Heron Update

Q2 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 and the completion of the private placement on the anticipated terms or at all; the potential market opportunities for ZYNRELEF in the U.S., Europe and Canada; 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 net product sales guidance for the oncology care franchise and the acute care franchise; the net cash guidance for operating activities; 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 impact of our restructuring plans; the ability for the Company to reach profitability; 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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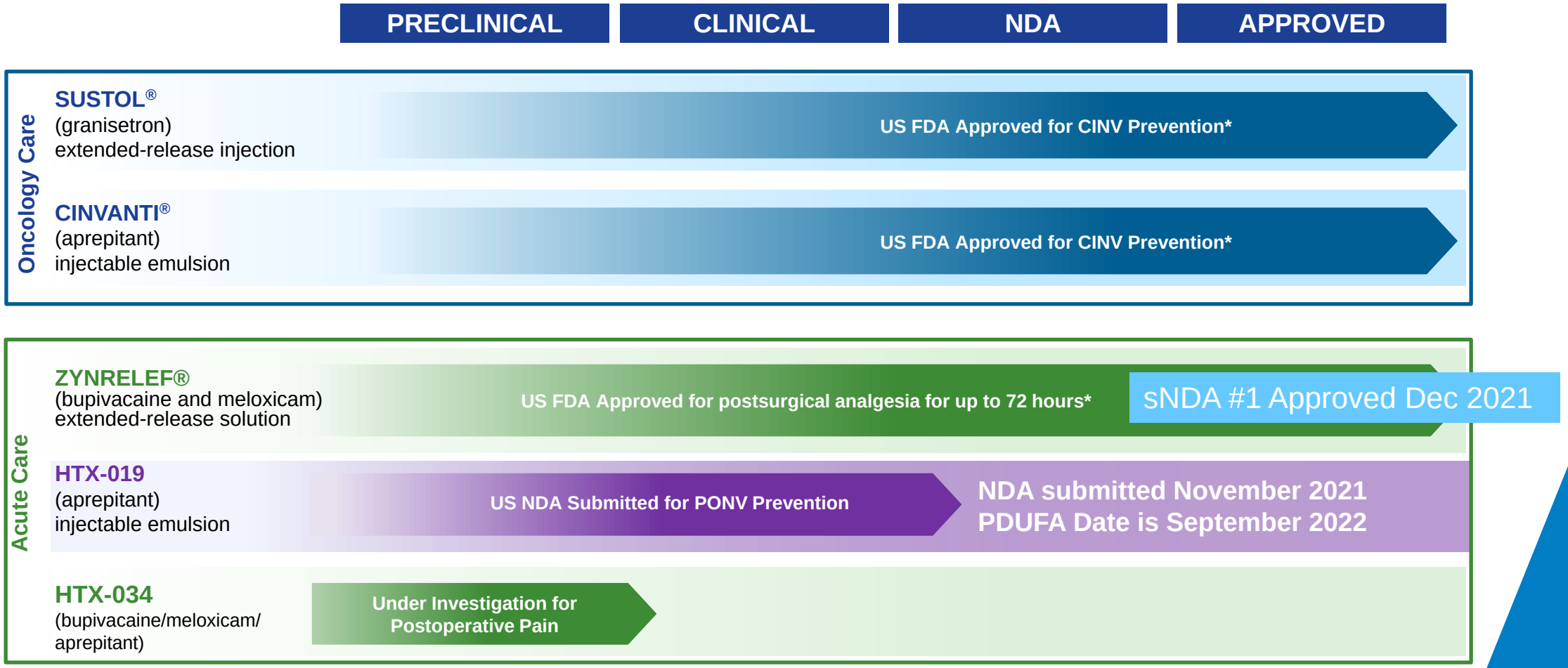
Heron Pipeline



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

Enrollment Completed in Clinical Studies Needed for sNDA #2 to Obtain Broadest Label

