Heron Update

Q1 2022 Earnings Call

HERON THERAPEUTICS

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 and Canada; the potential market opportunity for ZYNRELEF in the US, 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; 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 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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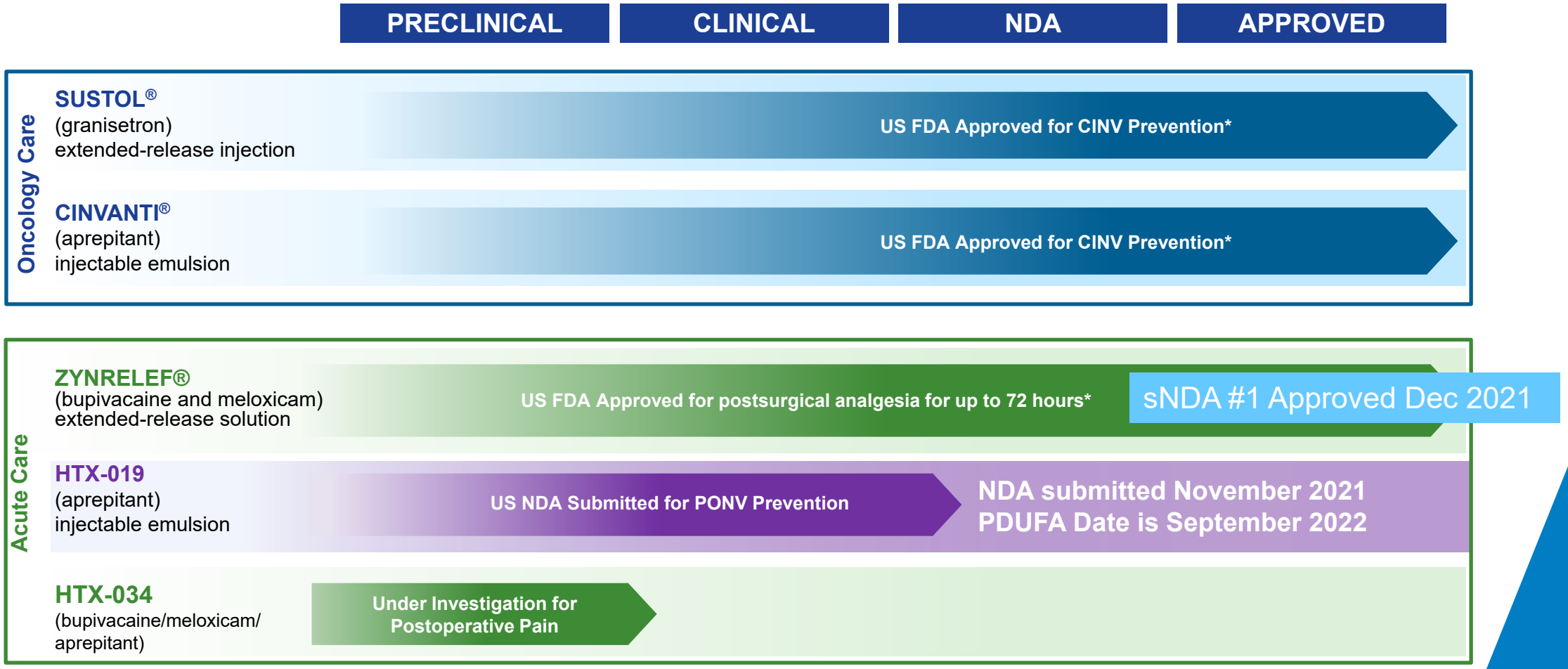
Heron Pipeline



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 Commercial Update

Q1 2022 Earnings Call

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ZYNRELEF Launch Progress Summary

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

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

- Effective April 1, 2022 - ZYNRELEF is separately reimbursed for Medicare patients in the HOPD under 3-year transitional pass-through status

