Heron Update

Q4 2022 Earnings Call

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: uncertainties related to market conditions; adjustments to the preliminary fourth-quarter 2022 and full-year 2022 net product sales for the acute care and oncology care franchises in connection with completion of financial closing procedures and an audit for the 2022 fiscal year; risks associated with the net product sales guidance for the oncology care franchise and acute care franchise; the timing of the FDA's review process and whether the FDA approves the supplemental new drug application (sNDA) for ZYNRELEF to expand the U.S. label; the potential additional market opportunity for the expanded U.S. label for ZYNRELEF; the results of the commercial launch of APONVIE in the U.S.; the potential market opportunities for ZYNRELEF, APONVIE, CINVANTI and SUSTOL; 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 ability of the Company to reach profitability; and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and we take no obligation to update or revise these statements except as may be required by law.

HERON
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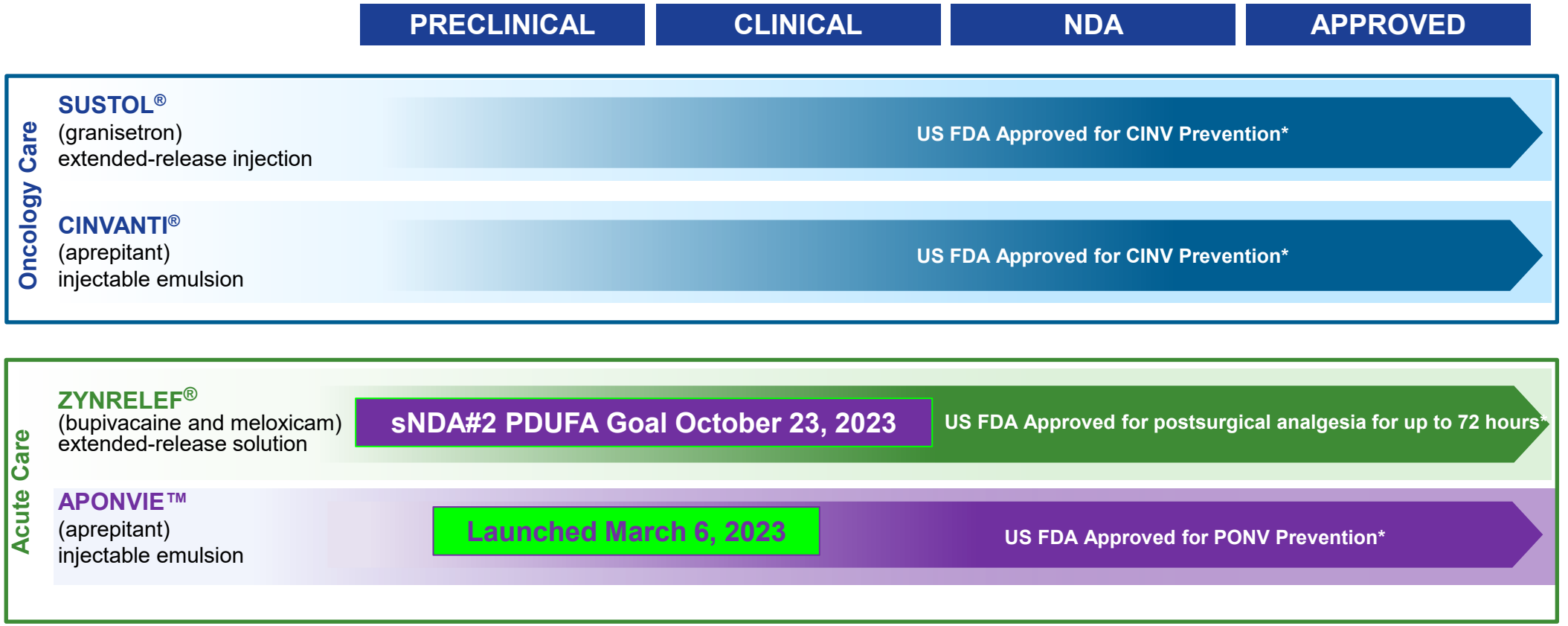
Heron Pipeline of 4 Approved Products With $107.7 million in 2022 Annual Net Product Sales, a 25% Increase Over 2021



CINV: Chemotherapy-induced nausea and vomiting. **PDUFA**: prescription drug user fee; **PONV:** postoperative nausea and vomiting. **sNDA:** supplemental new drug application

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. **APONVIE™ (aprepitant) injectable emulsion** is indicated for the prevention of postoperative nausea and vomiting (PONV) in adults.