- Study 220 C-section
- AMAZE Study:
  - Abdominoplasty
  - Total Shoulder Arthroplasty
- Study 221 Spine

sNDA #2 planned for year-end

ZYNRELEF
Commercial Update

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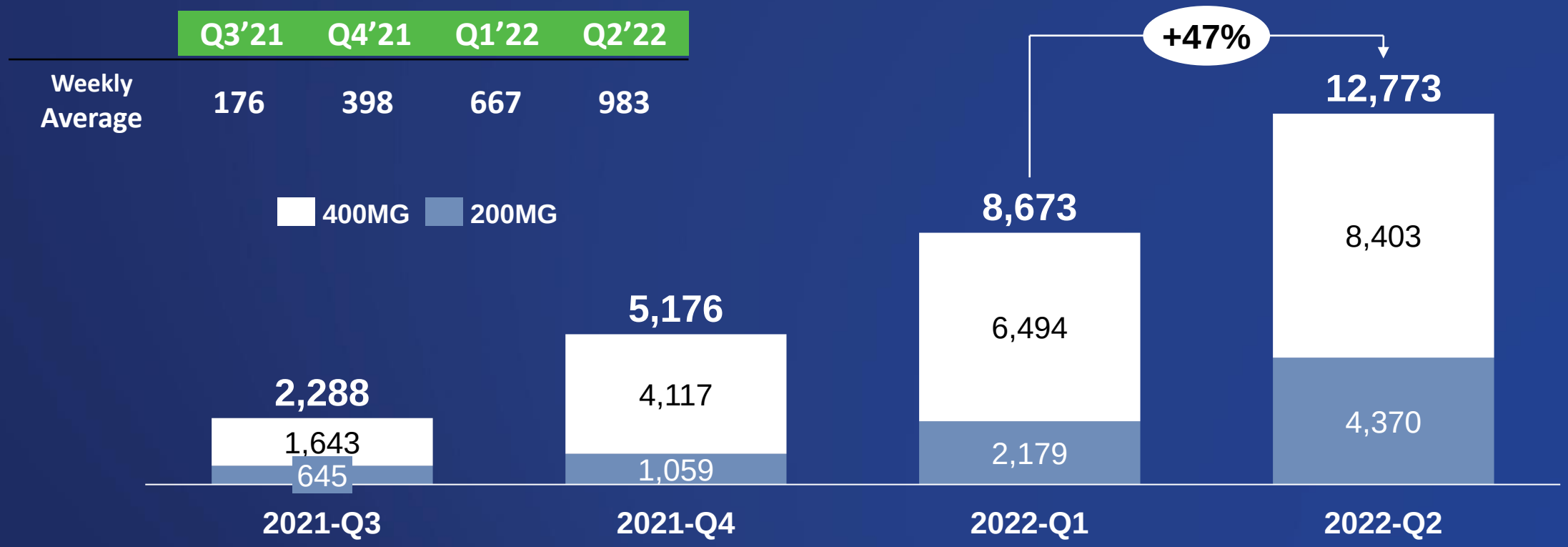
ZYNRELEF Inventory at Distribution Centers has Stabilized

- **Q2'22 Net Sales: $2.5 million**
  - 140% increase over prior quarter
  - Currently expect Q3'22 net sales increase of 40% to 50% vs. Q2'22
- **ZYNRELEF Ex-Factory reorders have stabilized at demand**

	Ex-Factory Reorder % of Demand Units			
SKU Dosage	Q4 2021	Q1 2022	Q2 2022	Q3 QTD thru 8/3
400 mg	97%	92%	> 100%	99%
200 mg	40%	41%	89%	105%

ZYNRELEF is Rapidly Increasing Quarterly Demand Volume

- Grew demand unit sales by **47%** from Q1 22 to Q2 22



ZYNRELEF data through 6/30/2022

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Continued Strong Progress Across All ZYNRELEF Launch Metrics

