Heron Corporate Update

January 10, 2022

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 timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunity for ZYNRELEF in the US and Europe; the potential additional market opportunity for the expanded U.S. label; the timing and results of studies for the further expansion of the U.S. label for ZYNRELEF; the timing and results of studies for the HTX-034 development program; the timing of the FDA's review process and whether the FDA approves the NDA for HTX-019 for prevention of postoperative nausea and vomiting; the potential market opportunity for HTX-019; 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.

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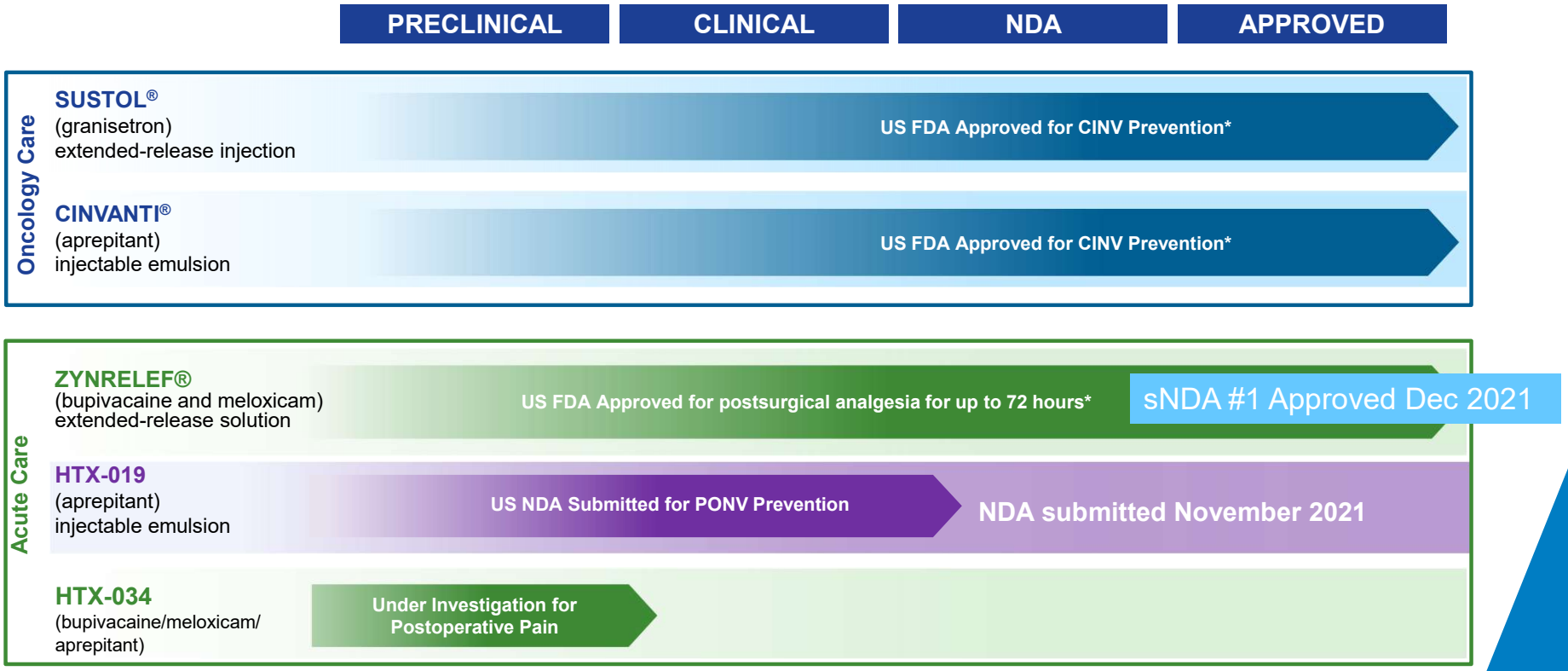
Heron Pipeline



CINV: Chemotherapy-induced nausea and vomiting. **PONV:** postoperative 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 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. **ZYNRELEF (bupivacaine and meloxicam) extended-release solution** is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures.

HTX-034 and HTX-019 (for PONV) are investigational new drugs and are not approved by the FDA

ZYNRELEF®
(bupivacaine and meloxicam)
Extended-Release Solution

Why Approval of ZYNRELEF is so Important
Postoperative Opioids Can Be a Doorway to Addiction

More than 50 million
surgical procedures happen in the United States.[1]

67% of patients
filled an opioid prescription between 30 days before through 14 days after surgery.[2*]

> 2 million Americans
may become persistent opioid users annually after surgery. [1]

In 2020, drug overdoses were linked to more than
90,000 deaths
the highest number ever recorded in a single year.[3]

In addition, most patients take fewer opioids than the amount prescribed after surgery, resulting in excess opioid pills that are accessible to others.[4]

80%
of patients report unused opioid tablets[4]

Up to **77%**
of opioid pills remain inside the home in unsecured locations[4]

51%
of nonmedical users of opioids received them from friends and family[5]

More than
$23.4 billion
in annual healthcare costs associated with persistent opioid users can be attributed to postoperative pain management.[1,6]

* This was determined using a 20% national sample of Medicare claims among beneficiaries aged 65 and older with Medicare Part D claims who underwent a major or minor surgical procedure between January 1, 2009 and June 30, 2015.

References: 1. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults [published correction appears in JAMA Surg. 2019 Mar 1;154(3):272]. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504. **2.** Santosa KB, Hu HM, Brummett CM, et al. New persistent opioid use among older patients following surgery: A Medicare claims analysis. *Surgery*. 2020;167(4):732-742. doi:10.1016/j.surg.2019.04.016. **3.** NCHS, National Vital Statistics System. Estimates for 2020 are based on provisional data. Estimates for 2015-2019 are based on final data (available from: https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm). **4.** Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surg*. 2017;152(11):1066–1071. doi:10.1001/jamasurg.2017.0831. **5.** Substance Abuse and Mental Health Services Administration . Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; Rockville, MD: 2019. Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf. Accessed April 19, 2021. **6.** Brummett CM, Evans-Shields J, England C, Kong AM, Lew CR, Henriques C, Zimmerman NM, Sun EC. Increased health care costs associated with new persistent opioid use after major surgery in opioid-naive patients. *J Manag Care Spec Pharm*. 2021 Feb 24:1-12. doi: 10.18553/jmcp.2021.20507. Epub ahead of print. PMID: 33624534.

