Heron Update

2023 COWEN Conference

March 7, 2023

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 full-year 2023 net product sales guidance for the oncology 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 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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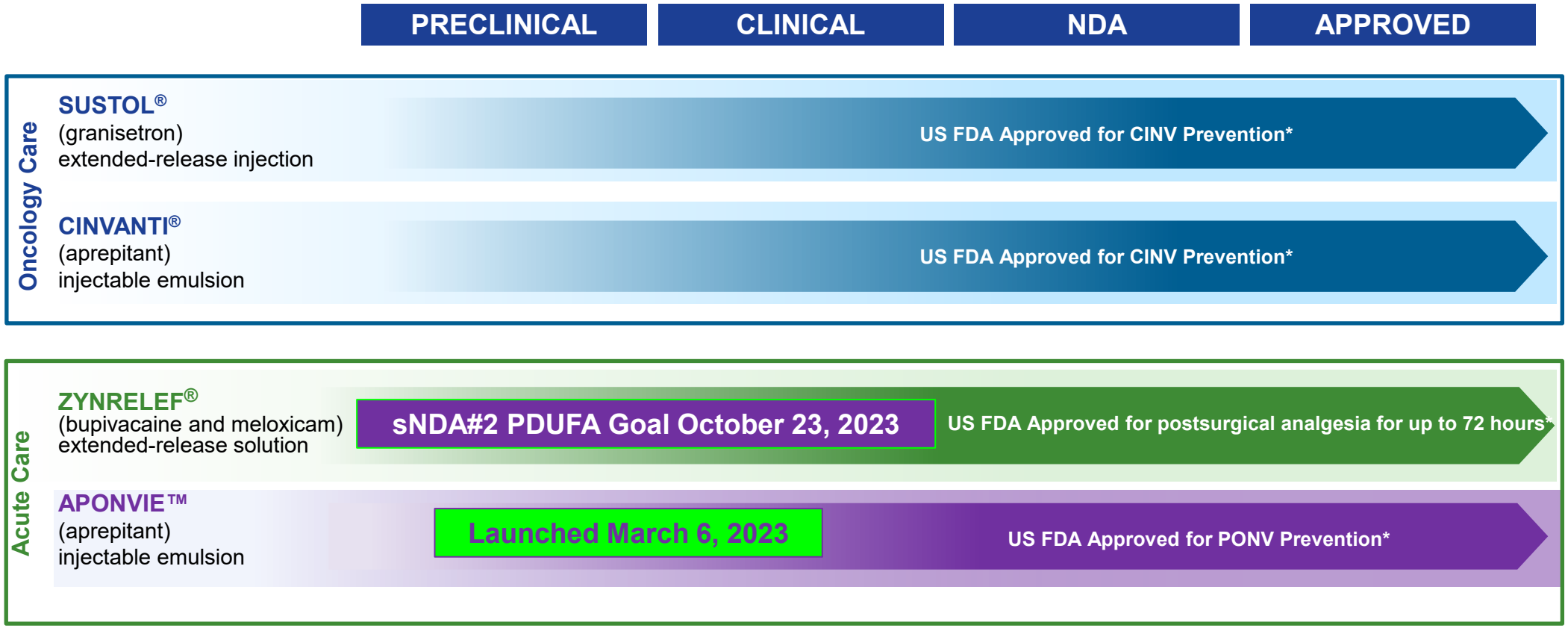
Heron Pipeline of 4 Approved Products With $106.7 million in Preliminary Annual Net Product Sales, a 24% Increase Over 2021



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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ZYNRELEF sNDA#2 for Expanded Indications
PDUFA Goal October 23, 2023

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 SNDA#2 for the Requested Broader Label for ZYNRELEF

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

No unique safety issues and consistent bupivacaine PK were observed following ZYNRELEF administration in additional procedures