Please See IMPORTANT SAFETY INFORMATION at the end of this presentation

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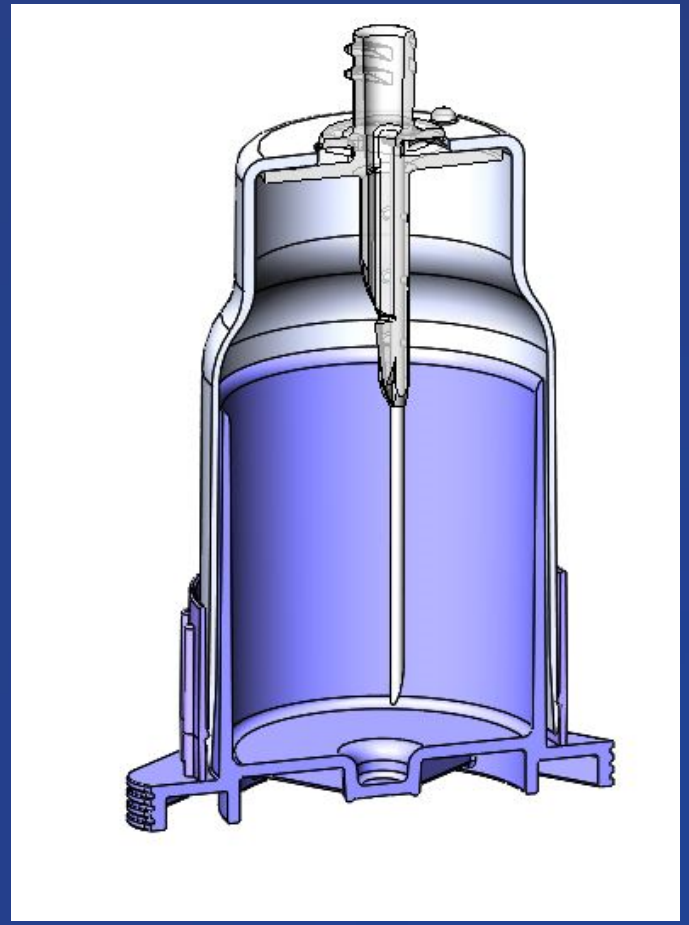
How to Accelerate ZYNRELEF Sales

- Expand indications
  - PDUFA Action Date for sNDA#2 for label expansion in 7 months
  - Proposed indications cover soft tissue and orthopedic surgical procedures, which will allow promotion to essentially all 14 million target procedures
- Make it easier to withdraw from vial
  - Due to viscosity, it can take > 1 minute to remove from vial
  - First step to improving withdrawal is custom Vial Access Needle (VAN)
  - Second step for most user-friendly presentation is a prefilled syringe (PFS)