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ZYNRELEF NEW Approved Expanded Indications

Indications

ZYNRELEF contains bupivacaine, an amide local anesthetic, and meloxicam, a nonsteroidal anti-inflammatory drug (NSAID), and is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.

Limitations of Use

Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures.

Successful FDA Interactions Resulted in Expansion of ZYNRELEF Label

- In a little over two months, the FDA approved our supplemental NDA to significantly expand ZYNRELEF indications to include foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.
  - Significantly expands the commercial opportunity to ~7 million procedures
  - Significantly improves the opportunity for therapeutic substitution
- FDA has agreed to contents of a second supplemental NDA to further expand the indications to orthopedic and soft tissue surgical procedures
  - Submission targeted for 2H2022
  - Expanded broad claim structure designed to cover the full 14 million target procedures

Activities Needed for sNDA #2 to Obtain Broadest Label Underway

- Study 220 C-section: enrollment completed
- Study 221 Spine: recruiting
- AMAZE Study:
  - Abdominoplasty – recruiting
  - Shoulder – recruiting
- sNDA #2 on target for 2H2022

Major ZYNRELEF 2021 Accomplishments

- Secured **over 200** P&T Approvals through 12/31/2021
- Scheduled **~ 160** P&T reviews for Q1'22
- **Over 300** unique ordering accounts with **over 70%** reordering through 12/31/2021
- Reimbursement for ZYNRELEF outside the surgical bundle is now up to **120 million** commercial and Medicaid covered lives in the ASC setting of care
- ZYNRELEF received a unique C-code effective January 1, 2022 for ASCs; pass-through for HOPD expected April 1, 2022
- Demand has increased significantly month over month with significantly greater acceleration expected in 2022 with the approval of the expanded label
- FDA approved manufacturing supplements to NDA to add large-scale supplier of our proprietary polymer and a 10X increase in drug product manufacturing
  - Allows for manufacturing of millions of doses of ZYNRELEF annually at a significantly reduced cost of goods

Overview 2021 – Headwinds or Challenges

- USPI initially limited to 3 indicated procedures
  - Made “Therapeutic Substitution” difficult
- Resurgence of COVID-19
  - Reduced surgeries
  - Delayed P&Ts
- TKA complicated and time consuming surgery

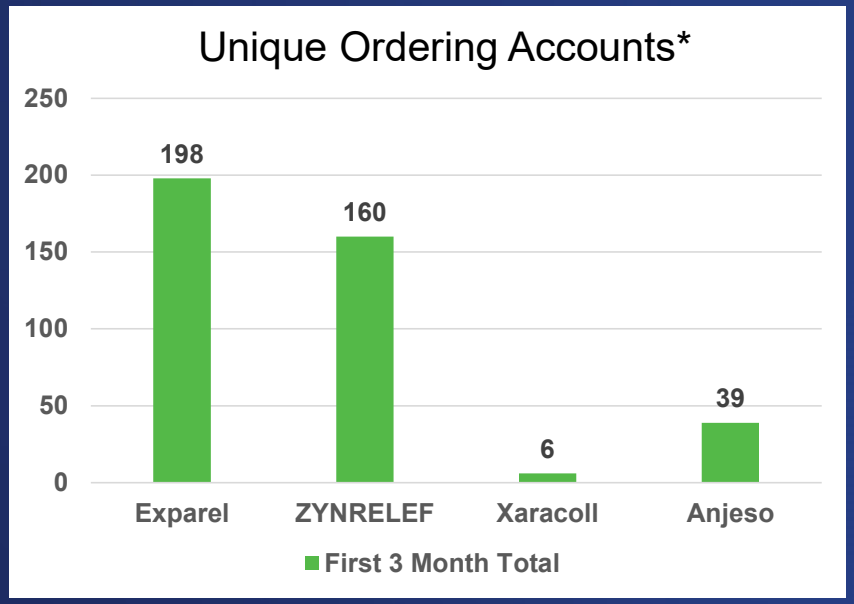
Key Learning: ZYNRELEF works as well or better in the commercial setting than we saw in clinical trials

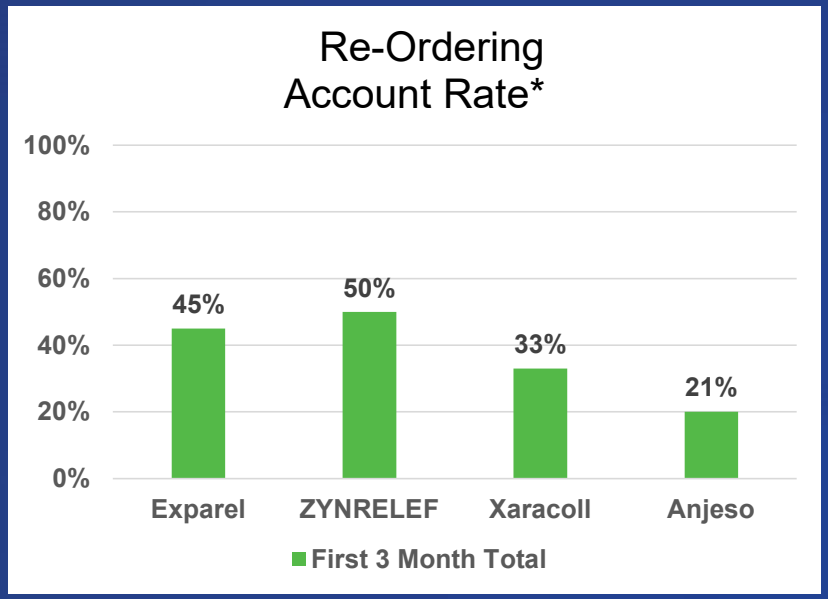
ZYNRELEF Priorities 2022 - Strategy

- Leverage **new label indication** for faster growth
  - Expand beyond TKA, Hernia and Bunion in unrestricted accounts
  - Expand / remove restrictions in open restricted accounts
  - Revisit “Therapeutic Substitution” accounts with expanded label
- Build consistent usage in open ordering accounts and increase average order size
- Maximize specific C-code and Commercial/Medicaid separate reimbursement in ASCs
- Reduce time from P&T approval to “Go live”
  - Leverage time between approval and Med Exec review to train and surgeons
  - Build additional surgical champions in delayed P&T accounts
- Continue to gain formulary access to new IDNs and Hospitals
- **2022 Challenges** – we are seeing reductions in elective surgeries due to the current spike in COVID; hopefully, Omicron burns out quickly

