Heron Q3 2021 Earnings Call

November 3, 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: the net product sales guidance for the oncology care franchise; the timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunity for ZYNRELEF in the US and Europe; the timing of the FDA's review process and whether the FDA approves the supplemental NDA for ZYNRELEF to expand the U.S. label to related procedures; 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 NDA submission for HTX-019 for prevention of postoperative nausea and vomiting; the net product sales guidance for the oncology care franchise; 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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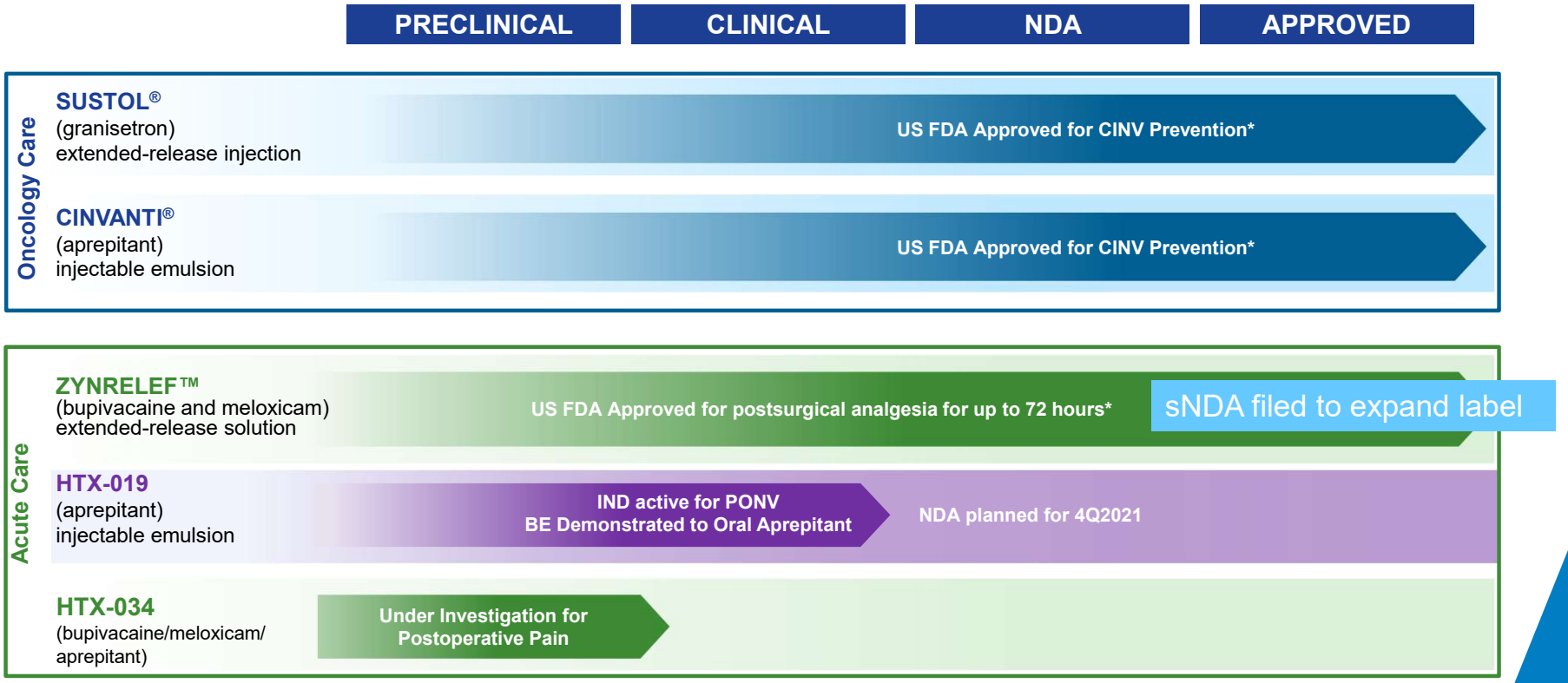
Heron Pipeline



CINV: Chemotherapy-induced nausea and vomiting. **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 bunionectomy, open inguinal herniorrhaphy, and total knee arthroplasty. 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