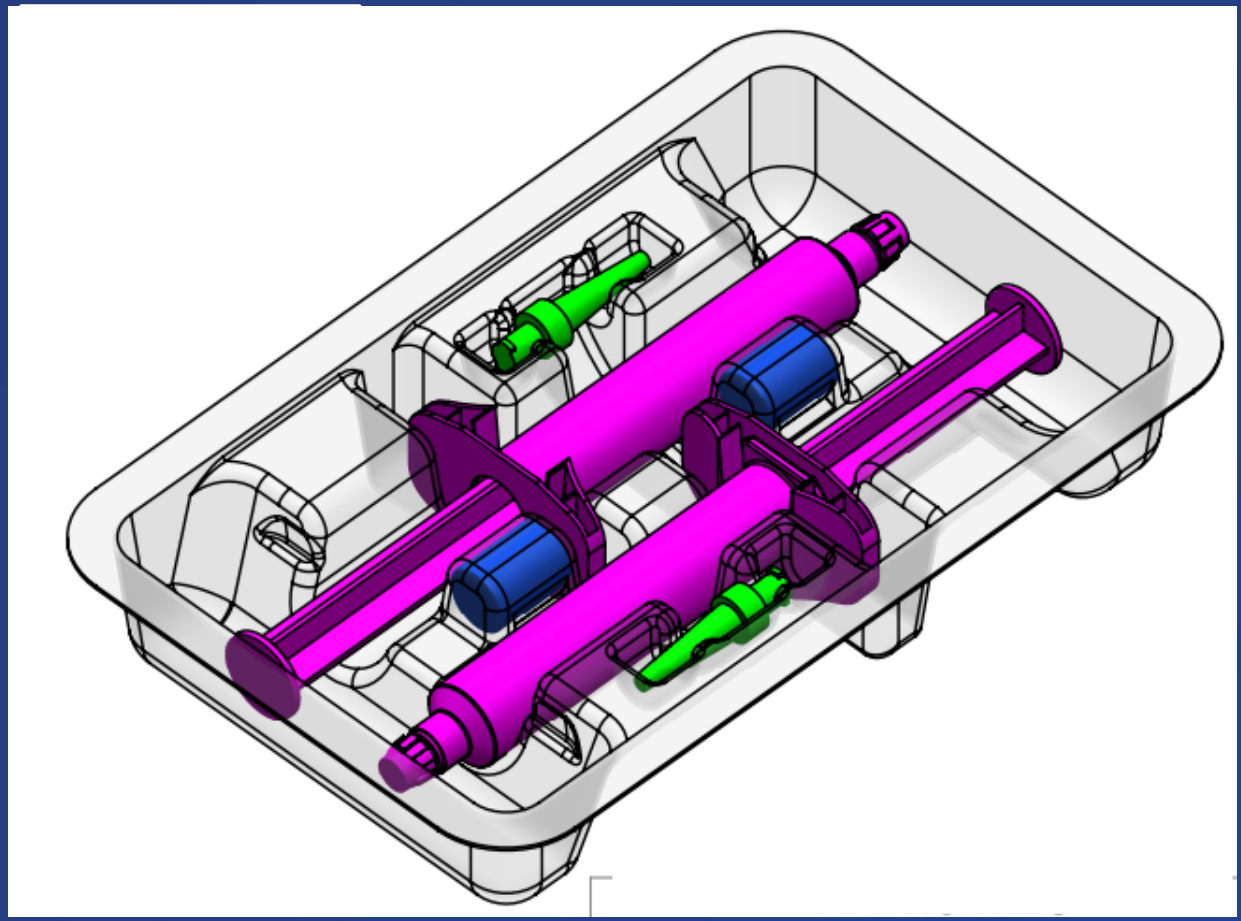
New Vial Access Needle (VAN) Designed Based on Feedback from ZYNRELEF Users

- Customers have told us that they would use more ZYNRELEF if it was easier to remove from the vial and even more if it was provided in a prefilled syringe (PFS)
- Due to moisture sensitivity of PFS it has been a challenging project, but recent advances support aggressively moving this forward. Unfortunately, this is a several-year project
- In the interim, we have developed a custom Vial Access Needle (VAN), which greatly simplifies product withdrawal and could be available by mid-2024
  - Withdrawal time of > 1 minute reduced to 20-30 sec
  - Sterile shroud eliminates need for non-sterile circulating nurse to participate in withdrawal process



Significant Progress Made With Prefilled Syringe

- Sterile prefilled syringe eliminates all preparation activities and is the ultimate presentation for ZYNRELEF
- COGS will also likely be reduced switching to the PFS



Acute Care Commercial Update

Q4’22 Earnings Call

ZYNRELEF Quarterly Performance Metrics

	Q4'22	Q3'22	% CHG vs. PQ	Q4'21	% CHG vs. PY
Net Sales	$3.9M	$2.7M	+44%	$0.8M	+362%
Demand Units	20,765	15,077	+38%	5,176	+301%

- **Total Unique Ordering Accounts: 793** (as of 12/31/2022)
- **Total Formulary Approvals: 522** (as of 2/28/2023)
- **IDN formulary Approvals: 74** (as of 2/28/2023)

Seasonality in Elective Procedures with Q4 as Largest Surgical Quarter Followed by Declines in Q1 is Expected

Non-Retail Drugs: Q4 2018- Q4 2022 SHA Non-Retail Drug Market
2020 Data not used do to drastic COVID swings

ZYNRELEF is Increasing Quarterly Demand Volume

- Weekly Demand Units Average up 38% from Q3 22 to Q4 22

Weekly Average ZYNRELEF data through 3/17/2023
ZYNRELEF Data 867 EDI

Targeting IDNs – Top-Down Strategy is Creating New Opportunities for Therapeutic Interchange