ZYNRELEF is Gaining Significant Traction Despite COVID-19

- 160 unique accounts ordered ZYNRELEF in Q3'21 (July '21 through Sept. '21)
  - Over 50% of accounts reordered ZYNRELEF in Q3'21 since their initial order





* Source: Symphony Heath SNR

Please see **IMPORTANT SAFETY INFORMATION** on pages 16 and 17 and full Prescribing Information, including **Boxed Warning**.

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Developing Best-in-Class Medicine. Improving Lives.™

ZYNRELEF Competitive Position Across Settings of Care

~14M
High Value Market Procedures[1]

Hospital Inpatient 46% (6.5M procedures)

- Bundled in DRG
- 57% (3.7M) of inpatient procedures are done in 340B hospitals

Hospital Outpatient 39% (5.4M procedures)

- **On 4/1/22, expect** 17% (0.9M) have Medicare reimbursement (3-year pass-through)
- 58% (3.1M) eligible for 340B discount
- Multiple SKUs – lower average costs

Ambulatory Surgical Centers 15% (2.1M procedures)

- 18% (0.4M) eligible for Medicare reimbursement at ASP + 6%
- 120 million Medicaid and commercial lives covered outside surgical bundle
- Multiple SKUs – lower average costs

54% of the opportunity lends itself to favorable reimbursement and access

OVERALL TOTAL

- **ZYNRELEF has lower acquisition cost benefit versus Exparel**
- **ZYNRELEF will have HOPD reimbursement – 3-year pass-through**
- **ZYNRELEF will offer 340B pricing**

SKU: stock keeping unit. **HOPD:** hospital outpatient department. 1. **Reference:** 2019 DRG Claims Data: Procedures selected on severity and duration of pain and opioid use validated thorough medical review

ZYNRELEF's Significant Economic Benefits Designed to Support Rapid Share Conversion and Broad Access

ZYNRELEF	WAC	340B
400 mg/12 mg	$267.50	$205.67
200 mg/6 mg	$135.50	$104.19

Exparel	WAC	340B
266 mg (20 mL)	$354.53	$354.53
133 mg (10 mL)	$198.84	$198.84

ZYNRELEF Savings vs Exparel			
WAC $/unit	WAC %	340B $/unit	340B %
~ $87	25%	~$149	42%
~ $63	32%	~$95	48%

Estimated Q1'22 Medicare NCR By Site of Care*			
	NCR 340B	NCR HOPD	ASC
ZYNRELEF 400 mg/12 mg	($205.67)	($267.50)	$8.50
Exparel 266 mg	($354.53)	($354.53)	$1.92
ZYNRELEF 200 mg/6 mg	($104.19)	($135.50)	$2.50
Exparel 133 mg	($198.84)	($198.84)	($20.62)

ZYNRELEF Economic Benefit vs. Exparel*

- 340B accounts: ~$149 (400 mg to 266 mg) and ~$95 (200 mg to 133 mg)
- HOPD accounts: ~$87 (400 mg to 266 mg) and ~$63 (200 mg to 133 mg)
- Anticipated pass-through status on 4/1/22 will more than double the economic benefits in 340B and HOPD
- Research has shown all customer segments were more sensitive to and favored acquisition cost over reimbursement**

Does not include additional cost of bupivacaine to admix with Exparel to achieve efficacy

*Estimates Comparing WAC (or 340B) acquisition cost to published ASP reimbursement for Medicare patients to calculate NCR.
WAC: wholesale acquisition cost. NCR: net cost recovery. HOPD: hospital outpatient department. ASC: ambulatory surgical center.
**DRG Research Pricing Research 2018 and Mock P&T Research 2019

ZYNRELEF Target Accounts Cover Majority of Opportunity

Hospitals	# Accounts	High Value Market Procedures (000s)[2]	Exparel WAC ($ in M's)[1]
340B / High Brand	487	3,237	$ 145.6
Non-340B / High Brand	450	2,425	$ 142.3
High Procedure / Low Brand	366	2,660	$ 19.5
Target Total	**1,303**	**8,322**	**$ 307.4**
All Hospitals	12,069	12,326	$ 392.3
% Capture	**11%**	**68%**	**78%**
ASC Market			
Target ASCs	**593**	**632**	**$ 30.9**
All ASCs	69,021	1,039	$ 45.3
% Capture	**1%**	**61%**	**68%**

*__ASC:__ ambulatory surgical center. __WAC:__ wholesale acquisition cost.
__References: 1.__ Symphony Drug Market – 12M ending 7/2021. __2.__ LexisNexis Procedure Data August 2019 YTD.

Please see __IMPORTANT SAFETY INFORMATION__ on pages 16 to 17 and full Prescribing Information, including __Boxed Warning__.

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Important Safety Information for Patients

Important Safety Information

ZYNRELEF contains an NSAID (non-steroidal anti-inflammatory drug), a type of medicine which:

- **can increase the risk of a heart attack or stroke that can lead to death. This risk increases with higher doses and longer use of an NSAID.**
- **cannot be used during heart bypass surgery**
- **can increase the risk of gastrointestinal bleeding, ulcers, and tears.**

ZYNRELEF should also not be used:

- if you are allergic to any component of ZYNRELEF, similar local anesthetics, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines.
- as a paracervical block, during childbirth.

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Important Safety Information for Patients (cont)

The most common side effects of ZYNRELEF are constipation, vomiting, and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) may affect the nervous and cardiovascular system; may reduce the effects of some blood pressure medications; should be avoided if you have severe heart failure; may cause adverse effects on cartilage; may cause liver or kidney problems, a rare blood disorder or life-threatening skin or allergic reactions; may harm your unborn baby if received at 20 weeks of pregnancy or later; and may cause low red blood cells (anemia).