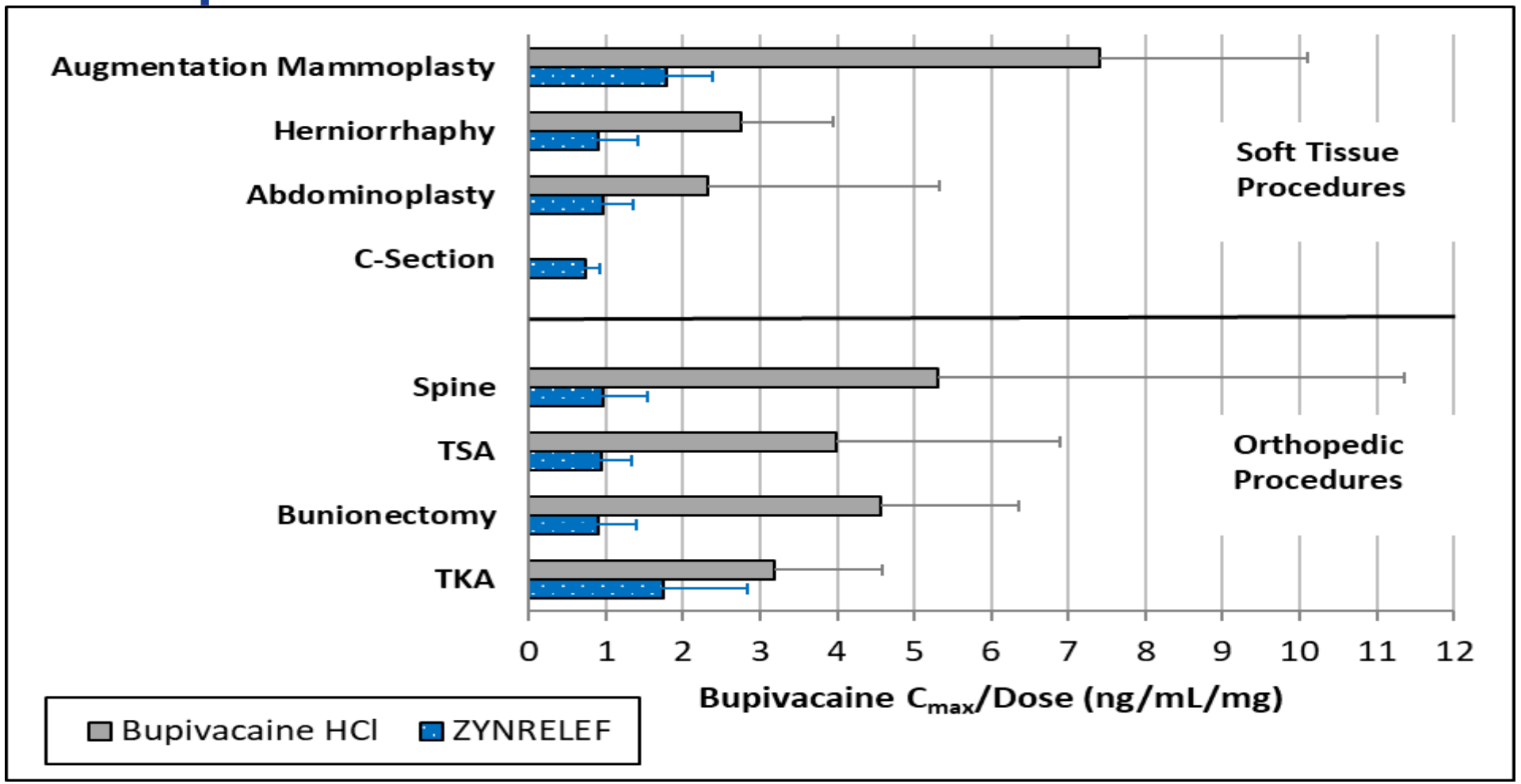
Overall Safety Summary Shows ZYNRELEF to be Well-Tolerated Across Soft Tissue and Orthopedic Procedures

Adverse Event (AE) Category	Saline Placebo (N=247) %	Bupivacaine HCl (N=450) %	ZYNRELEF (N=1,064) %
Any AE	81.4	82.0	67.6
AE possibly related to study drug	19.0	16.2	12.0
Severe AE	3.2	2.2	2.1
AE that led to study withdrawal	0.4	0	0.3
Potential ORAE	55.5	52.0	39.5
Local inflammatory AE	10.9	10.0	7.8
Potential LAST AE	32.4	36.7	18.9
Potential NSAID-related AE	33.2	26.7	24.8
Serious AE	2.0	2.0	1.8

Abbreviations: LAST, local anesthetic systemic toxicity; NSAID, nonsteroidal anti-inflammatory drug; ORAE, opioid-related adverse event

Consistent ZYNRELEF PK Across Surgical Procedures With Low Risk of LAST

Bupivacaine HCl vs. ZYNRELEF Cmax/Dose



Please see **IMPORTANT SAFETY INFORMATION** on pages 30 to 31 and full Prescribing Information, including **Boxed Warning**.