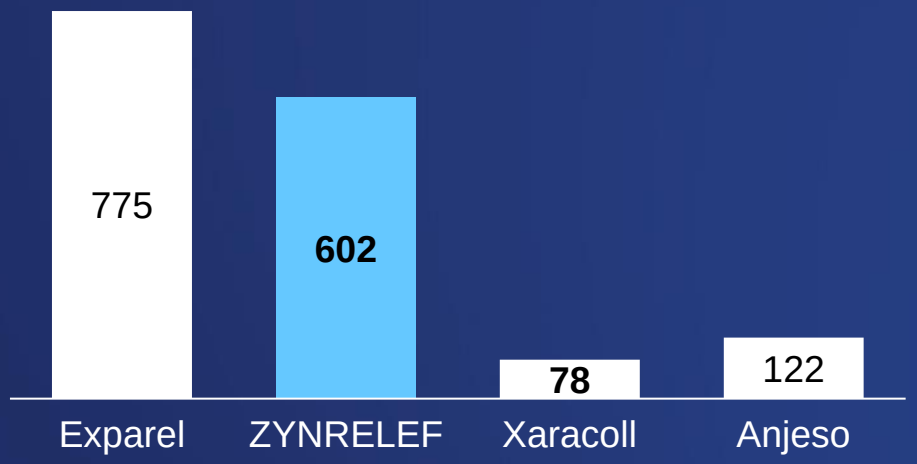
Account Growth	Q3'21 Earnings Call Sept 30, 2021	Q4'21 Earnings Call Dec 31, 2021	Q1'22 Earnings Call Mar 31, 2022	Q2'22 Earnings Call June 30, 2022
Unique Ordering Accounts	160	309	451	602
Average per Month	53	52	50	50
% Reorder Rate	50%	73%	80%	84%

P&T Decisions	Q3'21 Earnings Call Oct 31, 2021	Q4'21 Earnings Call Feb 25, 2022	Q1'22 Earnings Call Apr 30, 2022	Q2'22 Earnings Call July 31, 2022
Formulary Approvals	126	260	319	384
Average per Month	32	33	32	30
% Hospital Approvals	91%	> 90%	> 90%	> 90%
IDN Approvals	N/A	34	46	57

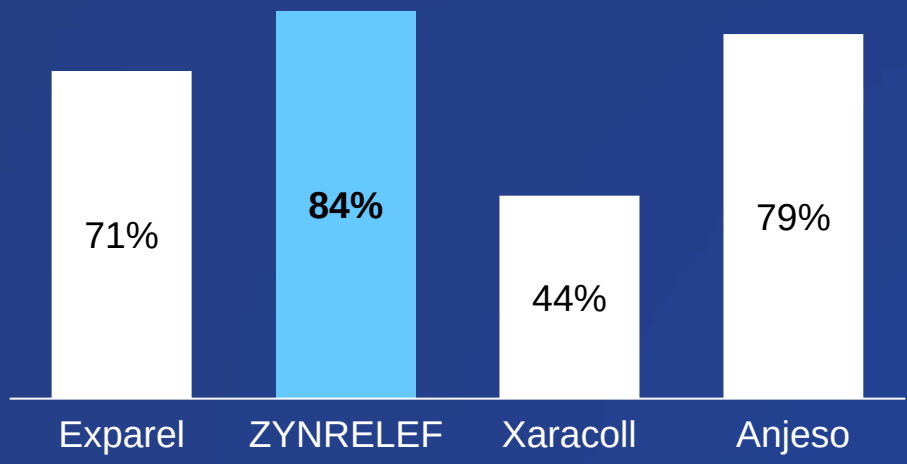
ZYNRELEF New Ordering Accounts Growth Continues

- **602** unique accounts ordered ZYNRELEF (July 2021 – June 2022)
  - +33% increase in unique accounts ordering ZYNRELEF from Q1’22 to Q2’22

Unique Ordering Accounts*
12 Months Post Launch



Reordering Account Rate*
12 Months Post Launch



* Source: Symphony Heath SNR / ZYNRELEF EDI 867

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ZYNRELEF Continues to Gain Rapid Formulary Approvals

- ZYNRELEF formulary approvals: **384** as of July 31, 2022
  - **P&T Committee approval rate > 90% in hospitals**

Formulary Approval Status	Estimated % of Approvals
Unrestricted Usage	**68%**
Restricted (Primarily for Trial Evaluations)	**32%**

- **> 80** additional P&T Committees are scheduled to review ZYNRELEF before the end of 2022
- Formulary approval → Medical Executive approval → CPOE → Pharmacy Orders → Patient

