potential approval in 2H2022

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