Successful FDA Interactions to Support Expansion of ZYNRELEF Label and Increase Product Supply

- FDA agreed to submission of supplemental NDA with existing data to significantly expand ZYNRELEF indications to include foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.
  - Supplemental NDA submitted in late September
- FDA also agreed to contents of a second supplemental NDA to substantially further expand the indications to orthopedic surgical procedures and soft tissue surgical procedures.
  - Submission targeted for 2H2022
  - Expanded broad claim structure designed to cover 14 million target procedures
- FDA approved manufacturing supplement to NDA to add secondary supplier of our proprietary polymer.
  - Approval received in under 4 months
  - Allows for polymer batch size sufficient to manufacture millions of doses of ZYNRELEF annually at a significantly reduced cost of goods

The Commercialization of ZYNRELEF

Advancing Postoperative Pain Management

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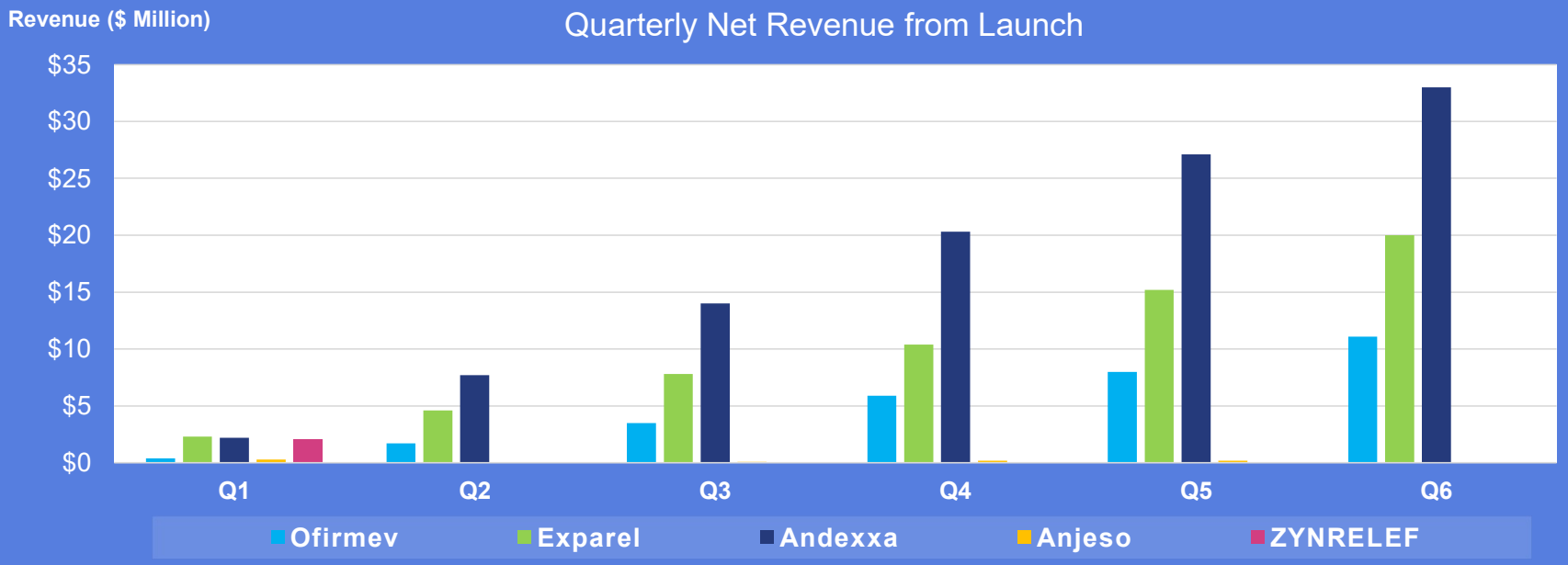
ZYNRELEF Launch is Off to a Strong Start