CPOE: computerized physician order entry

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

- **57** IDNs have added ZYNRELEF as formulary approved product

- **57** IDNs represent ~ **potential opportunity of $200M**** in annual ZYNRELEF net sales based on currently indicated surgical procedures
- **57** IDNs represent ~ **$135M* of Exparel** sales
  - 15 IDN's representing approximately **$42M* of Exparel** sales are currently evaluating switching to ZYNRELEF for indicated procedures

• Symphony DDD data July 2021 – June 2022 / based on WAC pricing
** Assumes 100% of share in currently indicated surgical procedures

Therapeutic Interchange: Opportunity to Accelerate Growth

- 15 IDNs have expressed interest in Therapeutic Interchange (TI) with ZYNRELEF for indicated procedures

Indicated Procedures	Exparel WAC	# of Hospitals	# of ASC
363,197	~ $42 million	234	169

- In all cases pharmacy is supportive and helping drive the evaluations for change
- Initial feedback on trials with ZYNRELEF has been positive

ZYNRELEF Branded Share is Growing in IDNs

- In 15 IDNs evaluating TI - ZYNRELEF units have grown ~ 290% in since label expansion (1st half 2022 vs. 2nd half 2021)

Approved IDN - ZYNRELEF Branded Mkt Sh (ZYNRELEF + Exparel Units)					
Category	**Q3'21**	**Q4'21**	**Q1'22**	**Q2'22**	**Exparel 12M WAC***
57 IDNs	**0.8%**	**2.1%**	**3.8%**	**6.5%**	**$135 M**
Highest ZYNRELEF Branded Market Share of IDNs Evaluating TI					
IDN #1	**0.0%**	**0.0%**	**13.6%**	**41.0%**	**$1.2 M**
IDN #2	**0.0%**	**1.9%**	**31.9%**	**40.4%**	**$0.6 M**
IDN #3	**0.0%**	**0.0%**	**4.8%**	**25.0%**	**$0.9 M**
IDN #4	**10.3%**	**17.4%**	**20.0%**	**22.0%**	**$1.3 M**
IDN #5	**0.0%**	**0.0%**	**4.3%**	**13.6%**	**$2.2 M**

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

ZYNRELEF is the Only Reimbursed Local Anesthetic in Hospital Outpatient, the Largest Setting of Care

- Effective April 1, 2022 - ZYNRELEF is separately reimbursed for Medicare patients in the Hospital Outpatient setting of care
  - 72% of indicated procedures were performed in outpatient settings in 2021 (59% in HOPD, 13% in ASC)[a]
- Effective January 1, 2022 - ZYNRELEF was separately reimbursed for Medicare patients in the ASC and a product specific C-code (C9088) is assigned
- Multiple commercial payers and state Medicaid agencies covering >123 million lives have agreed to reimburse ZYNRELEF outside of the surgical packaged payment in the ASC
- ZYNRELEF's lower price benefits all settings of care, including those in which local anesthetics are reimbursed as part of the surgical packaged payment

HOPD: Hospital Outpatient Department; **ASC**: Ambulatory Surgical Center

[a] Based on third party claims data

ZYNRELEF's Significant Economic & Reimbursement Benefits

ZYNRELEF	WAC	340B
400 mg/12 mg	$267.50	$205.17
200 mg/6 mg	$135.50	$104.05

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%

Medicare NCR By Site of Care*			
	NCR 340B	NCR HOPD	ASC
ZYNRELEF 400 mg/12 mg	$74.83	$12.50	$12.50
Exparel 266 mg	($354.53)	($354.53)	$12.55
ZYNRELEF 200 mg/6 mg	$35.95	$4.50	$4.50
Exparel 133 mg	($198.84)	($198.84)	($15.30)

*Estimates Comparing WAC (or 340B) acquisition cost to published ASP reimbursement for Medicare patients to calculate NCR based on ZYNRELEF Q3'22 rate and Exparel Q3'22 rate. Medicare reimbursement is subject to sequestration. .
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 Priorities 2022

- Leverage **new label indication** for faster growth
- Build consistent usage in formulary approved ordering accounts and increase average order size – expand number of surgeons using ZYNRELEF
- Continue to gain formulary access to new IDNs and Hospitals to build pipeline
- Maximize Pass-through status in HOPD and Commercial/Medicaid separate reimbursement in ASCs