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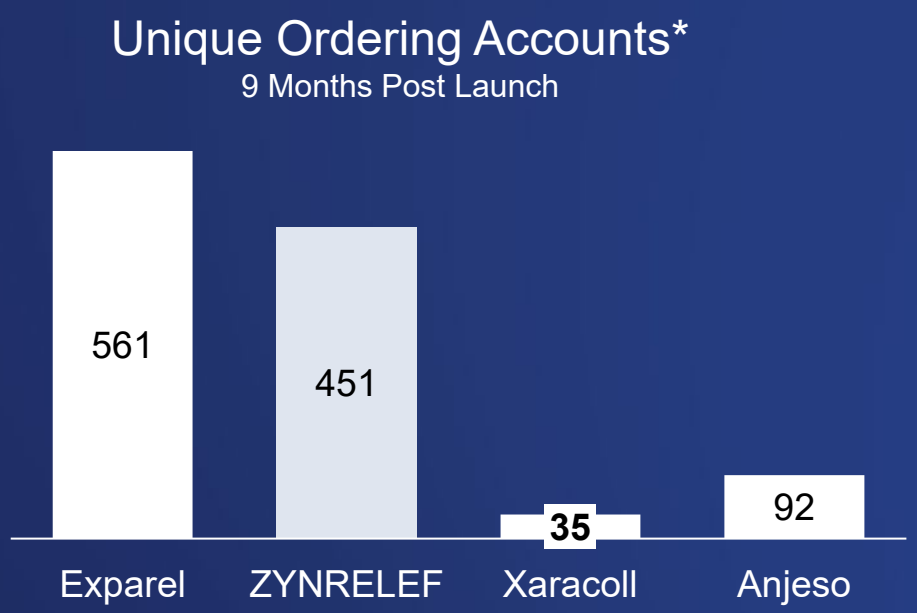
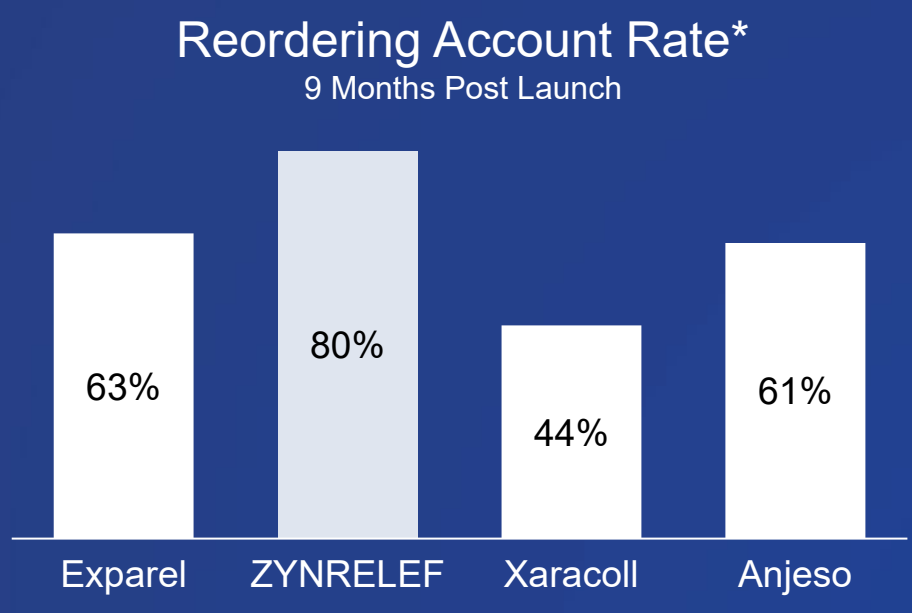
ZYNRELEF New Ordering Accounts Growth Continues

- **451** unique accounts ordered ZYNRELEF (July 2021 – March 2022)
  - +46% increase in unique accounts ordering ZYNRELEF from Q4'21 to Q1'22 QTD