ZYNRELEF
Commercial Update

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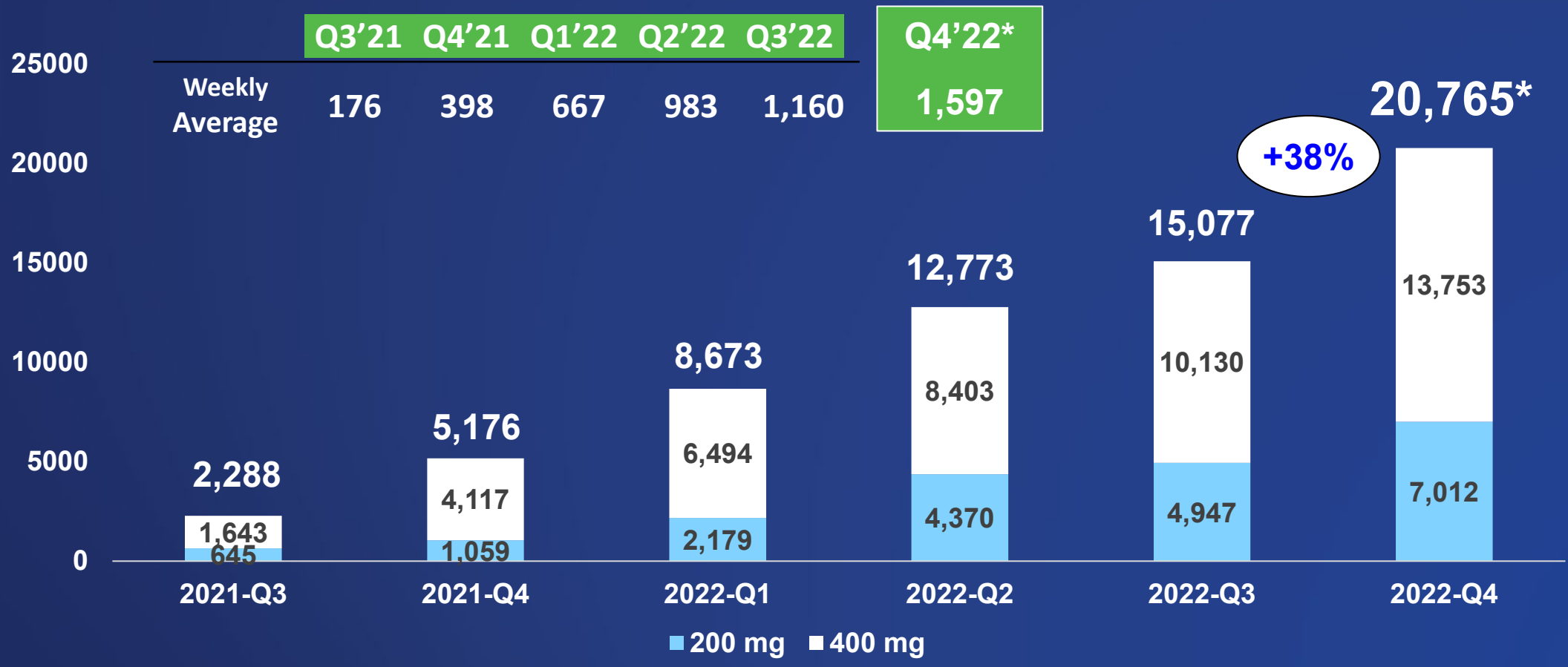
ZYNRELEF is Increasing Quarterly Demand Volume

- Weekly Sales Average up **38%** from Q3'22 to Q4'22



**Preliminary Symphony DDD data through 12/31/2022*

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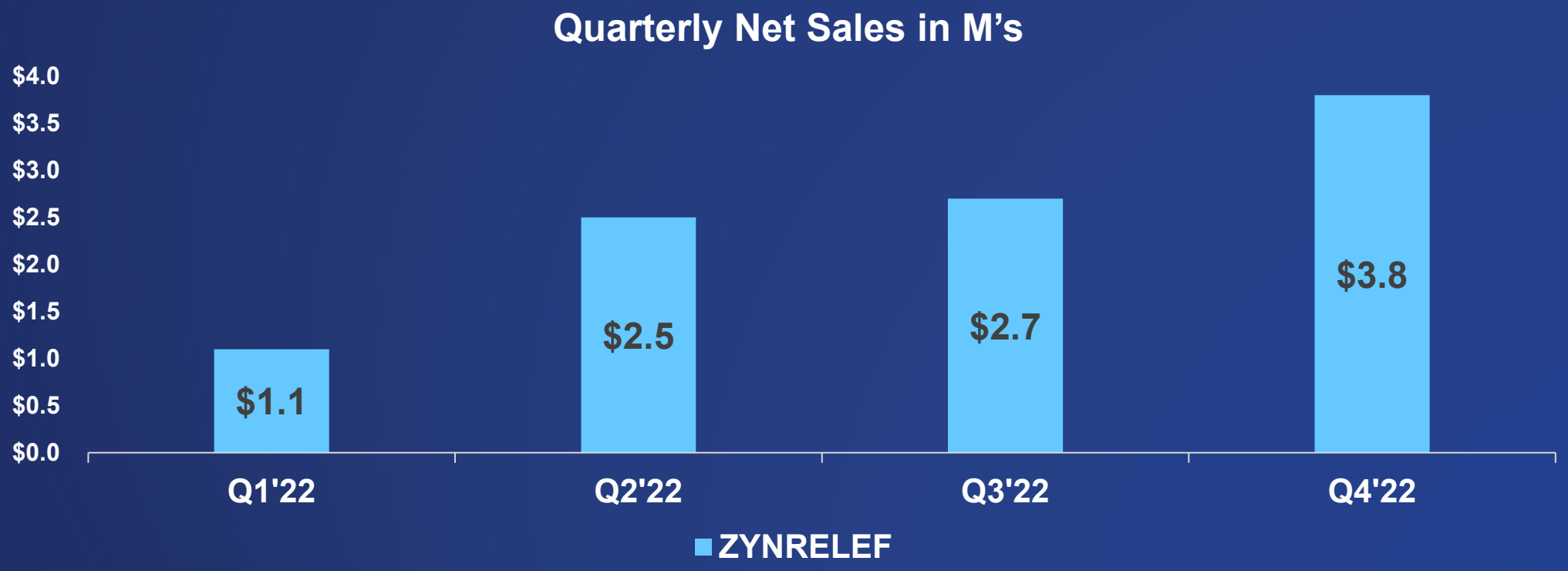
ZYNRELEF Net Sales Growth of 40% vs. Prior Quarter*