Oncology Care Franchise

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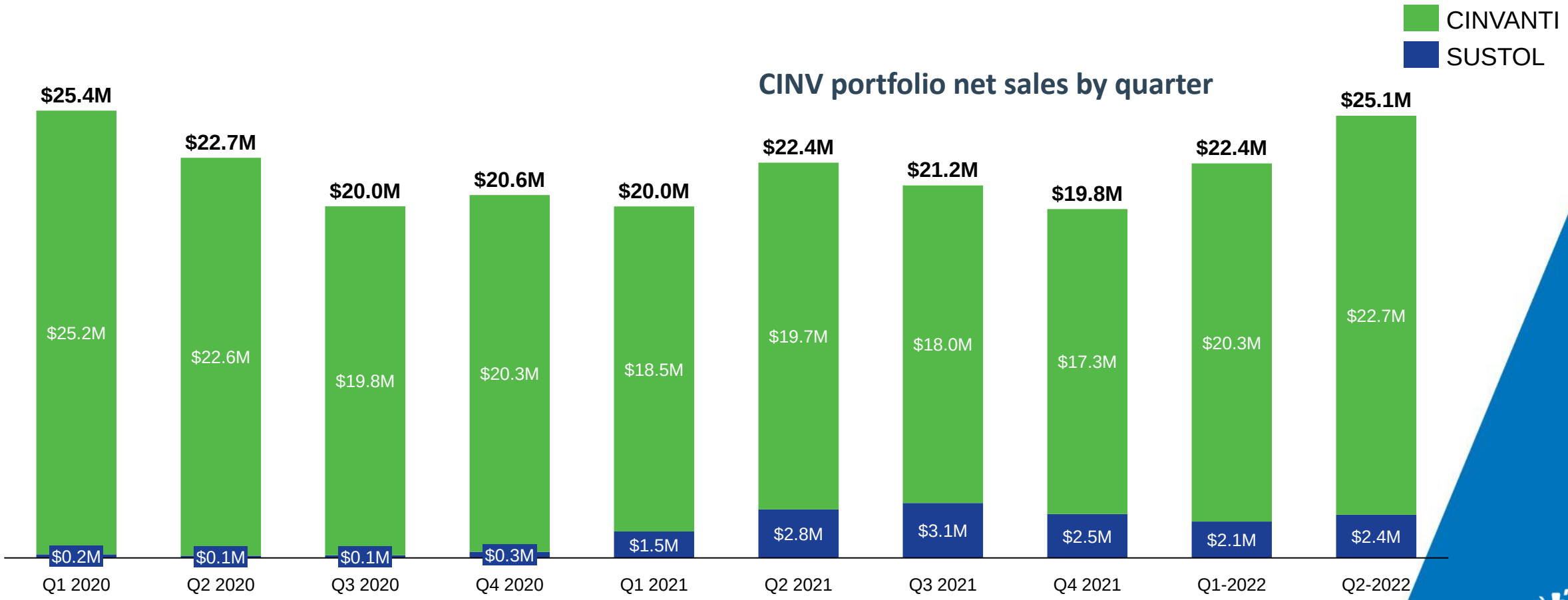
Heron's CINV Net Sales Grew by 12% over Prior Quarter