* Source: Symphony Heath SNR / ZYNRELEF EDI 867

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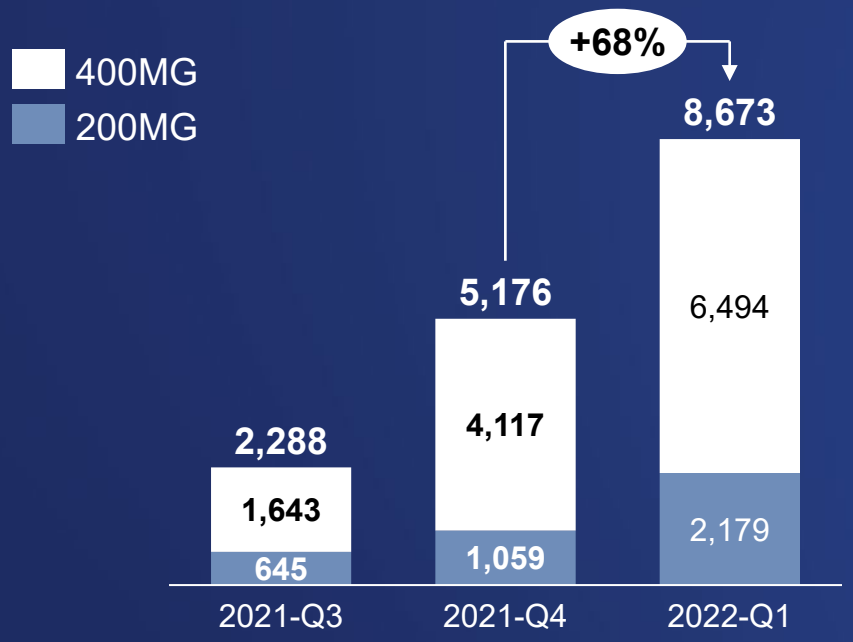
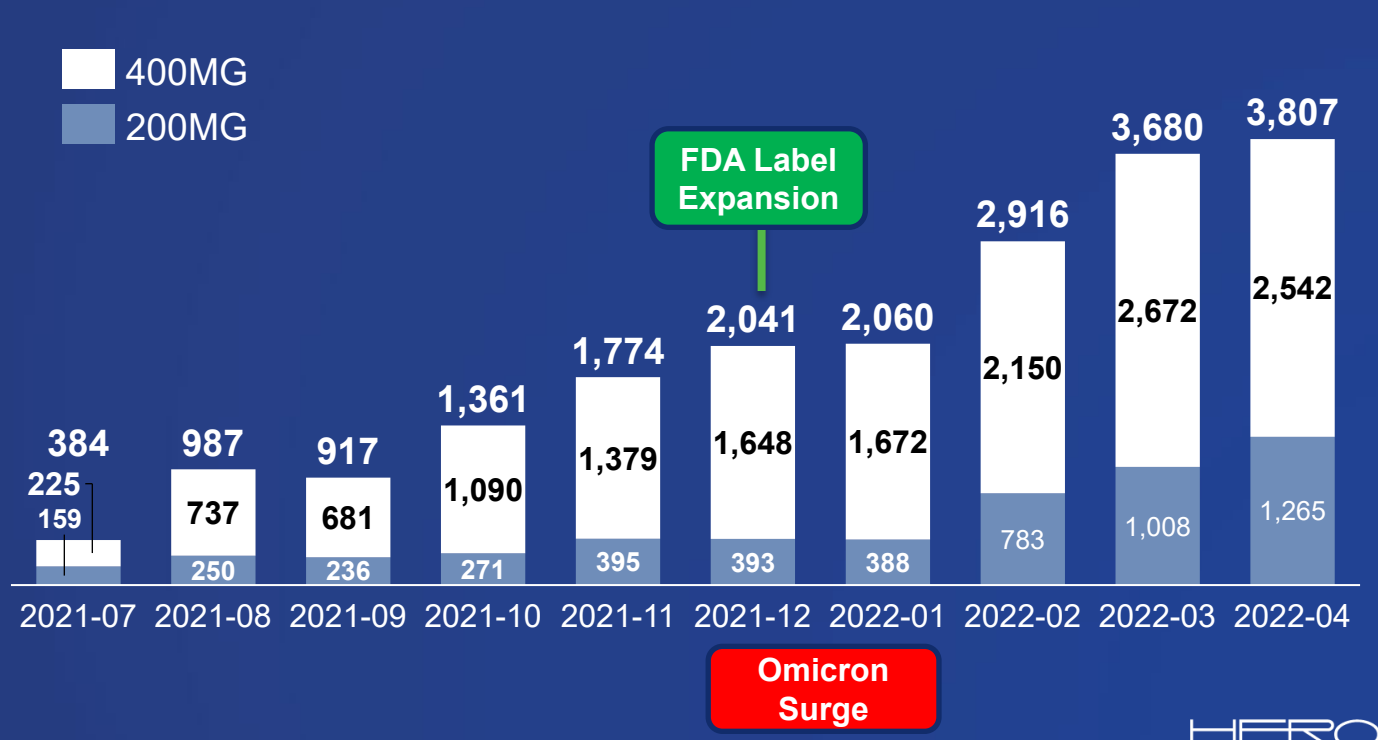
ZYNRELEF is Rapidly Increasing Quarterly Demand Volume

512 unique ordering accounts during first 10 months of launch (July 2021 to April 2022)

- Grew demand unit sales **+68%** from Q4 21 to Q1 22
- 400mg SKU represents **74%** of demand since launch





ZYNRELEF data through 5/1/2022

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ZYNRELEF Performance during Spring Break