- **Consensus for Q4'22: $3.6 M**

* Based on preliminary results

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

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

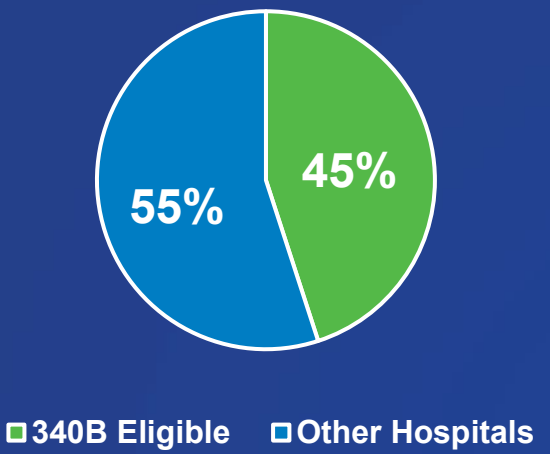
ZYNRELEF	WAC	340B
400 mg/12 mg	$267.50	$205.17
200 mg/6 mg	$135.50	$104.05

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.

H.R. 2617, SEC. 4135: ACCESS TO NON-OPIOID TREATMENTS FOR PAIN RELIEF Should Provide Almost Three Additional Years of Separate Payments

"No Pain ACT Approval"

H.R. 2617 Key Provisions:

- Provides for separate payment outside the surgical bundle for non-opioid treatments in the outpatient setting (including HOPD) from January 1, 2025 through December 31, 2027
- The non-opioid must have demonstrated the ability to replace, reduce, or avoid intraoperative or postoperative opioid use or the quantity of opioids prescribed
- Requires CMS to report to Congress the impact of using non-opioids on the use of opioids

ZYNRELEF Benefits of this legislation:

- Will continue to receive transitional pass-through payments from CMS through March 31, 2025
- From April 1, 2025 to December 31, 2027 will be eligible for separate payment under legislation

HOPD: Hospital Outpatient Department

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)

Launched March 6, 2023

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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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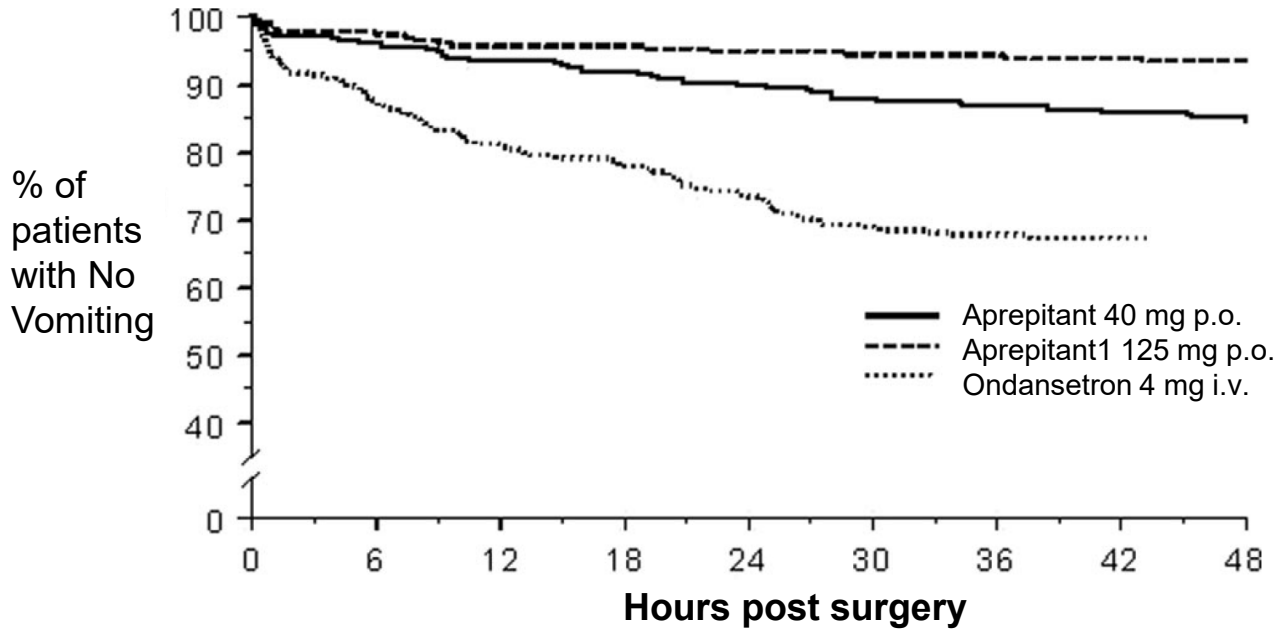
Aprepitant Reduced the Proportion of Patients Vomiting Through 48 hours by 17.7% (p<0.001*) vs. IV Ondansetron (SOC)



