Heron Update

Q3 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: uncertainties related to market conditions; the potential market opportunity for ZYNRELEF, including the potential additional market opportunity for a further expanded U.S. label for ZYNRELEF; the timing and results of studies for the further expansion of the U.S. label for ZYNRELEF; whether the U.S. Food and Drug Administration approves the further expansion of the U.S. label for ZYNRELEF; the potential market opportunity for APONVIE; the timing and results of the commercial launch of APONVIE; the net product sales guidance for the acute care and oncology care franchises; 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 ability of 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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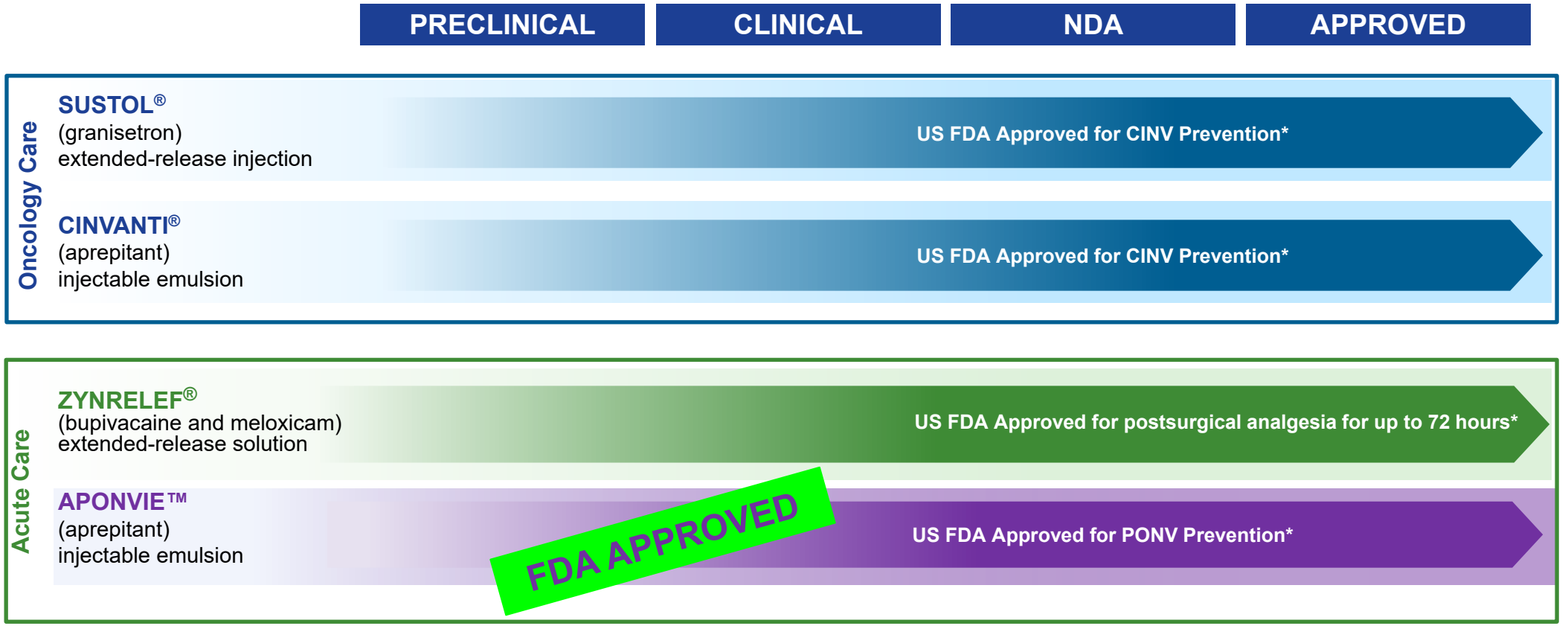
Heron Pipeline of 4 Approved Products



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. APONVIE™ (aprepitant) injectable solution is a substance P/neurokinin-1 (NK1) receptor antagonist indicated for the prevention of postoperative nausea and vomiting in adults. **APONVIE™ (aprepitant) injectable emulsion** is indicated for the prevention of postoperative nausea and vomiting (PONV) in adults.