- Q3'21 Net Sales: $2.1M
- ZYNRELEF has established nationwide access through broad distribution channel stocking
  - 4 Full-line Wholesaler with 68 distribution centers (DCs) have sold ZYNRELEF
    - 50% of DCs have reordered
  - 10 Specialty Distributor (DCs) have sold ZYNRELEF
    - 60% of DCs have reordered

Comparison of Select Hospital Launches



Product	Launch Date	Q1	Q2	Q3	Q4	Q5	Q6	Q1-Q6 TOTAL
Ofirmev	**Jan 2011**	$0.4	$1.7	$3.5	$5.9	$8.0	$11.1	**$30.6**
Exparel	**April 2012**	$2.3	$4.6	$7.8	$10.4	$15.2	$20.0	**$60.4**
Andexxa	**May 2018**	$2.2	$7.7	$14.0	$20.3	$27.1	$33.0	**$104.3**
Anjeso	**June 2020**	$0.3	$0.1	$0.1	$0.2	$0.2	--	**$0.9**
ZYNRELEF	**July 2021**	$2.1	--	--	--	--	--	**$2.1**

*Source: Net product revenue & launch dates based on SEC filings.

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ZYNRELEF is Gaining Rapid Formulary Access

- ZYNRELEF formulary approvals: **126** as of October 31, 2021
  - Over 91% P&T Committee approval rate in hospitals

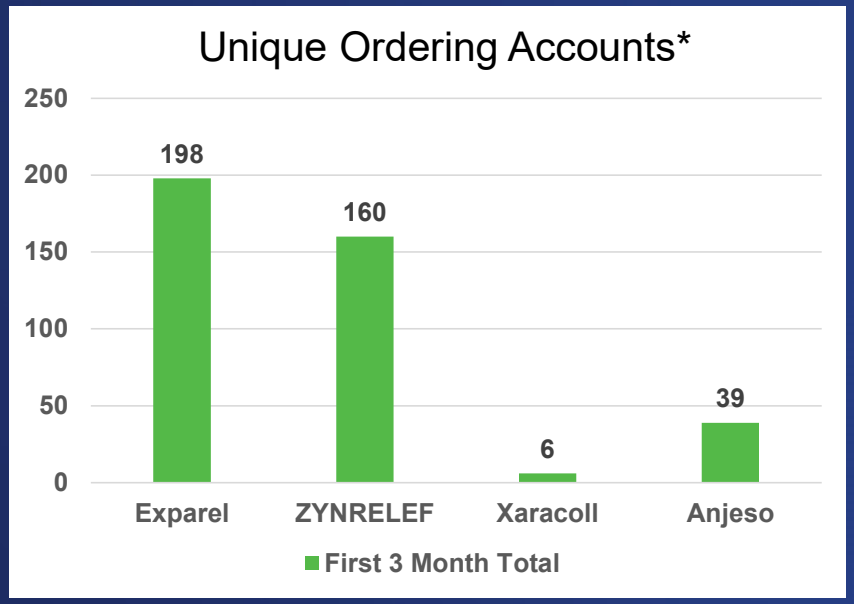
Formulary Approval Status	Estimated % of Approvals
Unrestricted Usage	**55%**
Restricted (Primarily for Indicated Procedures)	**45%**

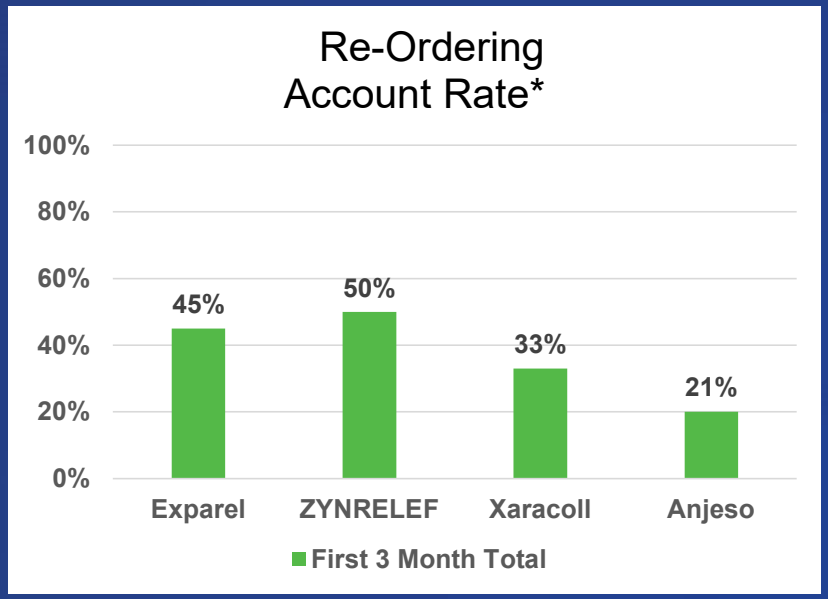
- Over 150 additional P&T Committees are scheduled to review ZYNRELEF before the end of 2021
- Formulary approval → Medical Executive approval → CPOE → Pharmacy Orders → Patient