Rolling 5-Week Comparison Ending April 15, 2022

Exparel – Symphony Healthcare Weekly Data Source
ZYNRELEF – 867 Data Source / WAC 200: $135.50 400: $267.50
***Rolling 5-week comparison:** 2022 Wks. 2/11 – 3/11/2022 vs 3/18 – 4/15/2022

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Meaningful Progress Burning through Initial DC* Inventory

- Q1’22 Net Sales: **$1.1 million**
  - Q1 Net Sales reflect $0.3M return of short-dated product and continue progress reducing the initial stocking inventory based on demand orders
- Q1’22 Ex-Factory Reorder Rate through 3/31/2022:
  - **92%** of ZYNRELEF 400mg demand units
  - **41%** of ZYNRELEF 200mg demand units
- Q2’22 Ex-Factory Reorder Rate through 5/03/2022:
  - **> 100%** of ZYNRELEF 400mg demand units
  - **67%** of ZYNRELEF 200mg demand units
  - 400mg SKU has stabilized / 200mg SKU expected to stabilize by end of Q2’22

* Distribution Center

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ZYNRELEF Continues to Gain Rapid Formulary Approvals

- ZYNRELEF formulary approvals: **319** as of April 30, 2022
  - **P&T Committee approval rate > 90% in hospitals**

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

- **~ 60** additional P&T Committees are scheduled to review ZYNRELEF before the end of Q2 2022
- Formulary approval → Medical Executive approval → CPOE → Pharmacy Orders → Patient

CPOE: computerized physician order entry

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

- 46 IDNs have added ZYNRELEF as formulary approved product
  - Represent 576 hospitals and 575 ASCs – many hospitals still require formulary approval
- 41% unrestricted / 59% restricted formulary approvals
- 46 IDNs represent ~ 676k of annual ZYNRELEF indicated surgical procedures
- 46 IDNs represent ~ **$77M* of Exparel** sales
- IDN's representing approximately **$40M* of Exparel** sales are currently evaluating switching to ZYNRELEF for indicated procedures

IDN: Integrated Delivery Network**; ASC:** Ambulatory Surgical Center; **WAC:** Wholesale Acquisition Cost
* Symphony DDD data April 2021 – March 2022 / based on WAC pricing

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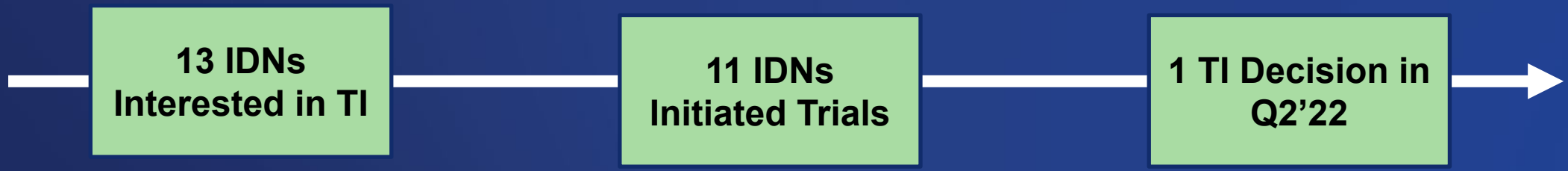
Therapeutic Interchange: Opportunity to Accelerate Growth

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

Target Procedures	Exparel WAC	Indicated Procedures	# of Hospitals	# of ASCs
599,212	~ $40 million	322,396	205	159

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



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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

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

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	$74.64	$12.50	$12.50
Exparel 266 mg	($354.53)	($354.53)	$1.92
ZYNRELEF 200 mg/6 mg	$35.86	$4.50	$4.50
Exparel 133 mg	($198.84)	($198.84)	($20.62)

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 based on Q2'22 rates. Medicare reimbursement is subject to sequestration.
WAC: wholesale acquisition cost. NCR: net cost recovery. HOPD: hospital outpatient department. ASC: ambulatory surgical center.