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ZYNRELEF sNDA for Expanded Indications Planned for 4Q22

Current Indications cover approximately 7 million procedures/year

ZYNRELEF 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.

Proposed Indications cover approximately 14 million procedures/year

ZYNRELEF is indicated in adults to produce postsurgical analgesia for up to 72 hours after soft tissue and orthopedic surgical procedures.

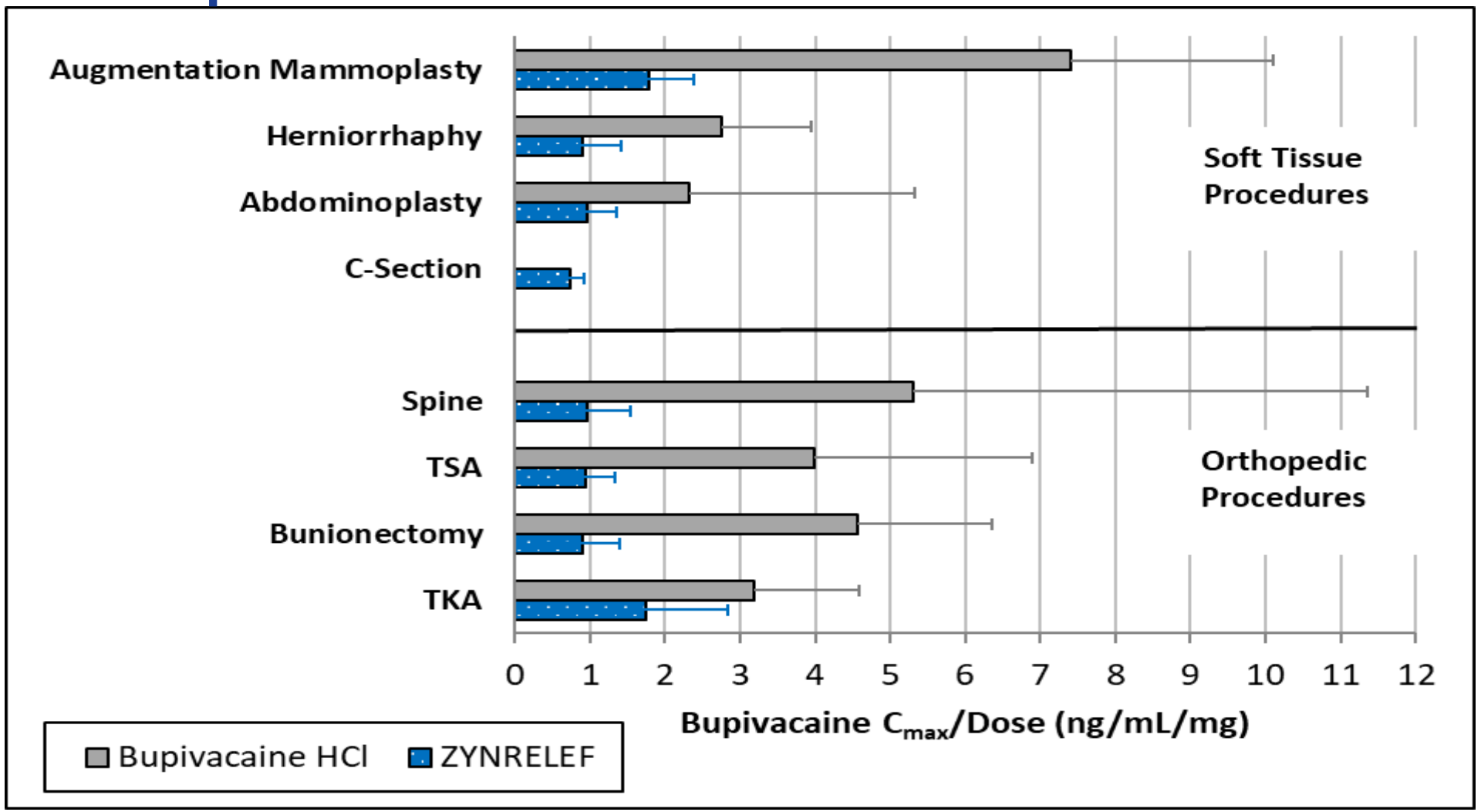
FDA Agreed the Following Studies Would Support a Significantly Broader Label for ZYNRELEF