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

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

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2020 Cochrane Meta-Analysis Concluded That Aprepitant is Most Effective Drug Approved for PONV*

Meta-analysis included 282 studies with 50,812 participants and 65 treatments (28 single agents, 36 drug combinations and placebo)

Drug	Vomiting (or dry retching) within 24 hours postoperatively RR	Number of Patients Vomiting out of 1000 Surgeries
Placebo	1	300
Droperidol	0.61	183
Ondansetron	0.55	165
Granisetron	0.45	135
Oral Aprepitant	0.26	78
Aprepitant + 5HT-3	0.01	3

Meta-analysis conclusions:

- Aprepitant was most effective single agent for prevention of vomiting in first 24 hrs after surgery*
- Aprepitant was most effective single agent for prevention of early (0-6 hrs or in PACU) vomiting*
- Aprepitant and it's prodrug provided similar or better reductions in vomiting compared to drug combinations evaluated
- Most effective 2-drug combination was aprepitant plus a 5HT-3 antagonist (palonosetron)
- Aprepitant had a favorable safety profile versus placebo

*Based on high-certainty evidence

*Weibel S, Rücker G, Eberhart LHJ, Pace NL, Hartl HM, Jordan OL, et al. *Cochrane Database of Systematic Reviews*. 2020

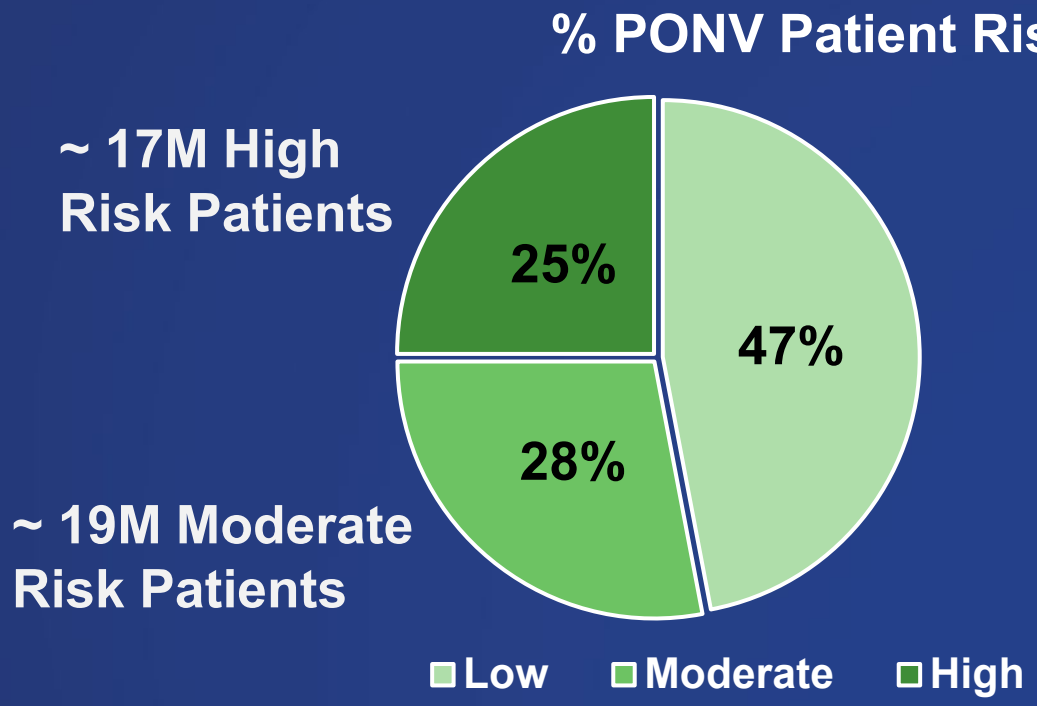
For 1000 Patients with Moderate to High Risk for PONV Addition of APONVIE Would be Expected to Save ~$80,000

PONV Prophylaxis	Cost of Vomiting in PACU[1,2]	Expected # of Patients Vomiting out of 1000[3]	Cost of PONV	Cost of APONVIE for all 1000 Patients	Total Cost for Prophylaxis and PONV
Ondansetron (OND)	$951	276	$262,476	0	$262,476
APONVIE + OND	$951	133	$126,483	$58,000	$184,483