Tell your healthcare provider about all your medical conditions and about all the medicines you take including prescription or over-the-counter medicines, vitamins, or herbal supplements to discuss if ZYNRELEF is right for you.

Talk to your healthcare provider for medical advice about side effects. Report side effects to Heron at 1-844-437-6611 or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The information provided here is not comprehensive.

Please see full Prescribing Information, including Boxed Warning

HERON THERAPEUTICS

HTX-019 for Postoperative Nausea and Vomiting (PONV)

NDA Submitted November 2021

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

HTX-019 for PONV

- PONV is a large market ~25x the size of CINV
- HTX-019 has significant potential advantages over oral aprepitant and IV fosaprepitant:
  - Therapeutic plasma concentrations where ≥97% receptor occupancy in the brain would be predicted are achieved in minutes versus >1 hour for oral aprepitant
  - 30-second administration of HTX-019 versus 20-30 minutes for fosaprepitant
  - IV fosaprepitant can be very painful when administered into a peripheral vein (In prior BE comparison HTX-019 was better tolerated than EMEND IV, with 65% fewer AEs at least possibly related to treatment and no AEs of greater than mild severity)
- NDA for prevention of PONV in adults submitted November 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*

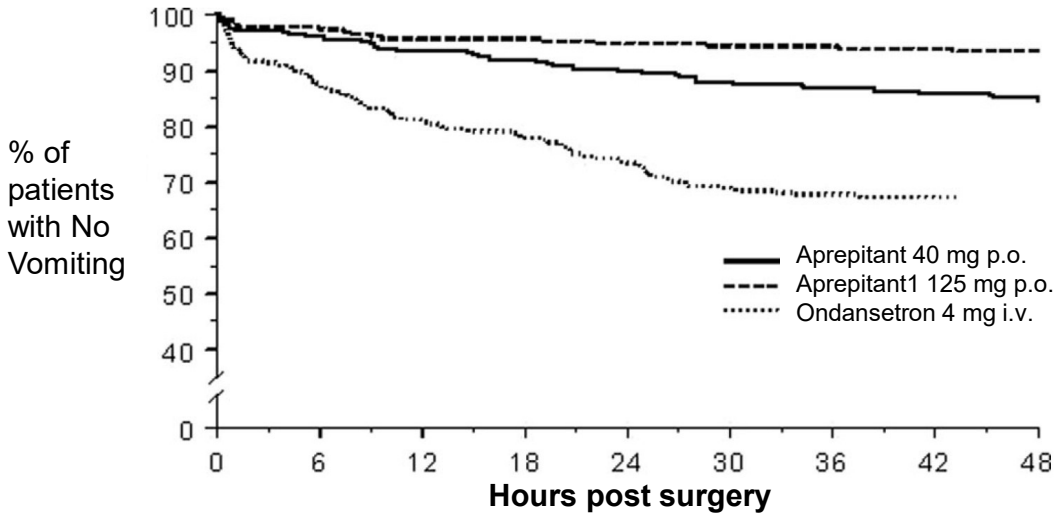


Figure 5. Kaplan-Meier curves for the time to first vomiting during the 48 h following surgery. The time to first vomiting was delayed by aprepitant; *P* 0.001 based on the log-rank test.

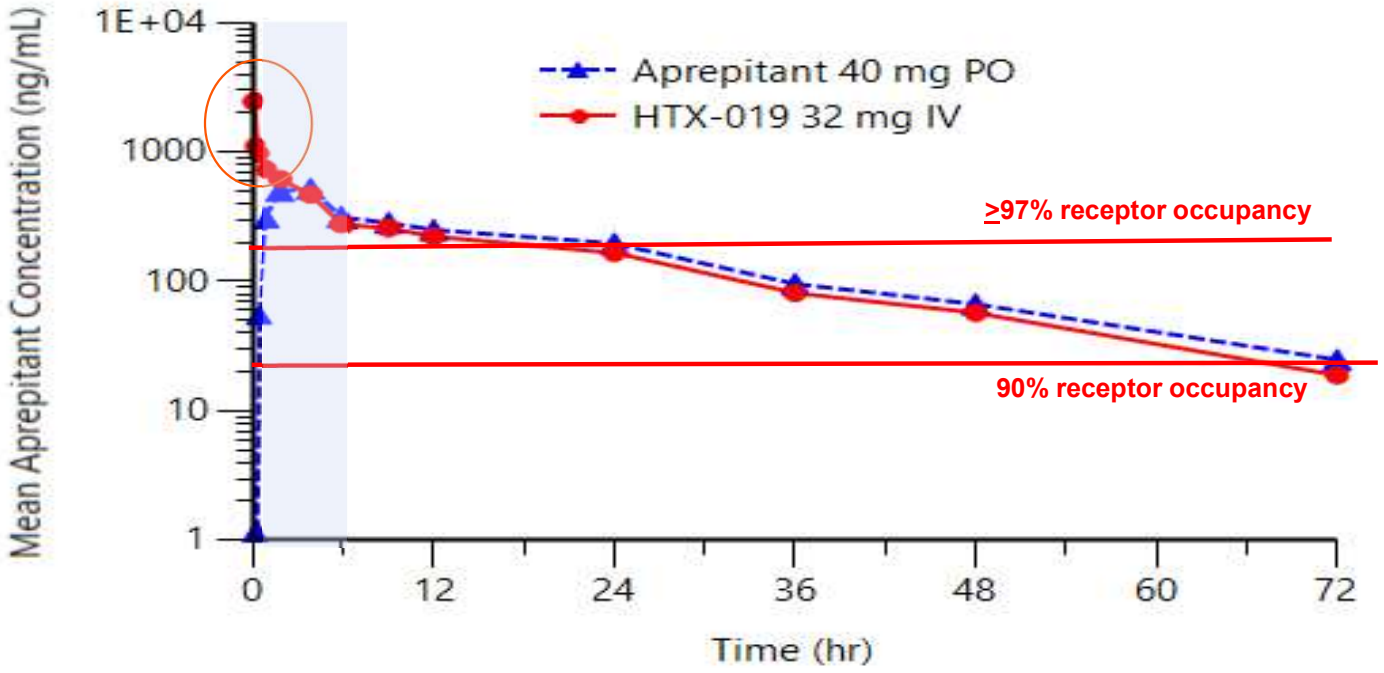
Aprepitant delayed the time to first vomiting episode compared with ondansetron.