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

All of the above studies have been fully enrolled as agreed with the FDA. No unique safety issues were observed and consistent bupivacaine PK following ZYNRELEF administration in additional procedures

Predictable ZYNRELEF PK Across Surgical Procedures

Bupivacaine HCl vs. ZYNRELEF Cmax/Dose



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ZYNRELEF
Commercial Update

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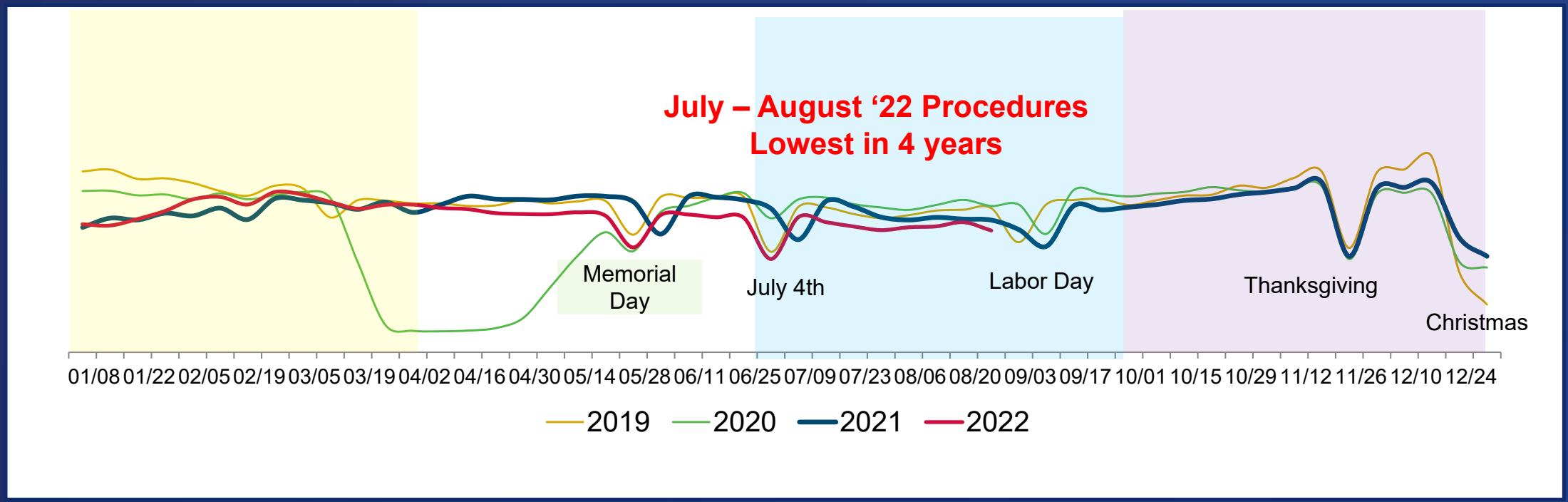
ZYNRELEF Quarterly Performance Metrics

- **Q3’22 Net Sales: $2.7 million**
- **Q3’22 Demand Units: 15,077**
- **Total Unique Ordering Accounts: 704** (as of 9/30/2022)
- **Total Formulary Approvals: 416** (as of 10/31/2022)
- **IDN formulary Approvals: 66** (as of 9/30/2022)

2019-2022 | Targeted Indicated Procedure Trends
Surgical Procedures Have Not Yet Returned to 2019 Levels