CPOE: computerized physician order entry

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

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ZYNRELEF Reimbursement Advantages

- Multiple Commercial and Medicaid payers covering >**88** million lives have agreed to reimburse ZYNRELEF outside of the surgical DRG bundled payment in the ASC
  - Many of these covered lives are also reimbursed separately in the HOPD
- ZYNRELEF's lower price benefits all settings of care where local anesthetics are reimbursed as part of the surgical bundle payment
- CMS is still evaluating ZYNRELEF's pass-through application for separate payment
  - Until December 31, 2021, HOPDs and ASCs may bill for ZYNRELEF using Misc. C-code (C9399) with reimbursement at 95% of AWP.
- On November 2, 2021, CMS published the CY 2022 OPPS final rule and issued ZYNRELEF a C-code (C9088) for separate reimbursement in the ASC setting of care effective January 1, 2022

HOPD: Hospital Outpatient Department; **ASC**: Ambulatory Surgical Center; **OPPS**: Outpatient Prospective Payment System

Please see **IMPORTANT SAFETY INFORMATION** on pages 23 to 24 and full Prescribing Information, including **Boxed Warning**.

ZYNRELEF Priorities in Q4

- In-service accounts with recent formulary approvals
- Grow formulary access in targeted accounts
- Expand reimbursement advantages
- Prepare for expanded label indications