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

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

100% Receptor Occupancy Occurs Much Faster With HTX-019 30-Second Administration Than with Oral Aprepitant

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



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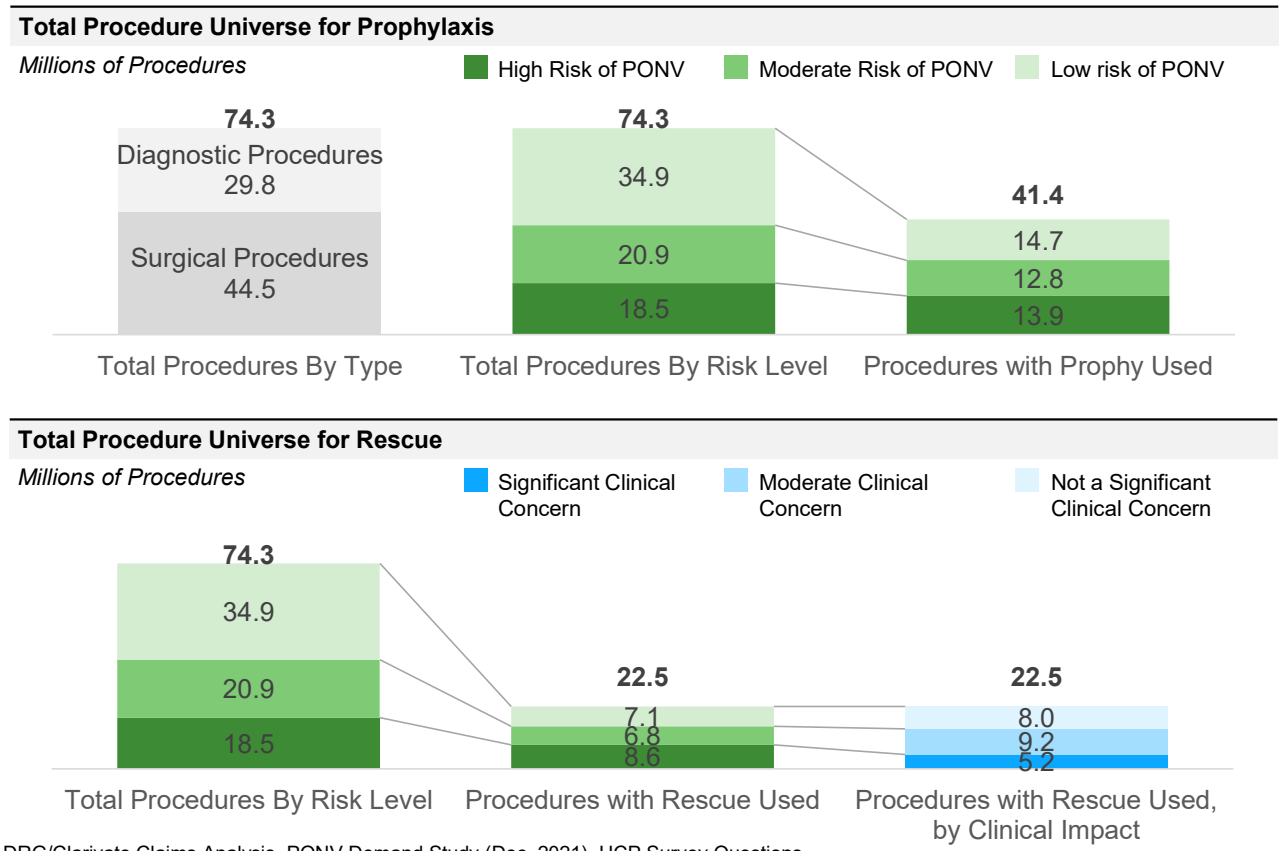
Total PONV Opportunity for HTX-019 is ~64M procedures; > 25X size of CINV Market (~41.4M in Prophylaxis & ~22.5M Rescue)