- **74** IDNs have added ZYNRELEF as formulary approved product an increase from the Q3'22 earnings call of **66** IDNs
- **74** IDNs represent ~ potential opportunity of **over 1.1 million** annual ZYNRELEF currently indicated surgical procedures
- **74** IDNs represent ~ **$149M* of Exparel** sales
  - **17** IDN's representing approximately **$46M* of Exparel** sales are currently evaluating switching to ZYNRELEF for indicated procedures

• Symphony DDD data January 2022 – December 2022 / based on WAC pricing

ZYNRELEF Branded Share is Growing in IDNs

- ~50% share is the upper limit - until our label is expanded in Q4 2023

ZYNRELEF Branded Market Share (ZYNRELEF + Exparel Units)							
Category	Q3'21	Q4'21	Q1'22	Q2'22	Q3'22	Q4'22	Exparel 12M WAC*
Total Market	0.6%	1.2%	2.2%	3.0%	3.7%	4.6%	$482 M
Approved IDN - ZYNRELEF Branded Mkt Sh (ZYNRELEF + Exparel Units)							
66 IDNs	0.8%	2.1%	3.8%	6.5%	8.1%	9.1%	$143 M
Highest ZYNRELEF Branded Market Share of IDNs Evaluating TI							
15 IDNs	1.5%	3.2%	6.3%	9.4%	12.4%	12.5%	$42 M
IDN #1	0.0%	0.0%	13.6%	41.0%	50.5%	48.0%	$1.2 M
IDN #2	0.0%	0.0%	4.3%	13.6%	27.8%	47.8%	$2.2 M
IDN #3	9.0%	18.3%	18.9%	22.1%	22.7%	27.1%	$1.4 M
IDN #4	0.0%	0.0%	4.8%	25.0%	1.1%	24.5%	$0.9 M
IDN #5	10.3%	17.4%	20.0%	22.0%	22.9%	20.5%	$1.3 M

* Symphony DDD data July 2021 – June 2022 / based on WAC pricing

ZYNRELEF Continues to Maintain Significant Economic & Reimbursement Benefits vs. Exparel

ZYNRELEF	WAC	340B
400 mg/12 mg	$280.87	$204.49
200 mg/6 mg	$142.27	$103.31

Exparel	WAC	340B*
266 mg (20 mL)	$365.17	$266.00
133 mg (10 mL)	$214.75	$151.00

ZYNRELEF Savings vs Exparel*			
WAC $/unit	WAC %	340B $/unit	340B %
~ $84	23%	~ $62	23%
~ $72	34%	~ $48	32%

Medicare Separate Reimbursement By Site of Care			
	340B HOPD	HOPD	ASC
ZYNRELEF	YES	YES	YES
Exparel	NO	NO	YES

Economic Advantages

- ZYNRELEF provides acquisition cost savings of 23% to 34% vs. Exparel
- Only ZYNRELEF has pass-through status for reimbursement in HOPD through 3/31/2025

* Estimated Exparel 340B pricing based on competitive intelligence
WAC: wholesale acquisition cost. HOPD: hospital outpatient department. ASC: ambulatory surgical center.
WAC prices effective 1/1/2023

ZYNRELEF Priorities 2023

- Build consistent usage in formulary approved ordering accounts
  - Heron sales reps – add new surgeons and service lines
  - Leverage new flexible resources deployed in Q4’22
    - Hospital Implementation Team – Operating Room Educators
    - Medical Device Reps – only paid for incremental units
- Increase communications of ZYNRELEF real world evidence
- Build pipeline with formulary access to new IDNs and Hospitals
  - Maximize ZYNRELEF usage at **17 IDNs** pursuing TI
- Improve the customer experience with the VAN and eventually the PFS

TI: Therapeutic Interchange

APONVIE – A Big Opportunity for Heron

Brand Name Conveys "Aprepitant for PONV"

- **Large target market opportunity**
  - **36 million** annual procedures in patients at moderate to high risk for PONV and **~12M** high to moderate risk patients currently not receiving prophylaxis
- **Significant Unmet Need**
  - Convenient, more effective and longer lasting treatments are needed
- **Synergies with Heron** commercial organization
  - Majority of same **ZYNRELEF** target accounts and audiences (ASA)
  - Existing positive experience with CINVANTI at major hospitals/IDNs

Source: DRG / Clarivate PONV Demand Study (Dec. 2021)
*** 2023 Procedure projections**

Please see **IMPORTANT SAFETY INFORMATION** at the end of this presentation

APONVIE Launch is Underway

- **Accelerate Access to APONVIE**
  - Strong value proposition: 340B pricing, 3-year pass-through status, GPO contracts, FLW prime vendor discounts
  - Effective targeting: oral aprepitant, CINVANTI & ZYNRELEF user accounts
  - Leverage 2020 Consensus PONV Guidelines
- **APONVIE Commercial Update**
  - March 6, 2023: completed initial stocking of distribution channel
  - CMS approved pass-through status for APONVIE for three years beginning April 1, 2023 under C-code C9145.