Oncology Care Franchise

Q3’21 Review

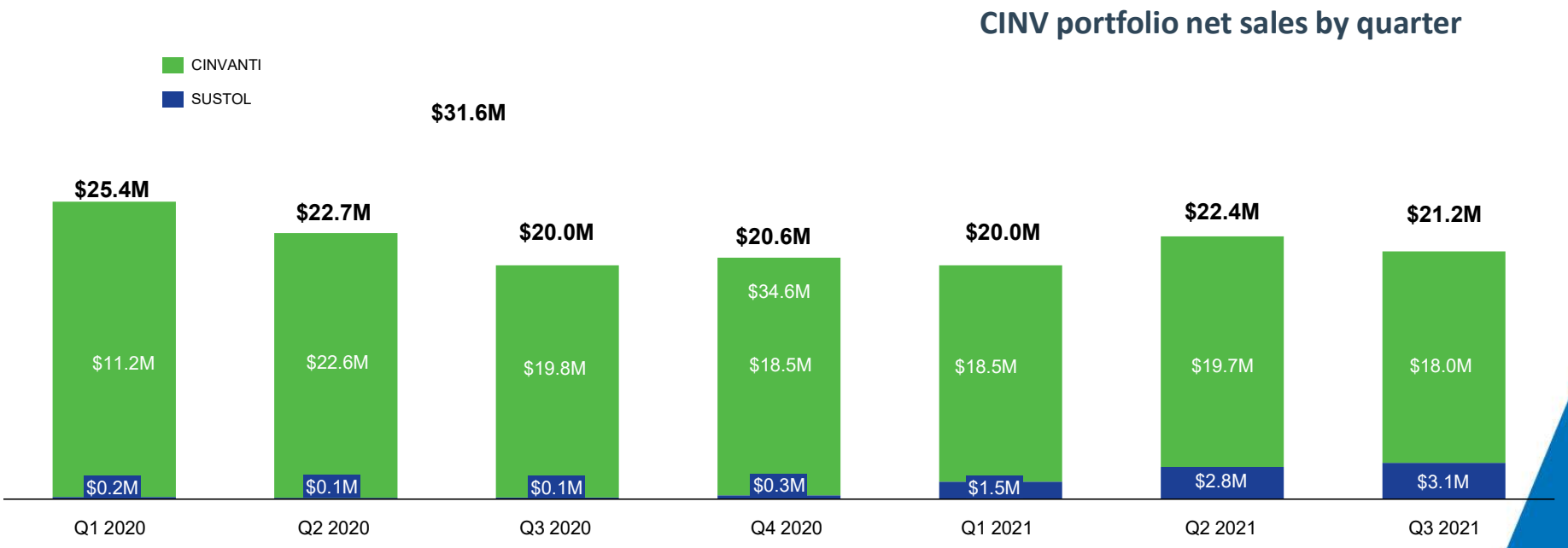
CINV Franchise 2021 Outlook

- Q3’21 CINV Franchise net product sales were **$21.1 million** (6% increase over prior year)
- Solid 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 clinic growth in 2022
  - Generic fosaprepitant ASP reimbursement decreased to **$36.45** in Q4’21 (decrease of 27% vs. prior QTR)
  - 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
- **CINV Franchise net product sales guidance: Q4’21 expected in $20M to $22M range**

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

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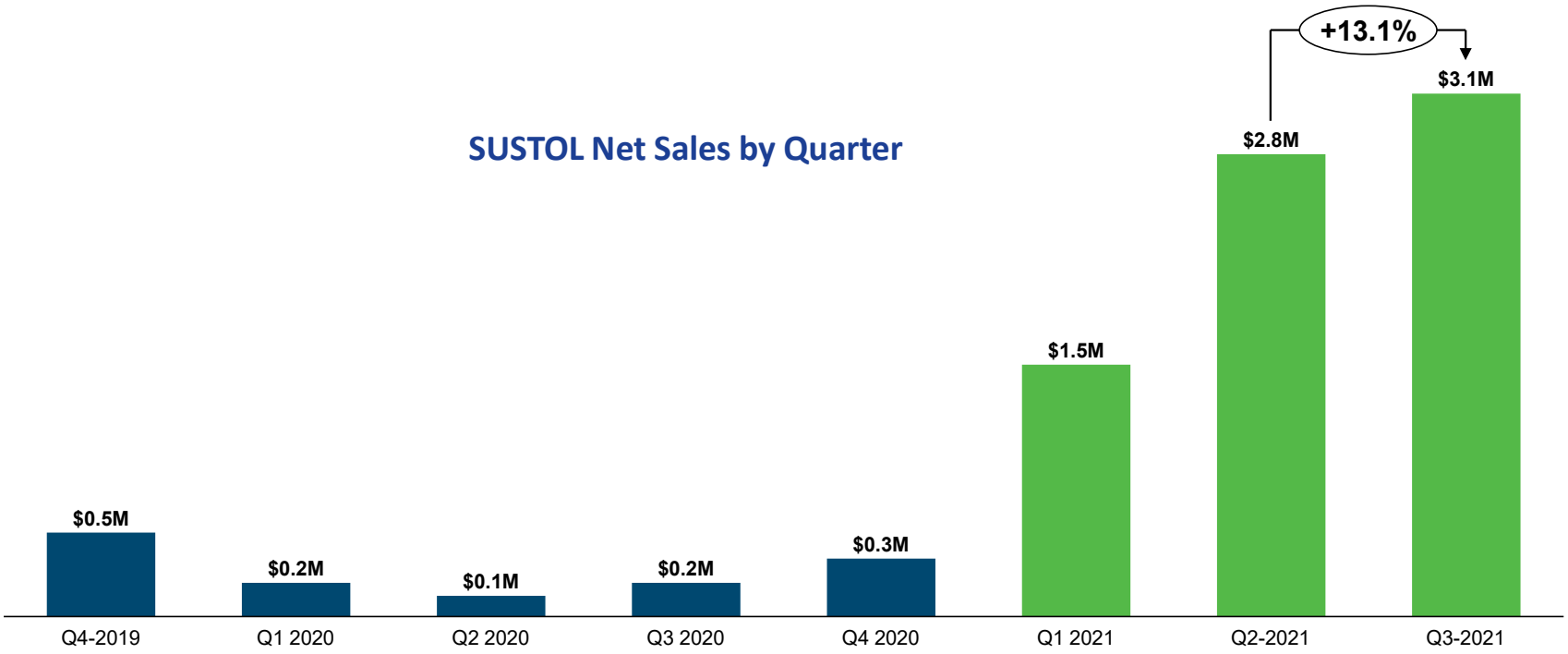
SUSTOL Removed Discounting in Q4'2019 with Refresh Program Completed in 2020 & Return to Growth in 2021