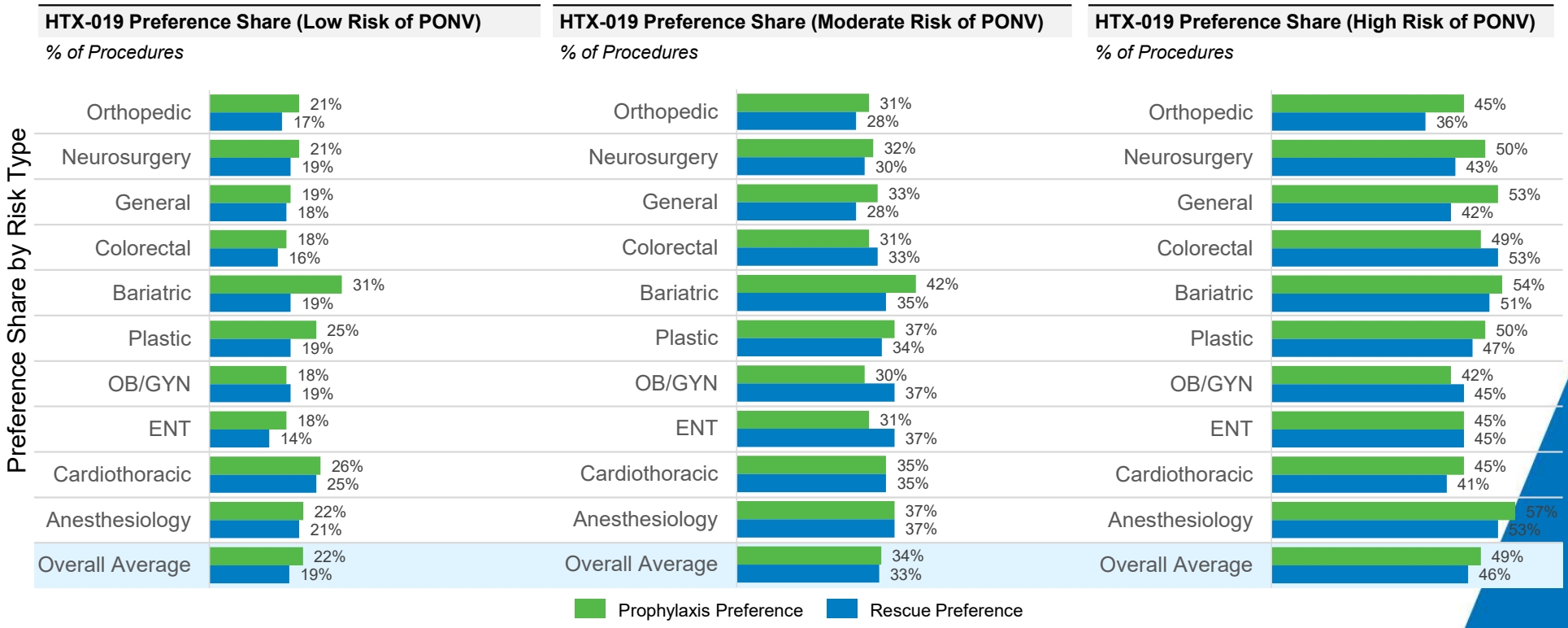


- Demand Survey considered ~30 procedures across Anesthesiology, 10 Surgical Specialties, and PACU Nurse respondents
- Procedures currently using prophylaxis were segmented as having High, Moderate, or Low Risk of developing PONV (Likelihood of PONV)
- Procedures currently using rescue were segmented as having Significant, Moderate, or No Significant Clinical Concern for clinical outcomes (Clinical Impact of PONV)

Source: DRG/Clarivate Claims Analysis, PONV Demand Study (Dec. 2021), HCP Survey Questions

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

Preference share for HTX-019 Grows as Patient Risk and Procedure Clinical Concern Increases – Approaching 50% at Highest Levels

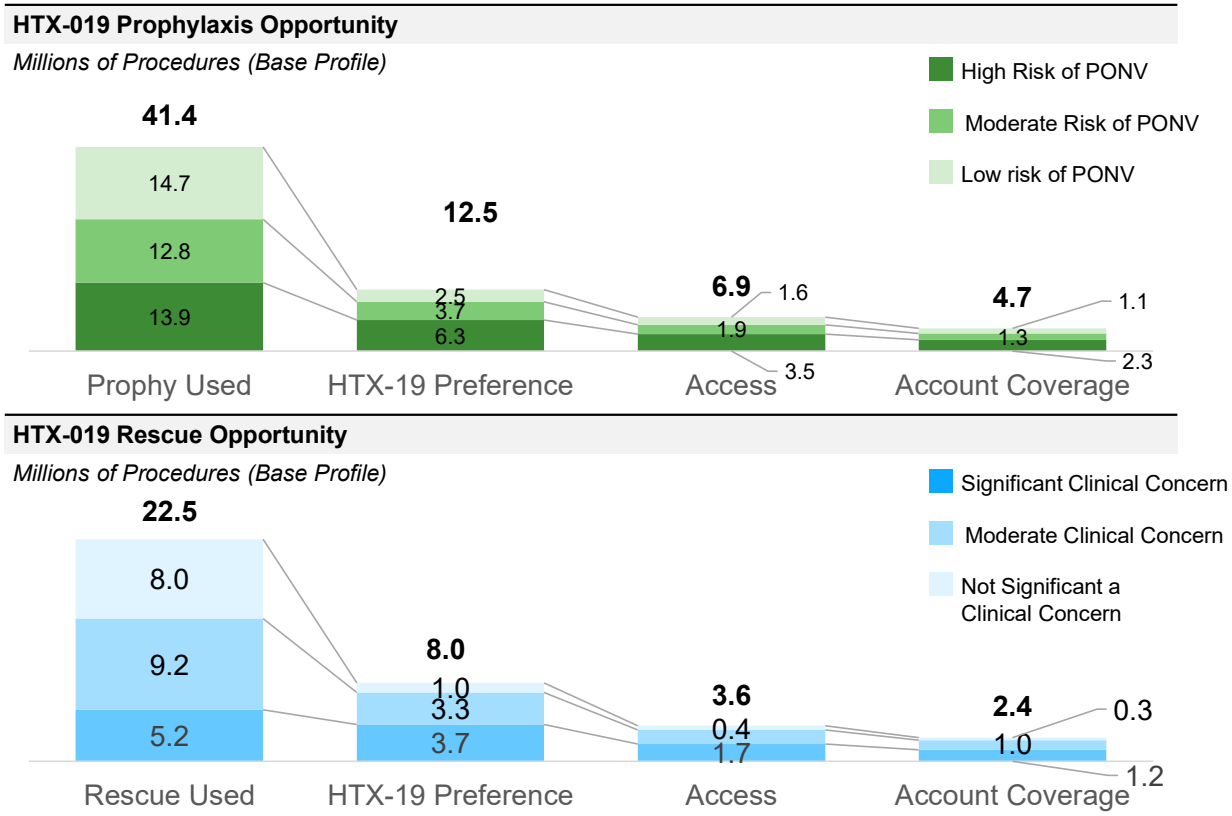


Source: DRG/Clarivate Claims Analysis, PONV Demand Study (Dec 2021), HCP Survey Questions