Note: SUSTOL sales from Q4 2016- Q4 2019 of 255.5 not shown in graph

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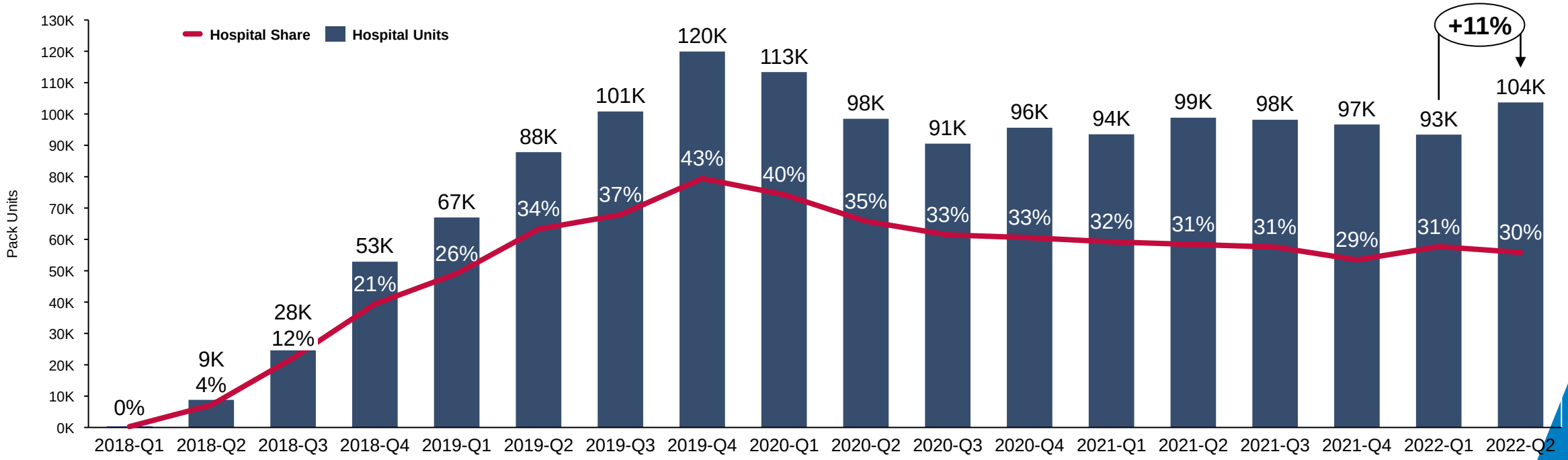
CINVANTI – Hospital Segment: Units Remain Strong Despite Significantly Lower Acquisition Cost of Generic Fosaprepitant



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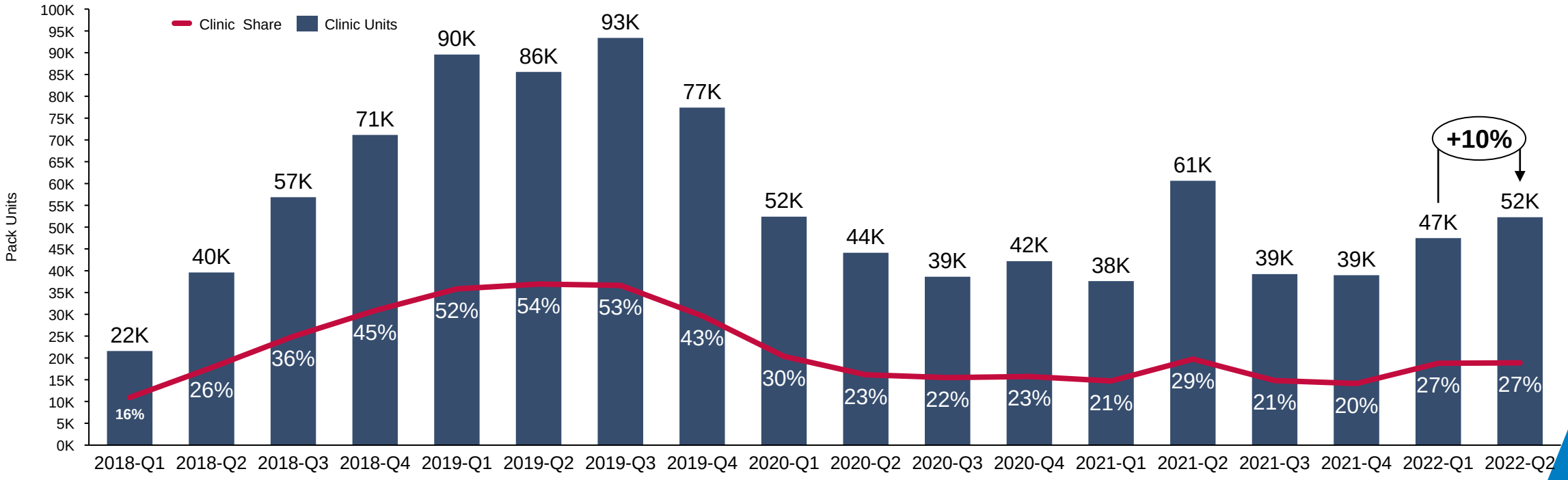
CINVANTI – Clinic Units Return To Growth in 2022 with End of Generic Abitrage