1. Dexter F, Tinker JH. Anesthesiology. 1995;82(1):94-101.
2. 2. Hill RP, Lubarsky DA, Phillips-Bute B, et al. Anesthesiology. 2000;92(4):958-967. Cost data has been adjusted to 2021 US dollars based on medical cost inflation, using the hospital services component of the CPI from the Bureau of Labor Statistics.
3. APONVIE [package insert]. San Diego, CA: Heron Therapeutics Inc; 2022.
4. Diemunsch P, Gan TJ, Philip BK, et al. Single dose aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting: a randomized, double blind Phase III trial in patients undergoing open abdominal surgery. Brit J Anaesth 2007;99(2):202 211. doi:10.1093/bja /aem133.
5. Gan TJ, Apfel CC, Kovac A, et al. A randomized, double blind comparison of the NK1 antagonist, aprepitant , versus ondansetron for the prevention of postoperative nausea and vomiting. Anesth Analg . 2007;104(5):1082 1089

APONVIE Target Market Opportunity ~ 36 Million Procedures in Patients at Moderate to High Risk for PONV[1] with 40-80% Risk of PONV[2]

PONV Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV and/or Motion Sickness	1
Postoperative Opioids	1
Sum of Points	**0 - 4**



Apfel Risk Score

Total Patient Risk Factors	Patient PONV Risk Level
0 – 1	Low Risk
2	Moderate Risk
3+	High Risk

Source: DRG / Clarivate PONV Demand Study (Dec. 2021)

1. 2023 Procedure projections 2. Gan TJ, Belani KG, Bergese S, et al. Anesth Analg. 2020;131(2):411-448

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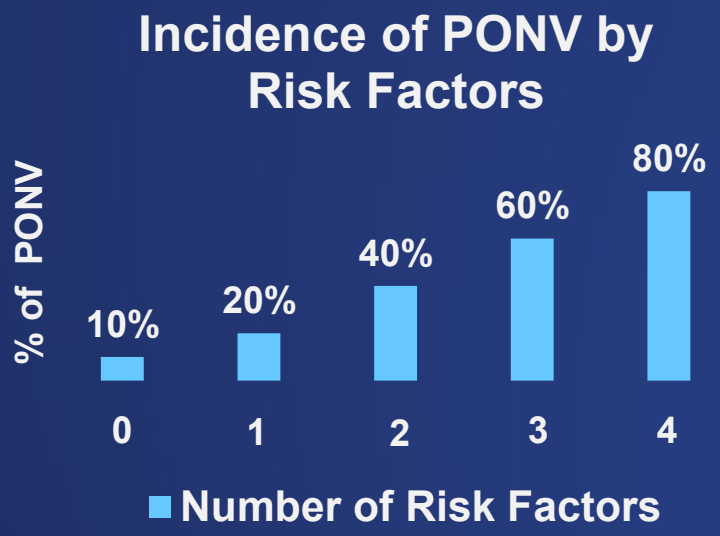
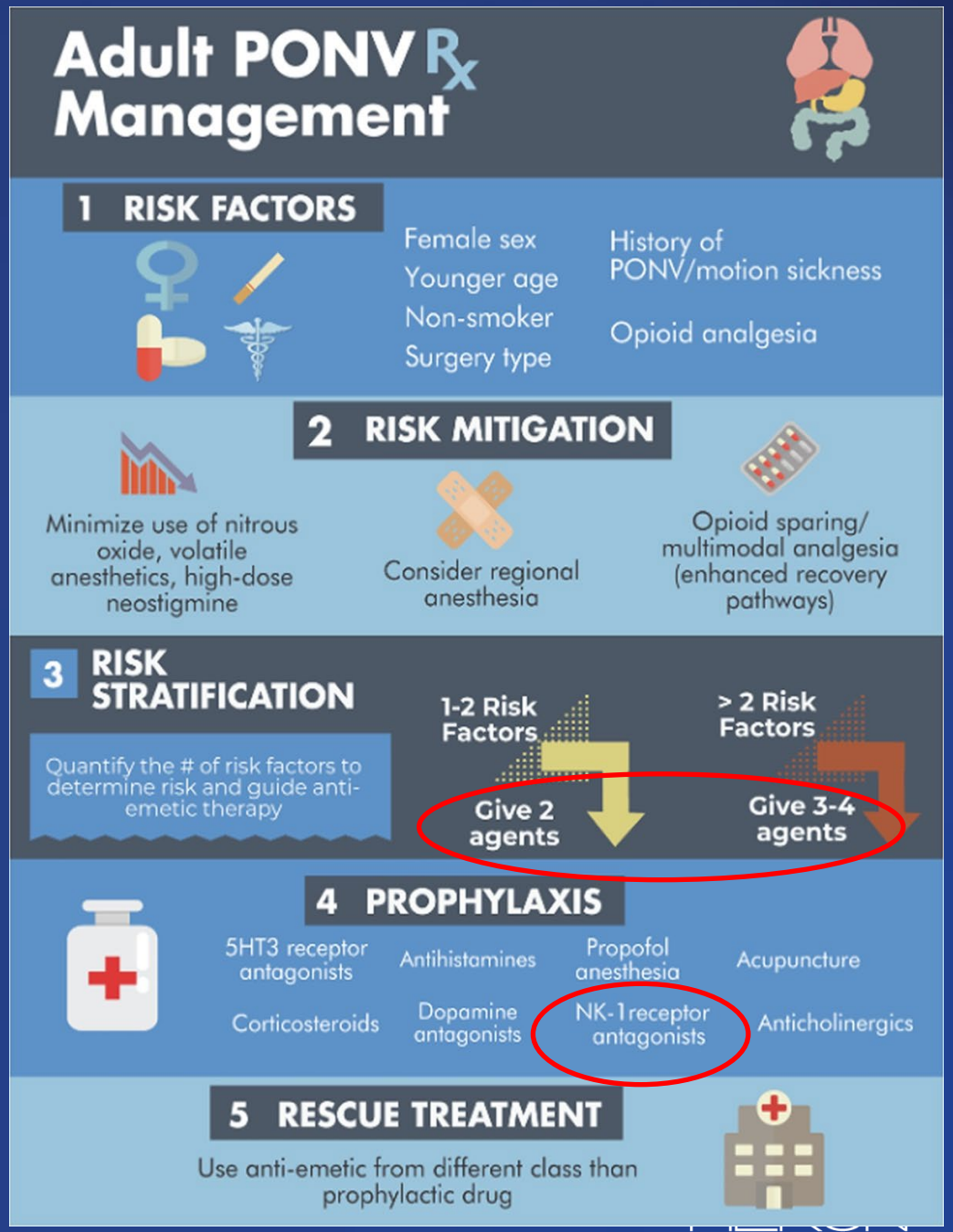
Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting[1]