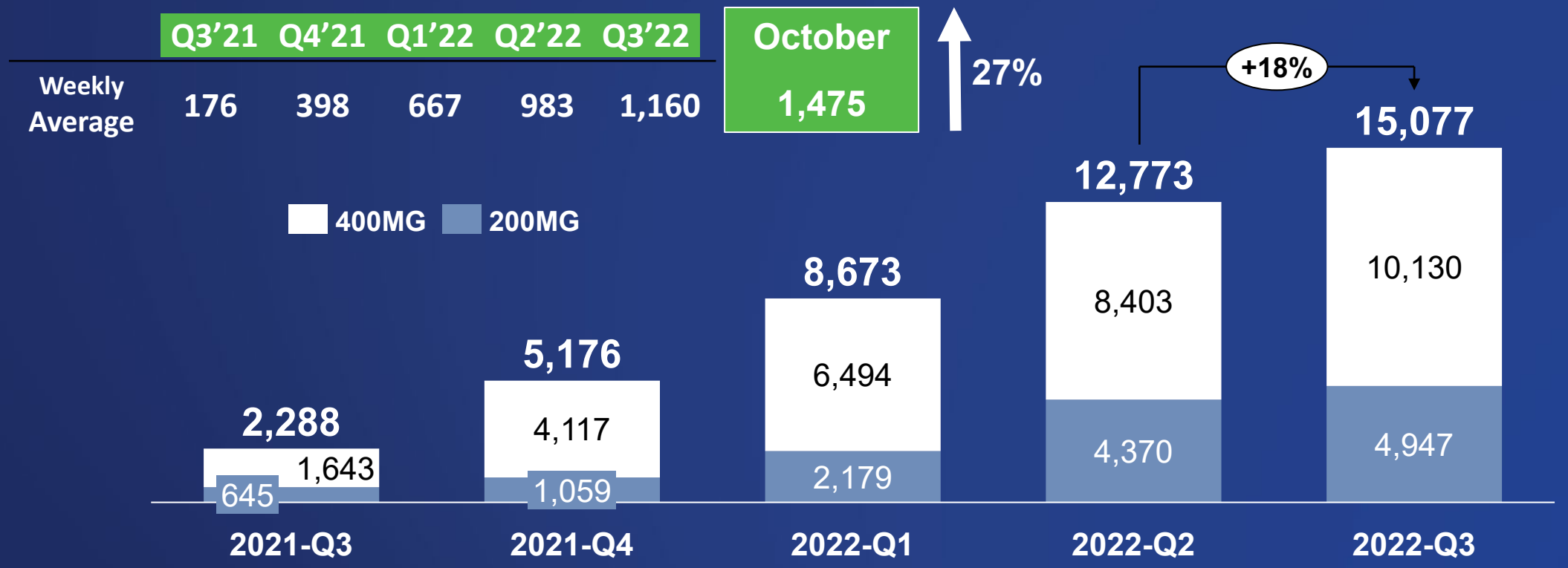


- **YoY 2022 vs 2021: - 4.5%**
- **QoQ 2022, Q2 vs Q3: - 11.1%**

YoY: Jan 3 - Sep 5, 2021 vs. Jan 2 - Sep 4, 2022 (36-Week Comparison)
QoQ: Apr 3 - Jun 5, 2022 vs. Jul 3 - Sep 4, 2022 (10-Week Comparison)

ZYNRELEF is Increasing Quarterly Demand Volume

- Weekly Sales Average up 18% from Q2 22 to Q3 22
- Based on strong growth in October, we anticipate net product sales to increase in the range of 30% to 40% in 4th quarter



ZYNRELEF data through 9/30/2022

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ZYNRELEF Continues to Gain Formulary Approvals

- ZYNRELEF formulary approvals: **416** as of October 31, 2022
  - **P&T Committee approval rate > 90% in hospitals evaluating the product**

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

- 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

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

- **66** IDNs represent ~ potential opportunity of **over one million** annual ZYNRELEF currently indicated surgical procedures
- **66** IDNs represent ~ **$143M* 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

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ZYNRELEF Branded Share is Growing in IDNs

- 15 IDNs evaluating TI share is > 50% higher than all IDNs
- ~50% share is the upper limit - until our label is expanded in 2H 2023