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

Estimated HTX-019 Usage Peaks at ~7M Annual Procedures

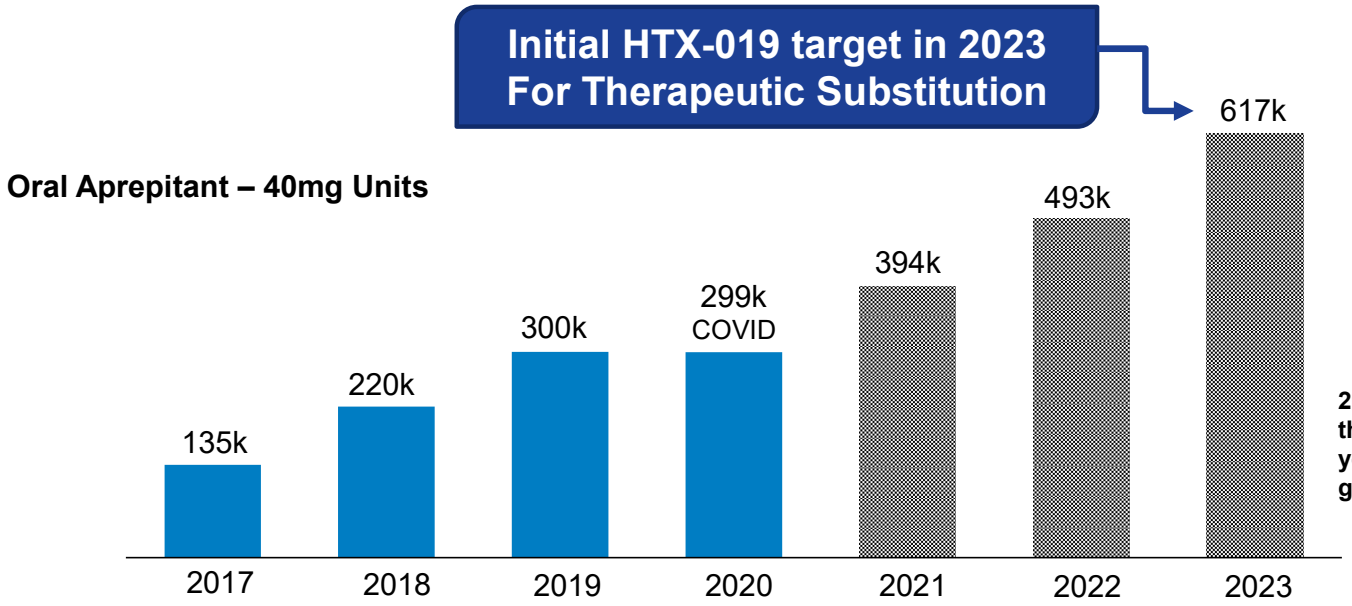
Strong HTX-019 Preference Share Adjusted for Access and Account Coverage



Source: DRG/Clarivate Claims Analysis, PONV Demand Study (Dec 2021), PD Survey Questions

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

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



2021-2023 Projected Totals: 2021 YTD thru 10 months 32% growth vs. prior year / 2022 & 2023 projected at 25% growth

- Oral Aprepitant volume is growing rapidly at premium price despite no promotion
  - Q2'21 WAC ~ $88/capsule
- ~ **1,100** current ordering accounts[1]

[1] Source IQVIA DDD Non-Retail data 2017 -2021

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

- Estimated peak HTX-019 usage at ~ 7M annual procedures based on significant unmet need for more convenient formulations of NK-1 class
- Potential Significant Advantages of HTX-019
  - 30-second IV Push injection with immediate onset of action and no difference in AEs versus oral formulation
  - Aprepitant is the most effective therapeutic agent for emesis
  - 505(b)(2) regulatory pathway for existing asset
  - Existing contract manufacturers: HTX-019 is a smaller vial of CINVANTI
- Synergies with ZYNRELEF commercial organization
  - Same target accounts and target audiences
  - Capacity & access advantages of adding a 2nd product to promote
  - No additional sales reps needed, so minimal incremental investment

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

Oncology Care Franchise

Q3’21 Review

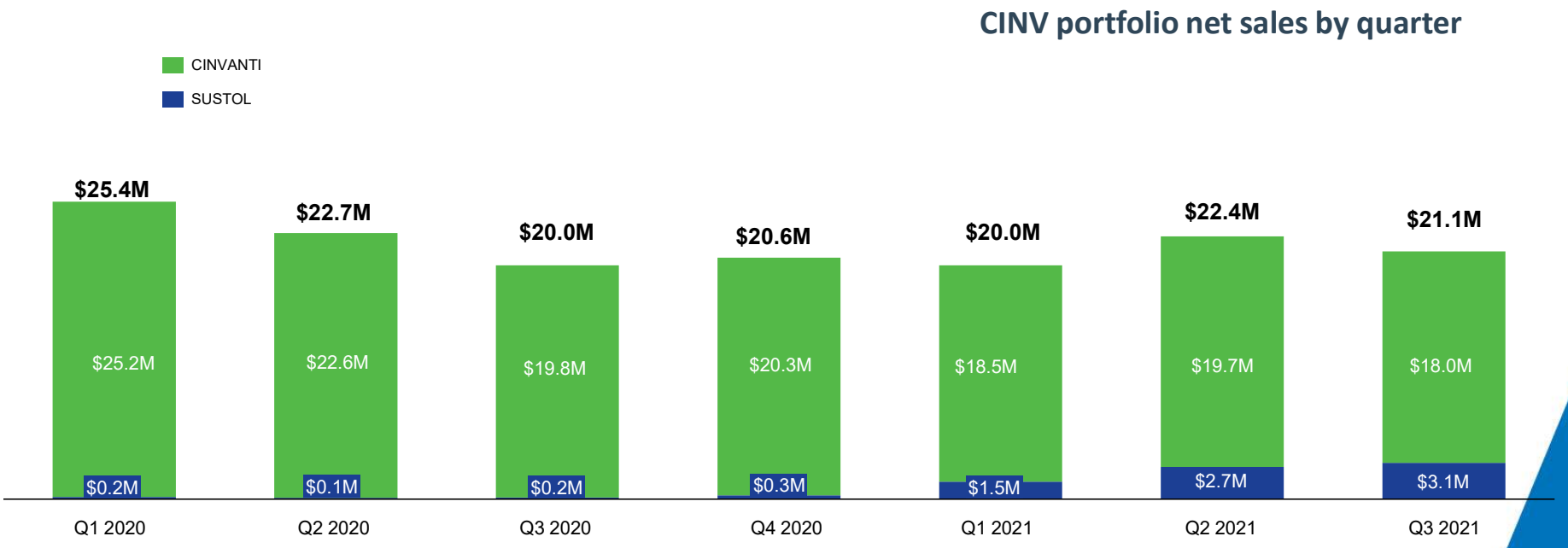
CINV Franchise 2022 Outlook

- Solid 2021 performance despite headwinds remaining in the CINV market
  - Reduction in the clinic anti-emetic market was due to COVID-related decreases in cancer screening and patient visits
  - OCM and value-based contracting reimbursement continues to drive generics market share
  - Continued aggressive competition from IV Akynzeo and generic fosaprepitant
- Sales for CINVANTI and SUSTOL are poised for moderate clinic growth in 2022
  - Generic fosaprepitant ASP reimbursement decreased to **$28.50** in Q1'22 (down 22% from Q4'21)
  - Effective January 1, 2022 – separate reimbursement for generic fosaprepitant ended in HOPD
  - IV Akynzeo ASP reimbursement decreased to **$503.98** in Q1'22 (decrease of > $190 over 2021)
  - Infusion bag shortages: CINVANTI – only NK-1 that does not need IV infusion bag
  - Virtually all HEC and majority of MEC regimens utilize 5HT3 + NK-1, thus the backlog of patients coming into treatment creates opportunities for both products