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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

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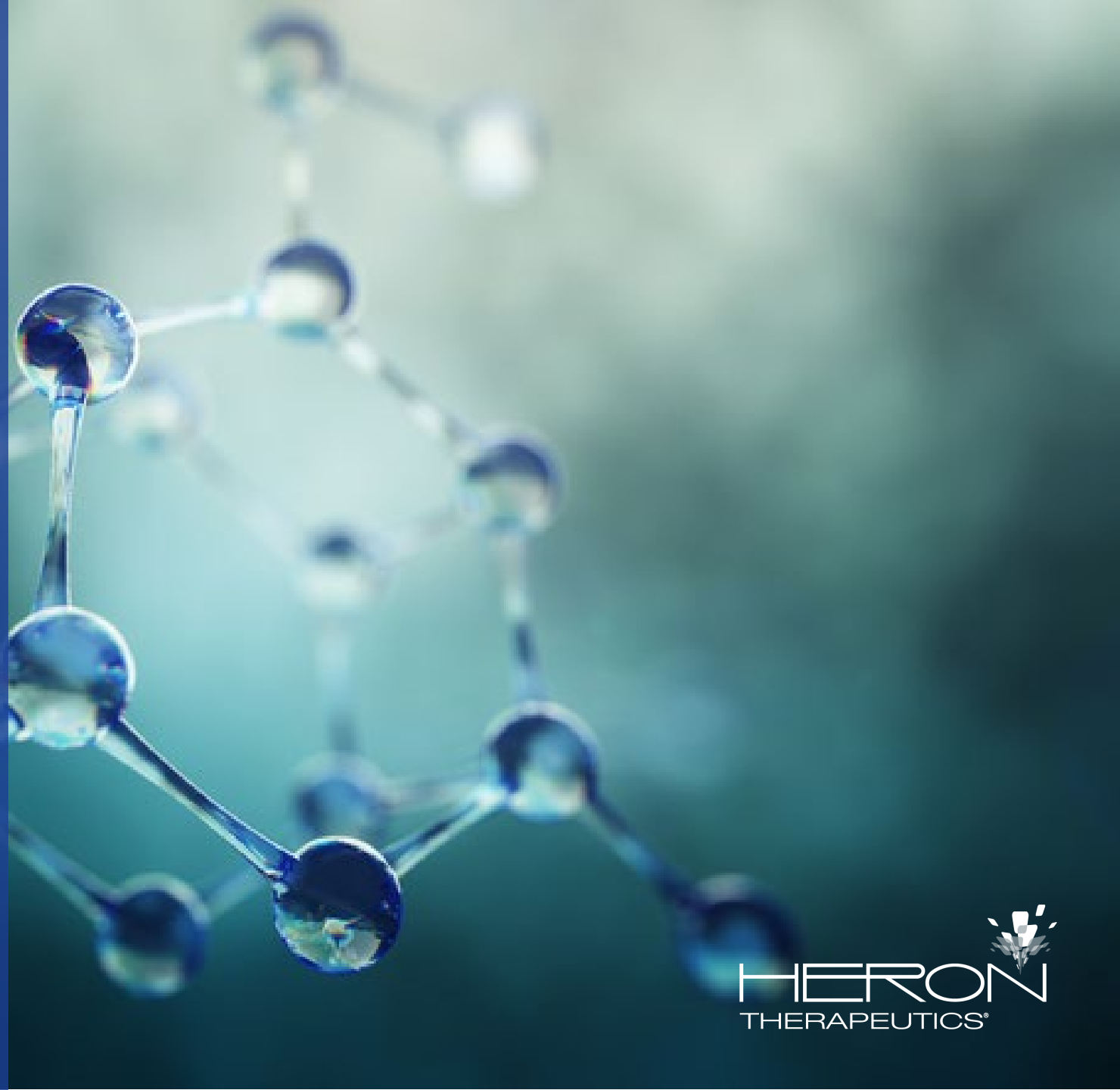
Oncology Care Franchise