HTX-019 for Postoperative Nausea and Vomiting (PONV)

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

HTX-019 for PONV

- PONV is a large market ~20x the size of CINV
- HTX-019 has significant potential advantages over oral aprepitant and fosaprepitant
- Successful Pre-NDA meeting with FDA with NDA for PONV prevention on-track 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*

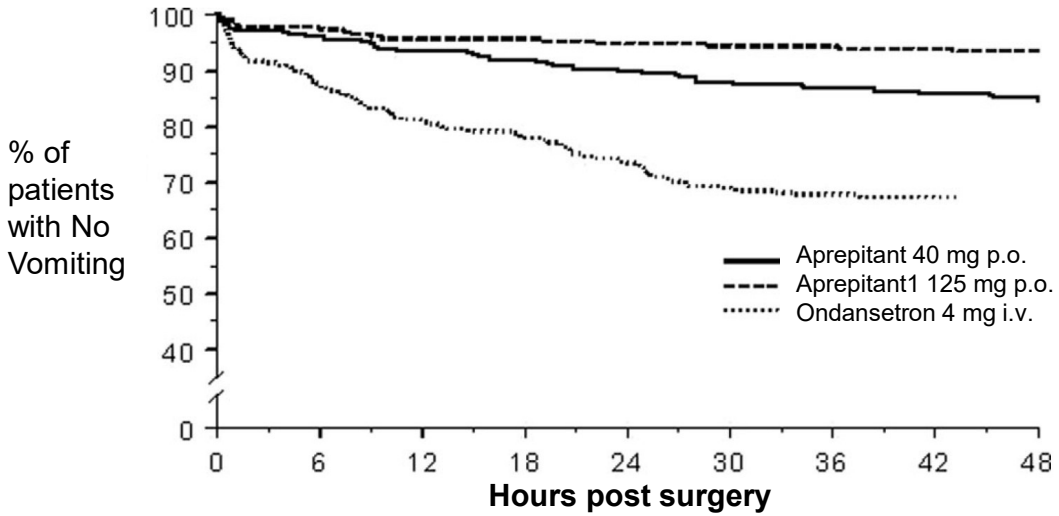


Figure 5. Kaplan-Meier curves for the time to first vomiting during the 48 h following surgery. The time to first vomiting was delayed by aprepitant; *P* 0.001 based on the log-rank test.

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

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

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

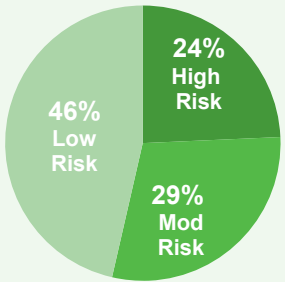
PONV Market is >20X the size of the CINV Market
PONV ~53M Treatments vs. ~2.5M CINV Treatments

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

High Risk Procedures

~5M

Clinically Concerning Cases of PONV in High Risk Patients

Source: *PONV quantitative survey DRG June 2020*

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

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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 2022

Return Growth and Maximize Profitability of Oncology Care

- Net sales stabilized in 2021 and poised for slow 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.

Q&A

November 3, 2021

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 components of ZYNRELEF, 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) can 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 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

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