HOPD: Hospital Outpatient Department; **OCM:** Oncology Care Model

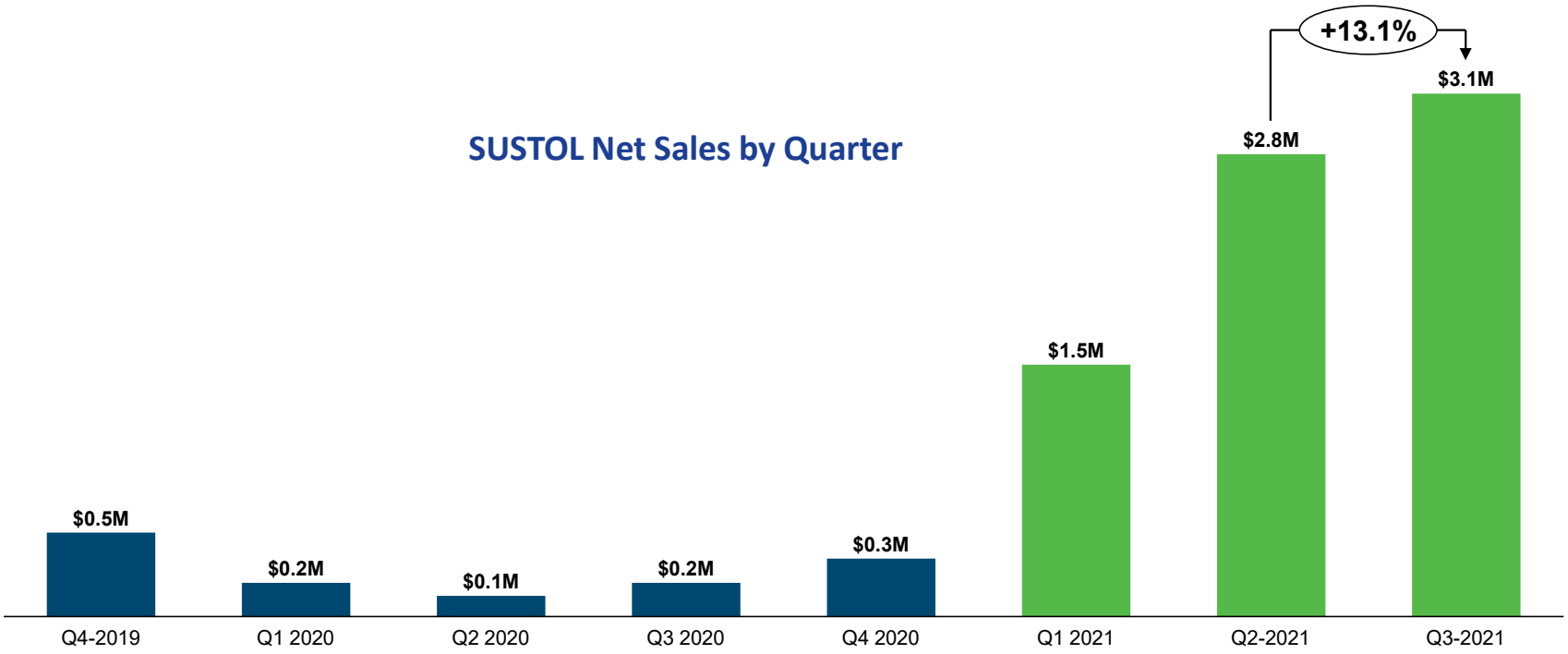
Heron's CINV Portfolio Net Sales Have Stabilized in Markets Dominated by Generics during 2021, Poised for Growth in 2022

- After declining after the launch of generic Emend IV in September 2019, CINVANTI sales have stabilized
- SUSTOL sales rebounding in 2021 following the Refresh Program



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

SUSTOL Removed Discounting in Q4'2019 with Refresh Program Completed in 2020 & Return to Growth in 2021



Heron's Commercial Strategy

Establish Heron as a leading company in Acute Care

- ZYNRELEF is off to a fast start and growing rapidly
- Growth will accelerate with ZYNRELEF's label expansion
- Expand Acute Care footprint with HTX-019 for PONV in Q4'22, if approved

Return Growth and Maximize Profitability of Oncology Care

- Net sales stabilized in 2021 and poised for moderate growth in 2022
- Reduce COGS through larger scale manufacturing in 2022
- Aligned resources to support the strategy

Financial Summary

Heron had cash, cash equivalents and short-term investments of $202.8 million as of September 30, 2021. We expect net cash used for operating activities of $45 million to $48 million in the fourth quarter of 2021, and we anticipate that our net cash usage will continue to moderate lower in 2022.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2021
Net product sales	$ 23,230	$ 65,691
Operating expenses[1]	74,938	229,982
Other income (expense), net	(700)	(1,746)
Net loss[1]	$ (52,408)	$ (166,037)
Net loss per share[2]	$ (0.51)	$ (1.71)
Net cash used in operations	$ (53,166)	$ (158,096)

Condensed Balance Sheet Data (In thousands)	September 30, 2021
Cash, cash equivalents and short-term investments	$ 202,820
Accounts receivable, net	$ 43,086
Total assets	$ 352,388
Total stockholders' equity	$ 118,843

Common shares outstanding as of September 30, 2021 totaled 101.9 million.

[1] Includes $11.2 million and $34.0 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2021, respectively.
[2] Based on 101.9 million and 97.3 million weighted-average common shares outstanding for the three and nine months ended September 30, 2021, respectively.