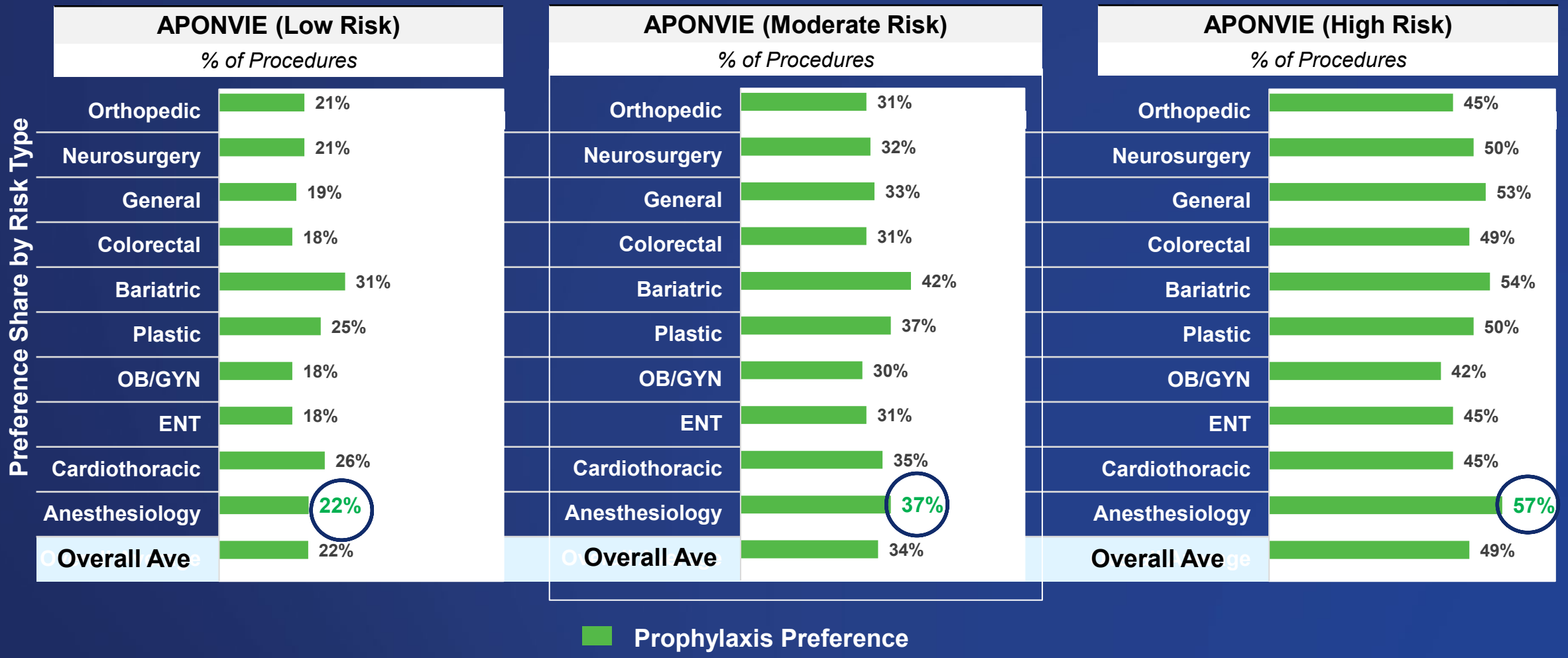


"In this iteration of the PONV guideline, one of the major changes is that we now recommend the use of multimodal prophylaxis in patients with one or more risk factors".