Oncology Care
Commercial Update

Q4’22 Earnings Call

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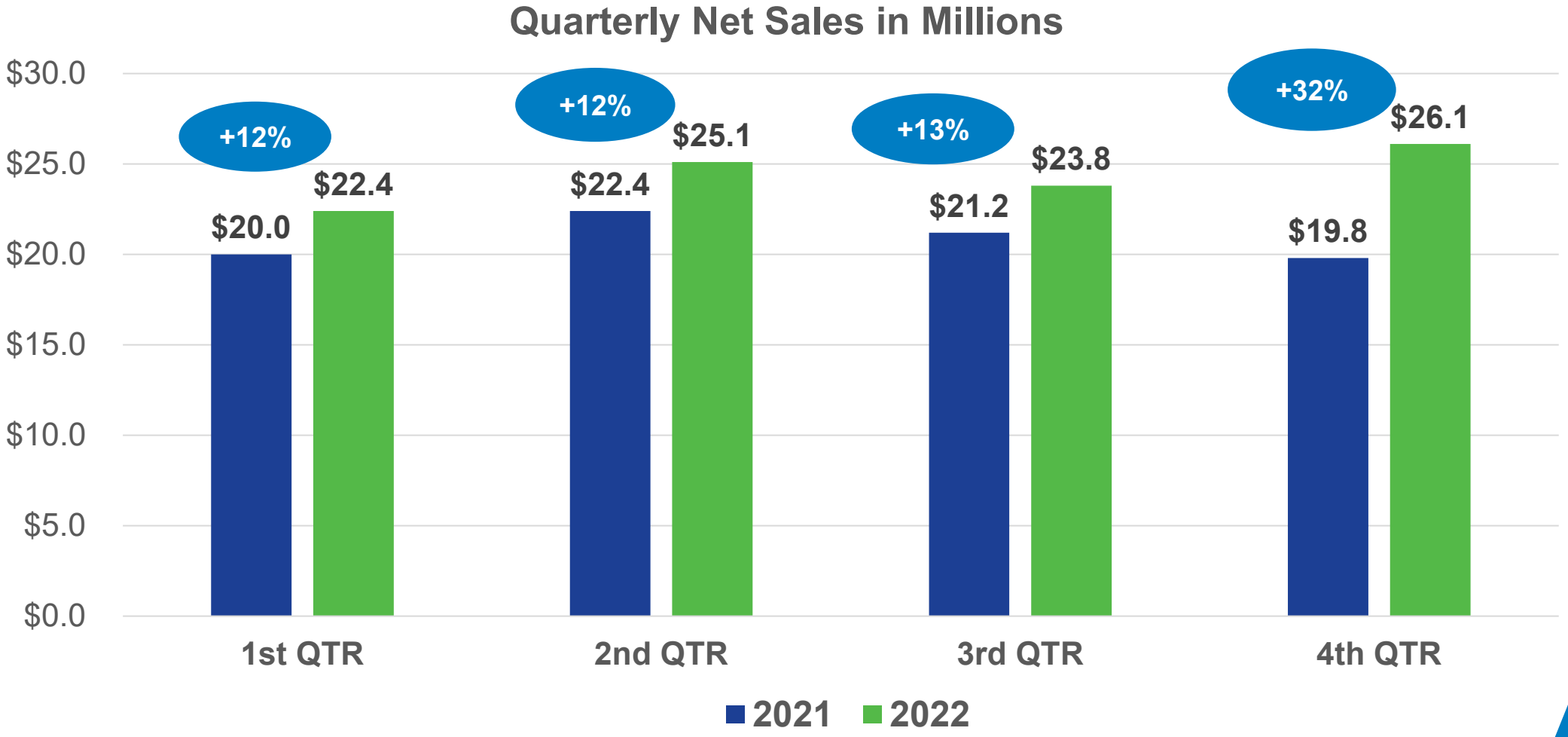
2022 CINV Franchise Net Sales Increased to $97.5M Demonstrating Growth of 17% vs. 2021