Approved IDN - ZYNRELEF Branded Mkt Sh (ZYNRELEF + Exparel Units)						
Category	**Q3'21**	**Q4'21**	**Q1'22**	**Q2'22**	**Q3'22**	**Exparel 12M WAC***
66 IDNs	**0.8%**	**2.1%**	**3.8%**	**6.5%**	**8.1%**	**$143 M**
Highest ZYNRELEF Branded Market Share of IDNs Evaluating TI						
15 IDNs	**1.5%**	**3.2%**	**6.3%**	**9.4%**	**12.4%**	**$42 M**
IDN #1	**0.0%**	**0.0%**	**13.6%**	**41.0%**	**50.5%**	**$1.2 M**
IDN #2	**0.0%**	**1.9%**	**31.9%**	**40.4%**	**47.9%**	**$0.6 M**
IDN #3	**0.0%**	**0.0%**	**4.3%**	**13.6%**	**27.8%**	**$2.2 M**
IDN #4	**10.3%**	**17.4%**	**20.0%**	**22.0%**	**22.9%**	**$1.3 M**
IDN #5	**9.0%**	**18.3%**	**18.9%**	**22.1%**	**22.7%**	**$1.4 M**

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

ZYNRELEF Continues to Maintain Significant Economic & Reimbursement Benefits vs. Exparel Even with 340B Pricing

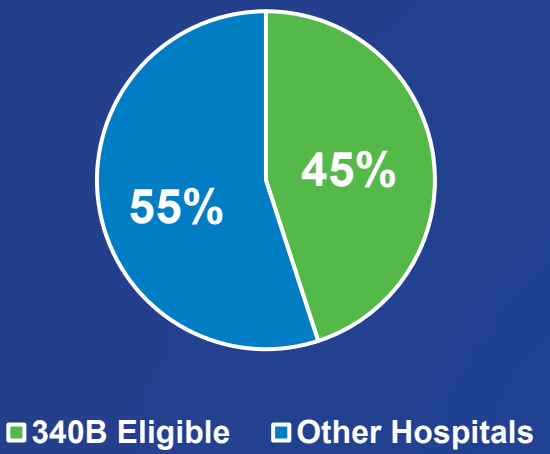
ZYNRELEF	WAC	340B
400 mg/12 mg	$267.50	$205.17
200 mg/6 mg	$135.50	$104.05

Exparel	WAC	340B*
266 mg (20 mL)	$354.53	$266.00
133 mg (10 mL)	$198.84	$151.00

ZYNRELEF Savings vs Exparel*			
WAC $/unit	WAC %	340B $/unit	340B %
~ $87	25%	~ $61	23%
~ $63	32%	~ $47	31%

Medicare NCR By Site of Care**			
	NCR 340B*	NCR HOPD	ASC
ZYNRELEF 400 mg/12 mg	$75.05	$12.50	$12.50
Exparel 266 mg	($266.00)	($354.53)	$12.55
ZYNRELEF 200 mg/6 mg	$36.09	$4.50	$4.50
Exparel 133 mg	($151.00)	($198.84)	($15.30)

Exparel Hospital Units***



* Estimated Exparel 340B pricing based on competitive intelligence
** Estimates Comparing WAC (or 340B) acquisition cost to published ASP reimbursement for Medicare patients to calculate NCR based on Q4'22 rates.
*** Symphony data: Rolling 12 months ending 9/30/2022
WAC: wholesale acquisition cost. NCR: net cost recovery. HOPD: hospital outpatient department. ASC: ambulatory surgical center.

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ZYNRELEF Refocused Priorities 2022

- Build consistent usage in formulary approved ordering accounts and increase average order size
  - Leverage new flexible resources deployed in Q4'22
  - Maximize 15 IDNs pursuing TI and accelerate other existing IDNs to advance to TI status
- Differentiate based on Pass-through status in HOPD and over **200 million covered lives** with Commercial/Medicaid separate reimbursement in ASCs
- Continue to gain formulary access to new IDNs and Hospitals to build pipeline

TI: Therapeutic Interchange

APONVIE™
(aprepitant) injectable emulsion

Postoperative Nausea and Vomiting (PONV)

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APONVIE – The Next Big Opportunity at 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**