SOURCE:867 7-13-22, : IMS DDD 7-1-22

CINV Franchise 2022 Outlook

- **Continued improving reimbursement tailwinds over the past year**

Product	J Code	Q3 2021	Q3 2022		
		ASP+6%	ASP+4.3%	$ Change	% Change
Fosaprepitant	J1453	$ 49.80	$ 27.01	$ (22.79)	-45.76%
CINVANTI	J0185	$ 209.56	$ 220.01	$ 10.45	4.99%
Palonosetron	J2469	$ 19.00	$ 8.90	$ (10.10)	-53.16%
SUSTOL	J1627	$ 707.20	$ 634.26	$ (72.94)	-10.31%
IV Akynzeo	J1454	$ 594.20	$ 458.60	$ (135.60)	-22.82%

  - Effective January 1, 2022 – separate reimbursement for generic fosaprepitant ended in HOPD
- **CINV Franchise net sales guidance: Full-year 2022 projections increased to a range of $93M to $95M**
  - Expect increased units at lower net price with CINV products in second half of 2022
  - **New CMS opportunity:** effective January 1, 2023, reimbursement for 340B at ASP+6% vs. ASP minus 22.5%
  - Large-scale manufacturing is expected to come on-line in 4th quarter with gross margin increasing from 50% to 75%

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

Financial Summary

Heron had cash, cash equivalents and short-term investments of $83.5 million as of June 30, 2022. Adjusting for net proceeds of $75.2 million from our August 2022 private placement, Heron had cash, cash equivalents and short-term investments of $158.7 million.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended June 30, 2022	Six Months Ended June 30, 2022
Net product sales	$ 27,630	$ 51,087
Operating expenses[1]	77,128	163,508
Other income (expense), net	(6,861)	(7,826)
Net loss[1]	$ (56,359)	$ (120,247)
Net loss per share[2]	$ (0.55)	$ (1.18)
Net cash used in operations	$ (28,373)	$ (72,312)
Condensed Balance Sheet Data (in thousands)		**June 30, 2022**
Cash, cash equivalents and short-term investments		$ 83,538
Accounts receivable, net		$ 40,303
Inventory[3]		$ 61,318
Total assets		$ 243,965
Total stockholders' equity (deficit)		$ (21,736)

Common shares outstanding as of June 30, 2022 totaled 102.5 million.

[1] Includes $10.4 million and $21.3 million of non-cash, stock-based compensation expense for the three and six months ended June 30, 2022, respectively.
[2] Based on 102.4 million and 102.3 million weighted-average common shares outstanding for the three and six months ended June 30, 2022, respectively.
[3] Includes $37.4 million for ZYNRELEF, $21.4 million for CINVANTI and $2.5 million for SUSTOL.

Key Catalysts in Pain Management & CINV Franchises

ZYNRELEF®	CINVANTI ® and SUSTOL® for CINV
✓ ZYNRELEF unit demand increased 47% in the second quarter compared to the prior quarter	✓ Net product sales in Q1 2022 increased by 13% compared to prior quarter
✓ Pass-through status began April 1 in HOPD	✓ Q2 2022 net sales guidance for CINV franchise: $22M - $23M BEAT @ $25.1M
• Complete partnership for Ex-US territory	• 2022 net sales guidance for CINV franchise: $89M - $93M increased to $93M - $95M
✓ Validation of large-scale manufacturing with significant reduction in COGS in Q3	• Large-scale manufacturing with 50% reduction on COGS validation in 3Q
• Publication of data: ✓ TKA with MMA ✓ C-Section poster	PONV
✓ Complete PK/safety studies in 3 additional surgical procedures to support NDA #2 in Q3 • Submit sNDA #2 for expanded indications Q4	• Obtain FDA approval for HTX-019 by Sept2022

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, 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.

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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