CINV Franchise in Excellent Position to Deliver Increasing Sales Through 2023

Continued Reimbursement Advantages

Product	J Code	Q2 2022	Q2 2023		
		ASP+5.2%	ASP+4.3%	$ Change	% Change
Fosaprepitant	J1453	$ 26.35	$ 27.90	$ 1.55	5.9%
CINVANTI	J0185	$ 223.20	$ 230.89	$ 7.69	3.4%
SUSTOL	J1627	$ 651.64	$ 580.34	$ (71.30)	-10.9%
IV Akynzeo	J1454	$ 460.88	$ 386.37	$ (74.51)	-16.2%

- Effective January 1, 2022 – separate reimbursement for generic fosaprepitant ended in HOPD
- **CMS opportunity:** effective January 1, 2023, reimbursement for 340B at ASP+6% vs. ASP minus 22.5% *(now retroactive to January 1, 2022)*
- CINVANTI large-scale manufacturing is now on-line with gross margin increasing from 50% toward 75%

CINV Franchise net sales guidance: Full-year 2023 expected in the range of $99M to $103M

ASP: Average Sales Price; **HOPD:** Hospital Outpatient Department

Financial Summary

Heron had cash, cash equivalents and short-term investments of $84.9 million as of December 31, 2022. The Company currently maintains a de minimis amount of cash and cash equivalents, in the low single digit millions of U.S. dollars, with Silicon Valley Bank ("SVB").

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended December 31, 2022	Twelve Months Ended December 31, 2022
Net product sales	$ 30,028	$ 107,672
Operating expenses[1]	50,383	282,330
Other income (expense), net	486	(7,366)
Net loss[1]	$ (19,869)	$ (182,024)
Net loss per share[2]	$ (0.17)	$ (1.67)
Net cash used in operations	$ (37,534)	$ (146,912)
Condensed Balance Sheet Data (in thousands)		**December 31, 2022**
Cash, cash equivalents and short-term investments		$ 84,852
Accounts receivable, net		$ 52,049
Inventory[3]		$ 54,573
Total assets		$ 250,951
Total stockholders' equity		$ 13,572

Common shares outstanding as of December 31, 2022 totaled 119.2 million.

[1] Includes $10.5 million and $43.0 million of non-cash, stock-based compensation expense for the three and twelve months ended December 31, 2022, respectively.
[2] Based on 119.0 million and 108.9 million weighted-average common shares outstanding for the three and twelve months ended December 31, 2022, respectively.
[3] Includes $30.9 million for ZYNRELEF, $19.9 million for CINVANTI, $2.6 million for SUSTOL and $1.2 million for APONVIE.

ZYNRELEF Important Safety Information for Patients

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, 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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ZYNRELEF 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 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

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APONVIE Important Safety Information for Patients

APONVIE should not be used:

- if you are allergic to aprepitant or any of the ingredients in APONVIE
- if you are taking pimozide

APONVIE may cause serious side effects. Tell your doctor or nurse right away if you have any of these signs or symptoms of an allergic reaction:

- trouble breathing or swallowing, shortness of breath or wheezing
- swelling of your eyes, face, tongue, or throat
- flushing or redness of your face or skin
- hives, rash, or itching
- dizziness, a rapid or weak heartbeat, or you feel faint

APONVIE may affect how other medicines work. Other medicines may affect how APONVIE works. Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, or herbal supplements. If you take the blood-thinner medicine warfarin, your doctor may do blood tests after you receive APONVIE to check your blood clotting.

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APONVIE Important Safety Information for Patients (cont)

The information provided here is not comprehensive. Women who use birth control medicines containing hormones to prevent pregnancy (birth control pills, skin patches, implants, and certain IUDs) should also use back-up methods of birth control (such as condoms and spermicides) for 1 month after receiving APONVIE.

Before you receive APONVIE, tell your doctor if you are pregnant or plan to become pregnant. APONVIE contains alcohol and may harm your unborn baby.

Before you receive APONVIE, tell your doctor if you are breast-feeding or plan to breastfeed because it is likely APONVIE passes into your milk, and it is not known if it can harm your baby. You and your doctor should decide if you will receive APONVIE, if breast-feeding.

The most common side effects of APONVIE are constipation, low blood pressure, tiredness, and headache.

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.

Please see full Prescribing Information.

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