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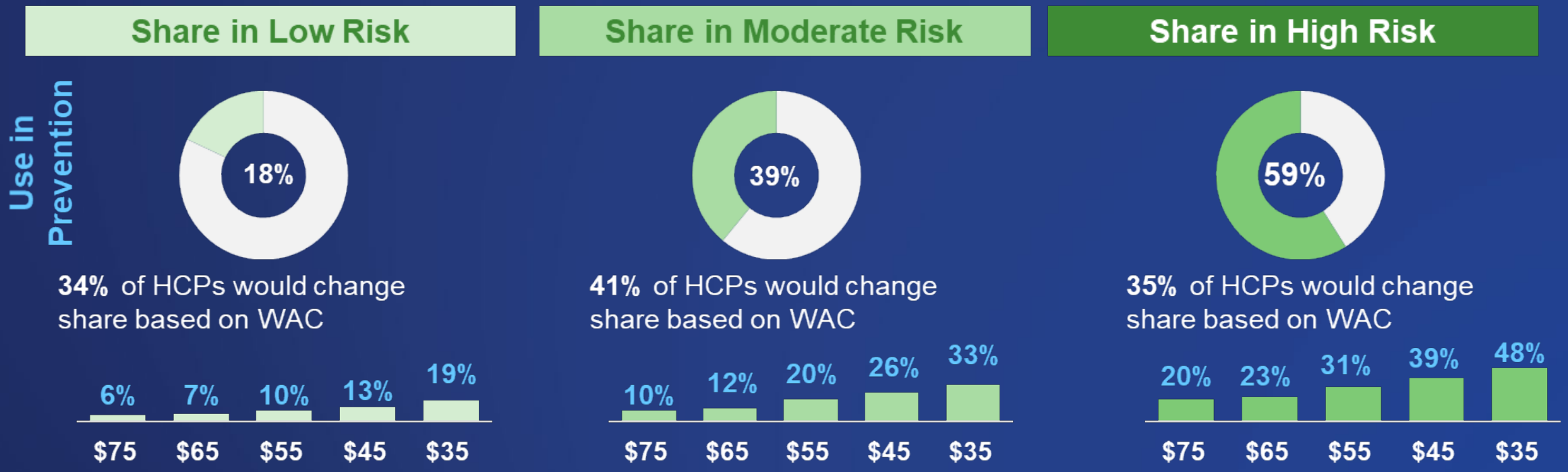
APONVIE Pricing Impact on HPC Market Share by Patient Risk Factors



Source: DRG / Clarivate PONV Pricing Study (2021)
HCP: Health Care Providers

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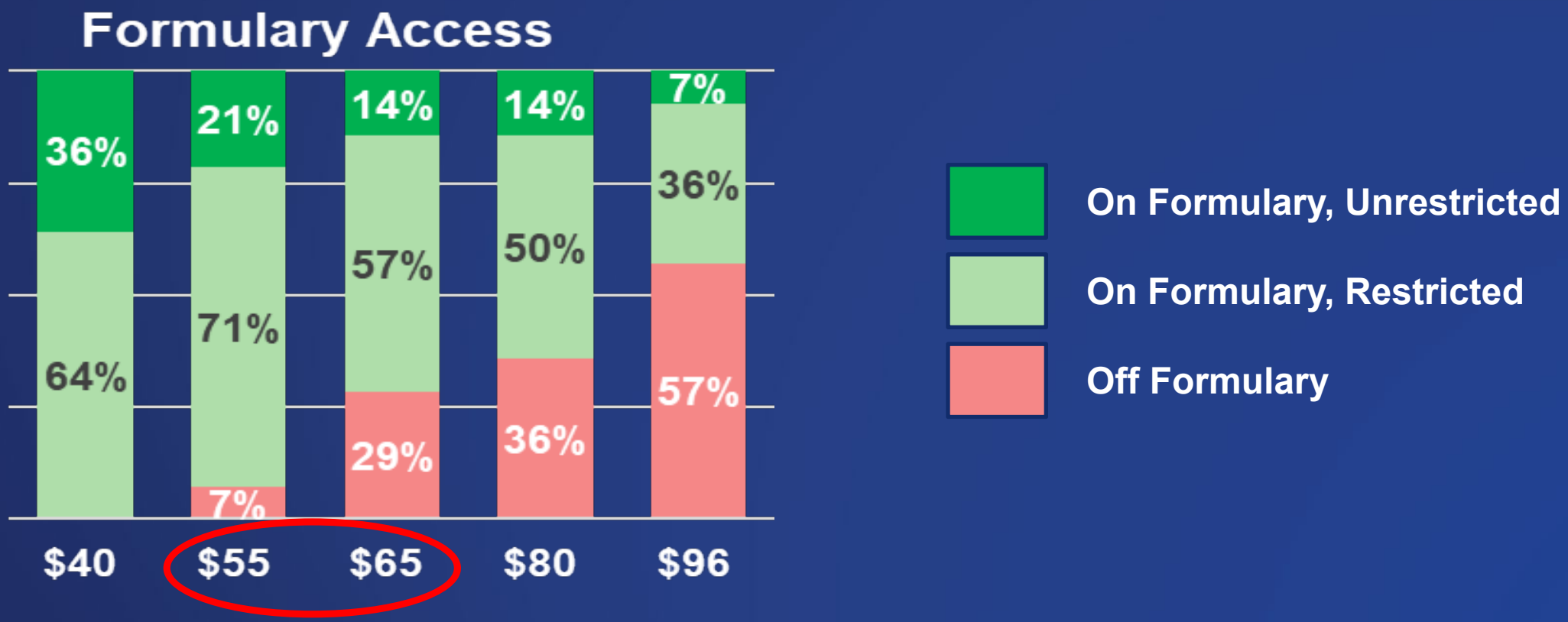
APONVIE Pricing Impact on Formulary Inclusion – Pharmacy Directors