[1] Gan TJ, Belani KG, Bergese S, et al. Anesth Analg. 2020;131(2):411-448.

APONVIE Attributes Resulted in High Physician Preference Share Which Grows as Patient PONV Risk Increases



Source: DRG/Clarivate Claims Analysis, PONV Demand Study (Dec 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 in Distribution Channel: March 6, 2023

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Oncology Care Franchise

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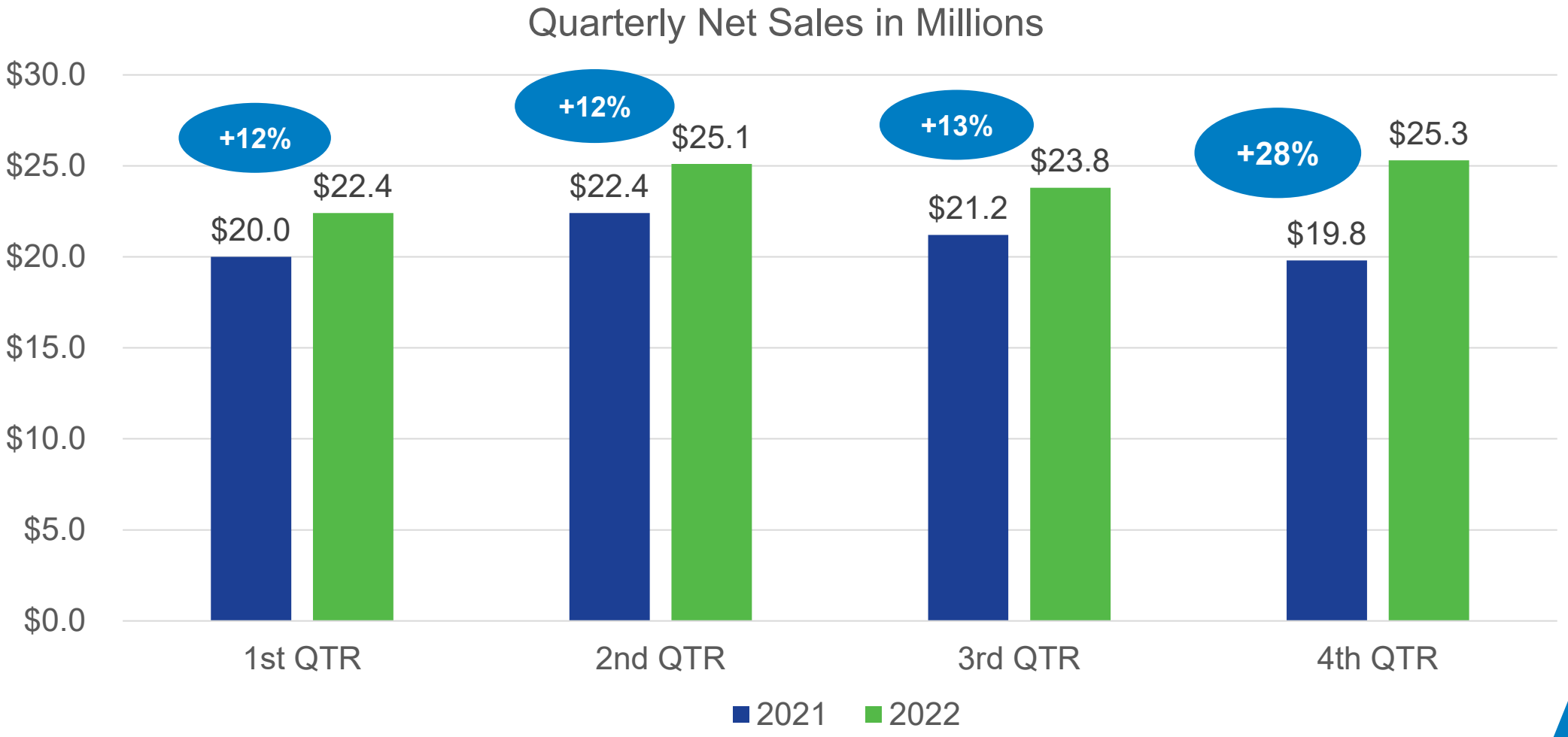
CINV Franchise Demonstrating 16% Growth vs. 2021 Preliminary 2022 net product sales of $96.6 million



CINV Franchise in Excellent Position to Deliver Increasing Sales Through 2023

Continued Reimbursement Advantages

Product	J Code	Q1 2023 ASP+4.3%	Reimbursement Benefit (Clinics)
Fosaprepitant	J1453	**$ 25.83**	
CINVANTI	J0185	**$ 221.17**	**$ 195.34**
IV Akynzeo	J1454	**$ 459.57**	
SUSTOL	J1627	**$ 593.33**	**$ 133.76**

Opportunity to offer greater value

- 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 $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.

Please see full Prescribing Information.

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