Q1’22 Review



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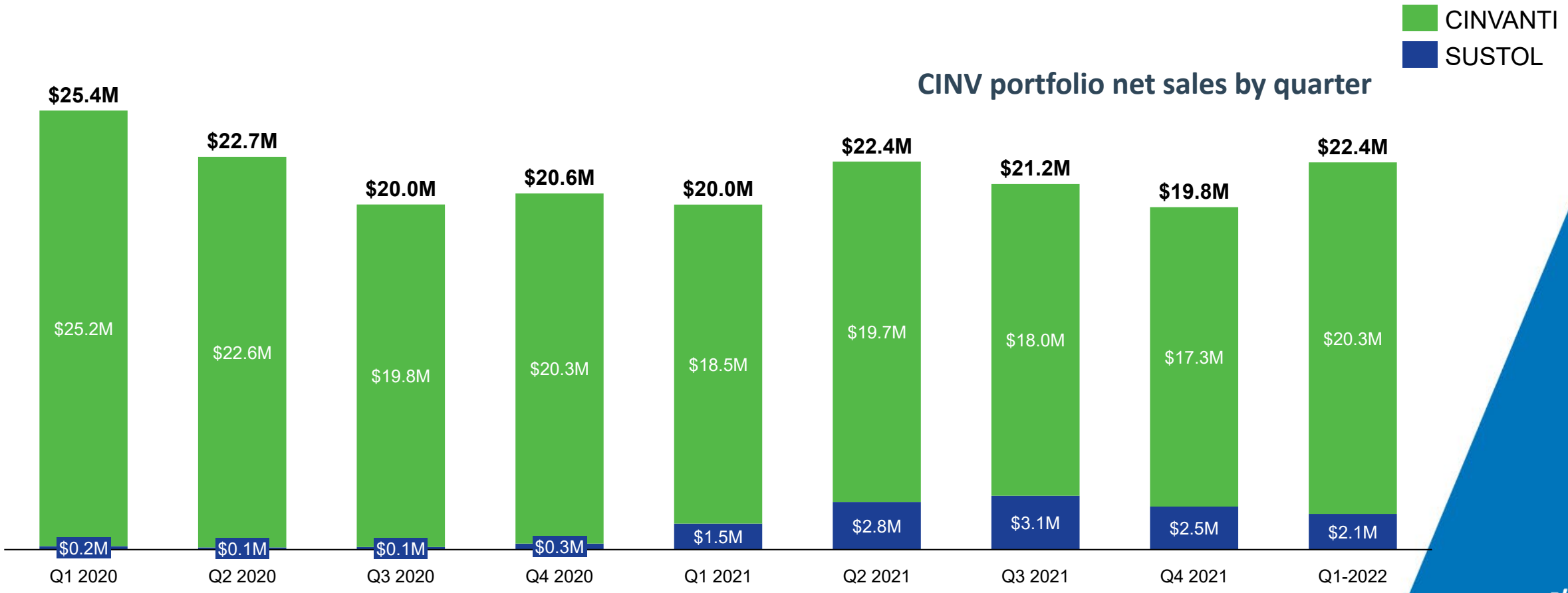
Heron's CINV Net Sales Grew by 13% over Prior Quarter

- Q2 2022 CINV Net Sales Guidance in range of **$22M to $23M**



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

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CINV Franchise 2022 Outlook

- Sales for CINVANTI and SUSTOL are poised for growth in 2022 based on improving reimbursement tailwinds
  - Generic fosaprepitant ASP reimbursement decreased to **$26.35** in Q2'22 (decrease of 49% from Q2'21)
  - Effective January 1, 2022 – separate reimbursement for generic fosaprepitant ended in HOPD
  - IV Akynzeo ASP reimbursement decreased to **$460.88** in Q2'22 (decrease of >$180 vs. Q2'21)
  - CINVANTI ASP reimbursement is **$223.20** in Q2'22 (increase of 19% from Q2'21)

- **CINV Franchise net sales guidance: Full-year 2022 expected in the range of $89M to $93M**
  - 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

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

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Financial Summary

Heron had cash, cash equivalents and short-term investments of $111.9 million as of March 31, 2022. We expect net cash used for operating activities of $37 million to $39 million in the second quarter of 2022.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended March 31, 2022
Net product sales	$ 23,457
Operating expenses[1]	86,380
Other income (expense), net	(965)
Net loss[1]	$ (63,888)
Net loss per share[2]	$ (0.63)
Net cash used in operations	$ (43,939)

Condensed Balance Sheet Data (in thousands)	March 31, 2022
Cash, cash equivalents and short-term investments	$ 111,910
Accounts receivable, net	$ 41,103
Inventory[3]	$ 56,470
Total assets	$ 273,723
Total stockholders' equity	$ 23,958

Common shares outstanding as of March 31, 2022 totaled 102.1 million.

[1] Includes $10.9 million of non-cash, stock-based compensation expense for the three months ended March 31, 2022.
[2] Based on 102.1 million weighted-average common shares outstanding for the three months ended March 31, 2022.
[3] Includes $34.3 million for ZYNRELEF, $20.9 million for CINVANTI and $1.3 million for SUSTOL.

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Key Catalysts in Pain Management & CINV Franchises

ZYNRELEF®	CINVANTI ® and SUSTOL® for CINV
✓ ZYNRELEF unit demand increased 68% in the first 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
• Complete partnership for Ex-US territory Q2	• 2022 net sales guidance for CINV franchise: $89M - $93M
• 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

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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 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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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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