Source: DRG / Clarivate PONV Pricing Study (2021)

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APONVIE Pricing Strategy Maximizes Profit Contribution

- Final pricing decision balances projected HCP market share in moderate to high risk patients, with impact on formulary access (level of potential restrictions)
- APONVIE Launch with WAC price of **$58.00 per vial**
  - Only sold as 10 vials per pack
- We will offer 340B pricing on APONVIE to strengthen the value proposition and accelerate access
  - Market research shows leveraging 340B price increases HCP market share and improves formulary access
- APONVIE availability: Q1 2023

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Oncology Care Franchise

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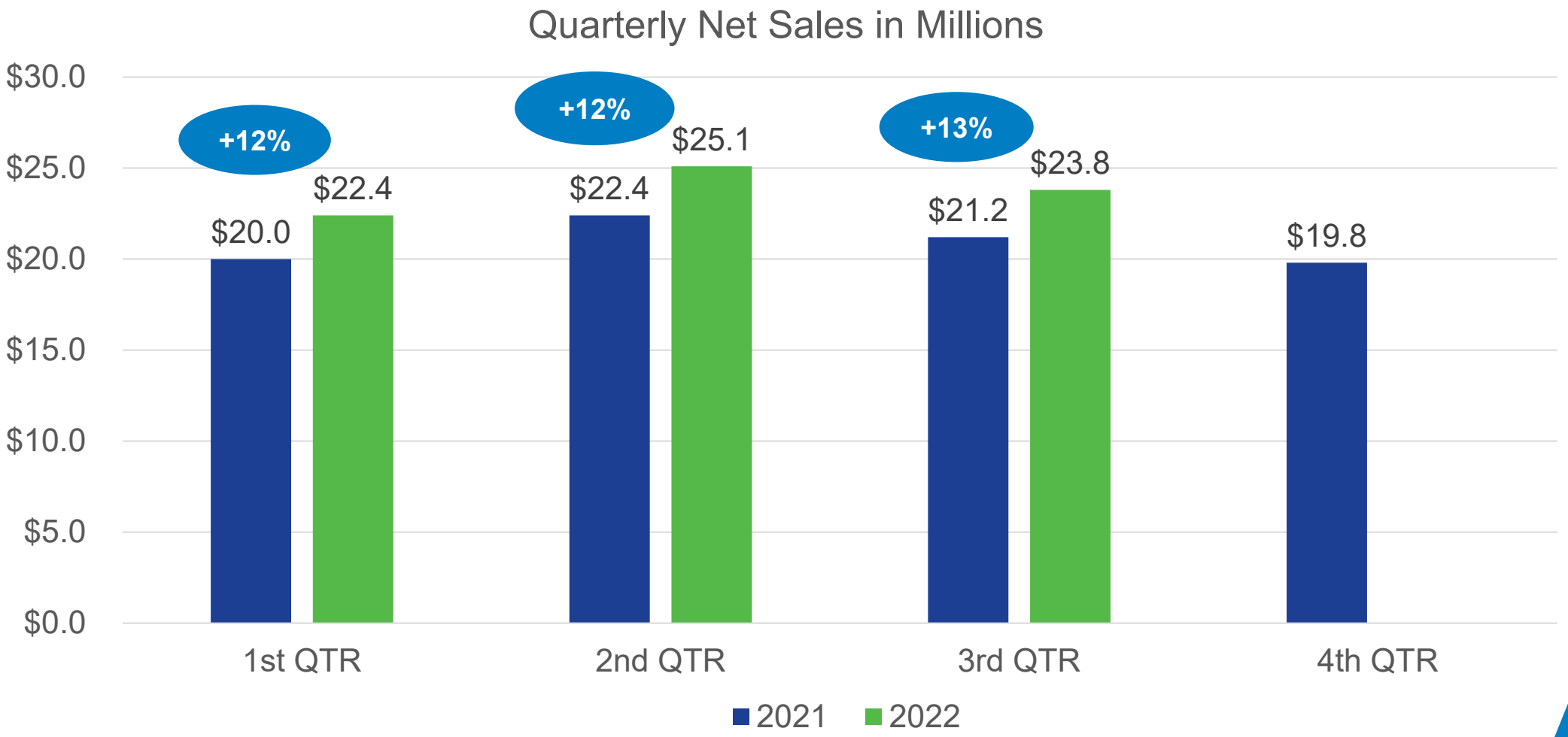
CINV Franchise Demonstrating Solid Quarterly Growth vs. Prior Year



- On-track for $93M to $95M net product sales in 2022

CINV Franchise in Excellent Position to Deliver Increasing Sales Through 2023

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

Product	J Code	Q4 2021	Q4 2022		
		ASP+6%	ASP+4.3%	$ Change	% Change
Fosaprepitant	J1453	**$ 36.45**	**$ 20.66**	**$ (15.79)**	**-43.3%**
CINVANTI	J0185	**$ 219.83**	**$ 215.15**	**$ (4.68)**	**-2.1%**
SUSTOL	J1627	**$ 693.80**	**$ 597.56**	**$ (96.24)**	**-13.9%**
IV Akynzeo	J1454	**$ 571.22**	**$ 423.12**	**$ (148.10)**	**-25.9%**

- 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%

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

Financial Summary

Heron had cash, cash equivalents and short-term investments of $121.7 million as of September 30, 2022.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended September 30, 2022	Nine Months Ended September 30, 2022
Net product sales	$ 26,557	$ 77,644
Operating expenses[1]	68,439	231,947
Other income (expense), net	(26)	(7,852)
Net loss[1]	$ (41,908)	$ (162,155)
Net loss per share[2]	$ (0.38)	$ (1.54)
Net cash used in operations	$ (37,066)	$ (109,378)
Condensed Balance Sheet Data (in thousands)		**September 30, 2022**
Cash, cash equivalents and short-term investments		$ 121,746
Accounts receivable, net		$ 42,188
Inventory[3]		$ 52,239
Total assets		$ 271,952
Total stockholders' equity		$ 22,450

Common shares outstanding as of September 30, 2022 totaled 118.8 million.

[1] Includes $11.2 million and $32.5 million of non-cash, stock-based compensation expense for the three and nine months ended September 30, 2022, respectively.
[2] Based on 111.7 million and 105.5 million weighted-average common shares outstanding for the three and nine months ended September 30, 2022, respectively.
[3] Includes $36.2 million for ZYNRELEF, $13.4 million for CINVANTI and $2.6 million for SUSTOL.

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.

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