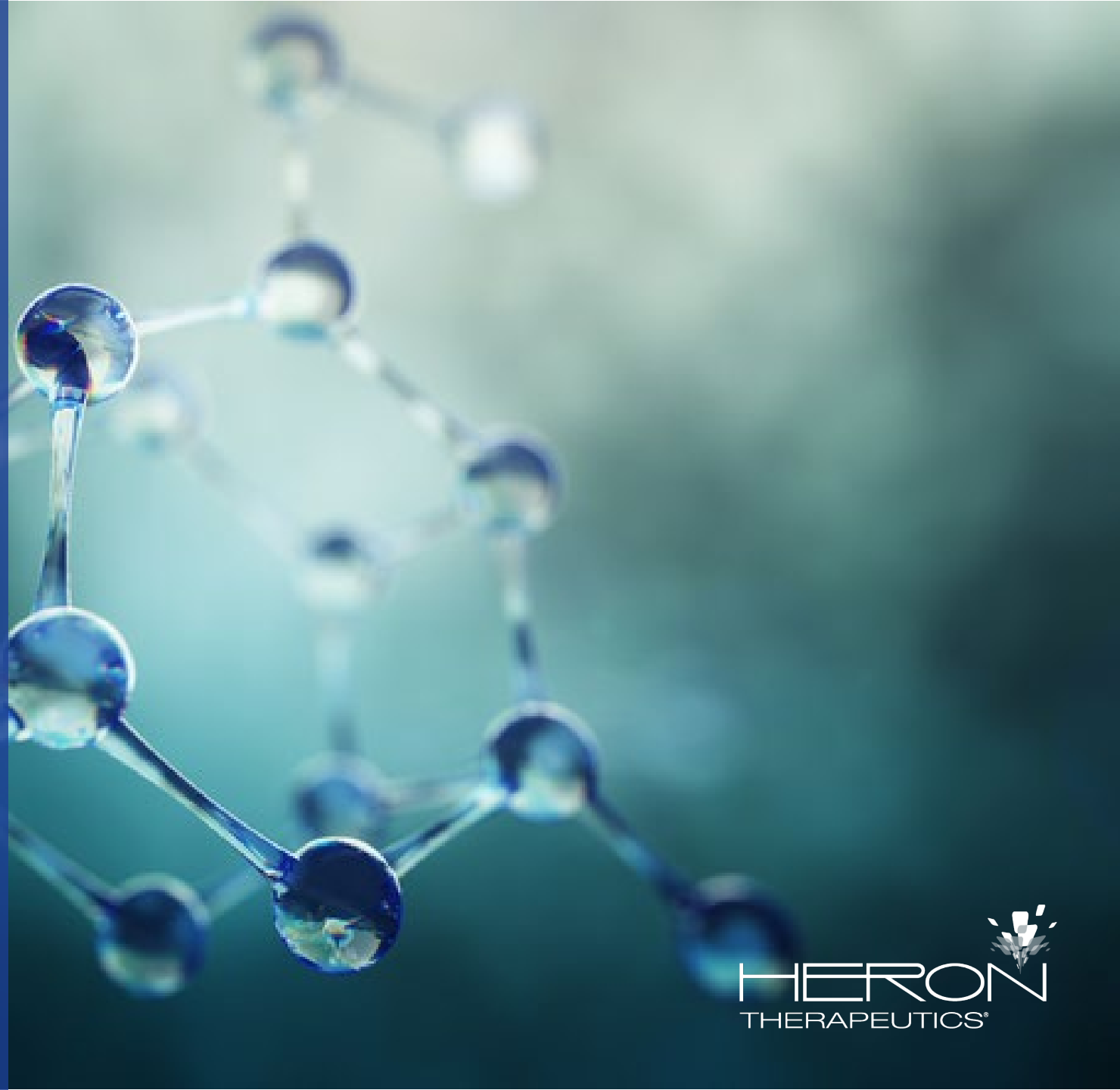
Heron Therapeutics, Inc. Investor Day

May 15th, 2024



Forward-looking Statements and non-GAAP Disclosures

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 news release and are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, uncertainties related to market conditions; the potential market opportunities for ZYNRELEF®, APONVIE®, CINVANTI® and SUSTOL®; the net product sales guidance for the oncology care franchise and the acute care franchise; the EBITDA guidance provided by the Company; the results of the commercial launch of APONVIE; the timing of the FDA's review process and whether the FDA approves the sNDA for ZYNRELEF to further expand the U.S. label; the potential additional market opportunity for the expanded U.S. label for ZYNRELEF, if approved; the timing of the Company's development of the VAN program; the timing of the Company's submission of the PAS to the FDA for the VAN; the timing of the FDA's review process and whether the FDA approves the PAS for the VAN; the outcome of the Company's pending ANDA litigation related to CINVANTI; whether the Company is required to write-off any additional inventory in the future; 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 and the risk that future equity financings may be needed; any inability or delay in achieving profitability; and other risks and uncertainties identified in the Company's filings with the U.S. Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and Heron takes no obligation to update or revise these statements except as may be required by law.

In addition to the company's financial results determined in accordance with U.S. GAAP, the company provides non-GAAP measures that it determines to be useful in evaluating its operating performance and liquidity. Management believes that presentation of operating results using non-GAAP financial measures provides useful supplemental information to investors and facilitates the analysis of the Company's core operating results and comparison of operating results across reporting periods. Management uses non-GAAP financial measures to establish budgets, manage the Company's business, and set incentive and compensation arrangements. The company presents adjusted EBITDA and adjusted operating expenses. The Company has not provided a reconciliation of its full-year 2024 guidance for adjusted EBITDA or adjusted operating expenses to the most directly comparable forward-looking GAAP measures, in reliance on the unreasonable efforts exception provided under Item 10(e)(1)(i)(B) of Regulation S-K, because the Company is unable to predict, without unreasonable efforts, the timing and amount of items that would be included in such a reconciliation, including, but not limited to, stock-based compensation expense, acquisition related expense and litigation settlements. These items are uncertain and depend on various factors that are outside of the Company's control or cannot be reasonably predicted. While the Company is unable to address the probable significance of these items, they could have a material impact on GAAP net income and operating expenses for the guidance period.

Heron Therapeutics, A Year Ago

- Heron entered into a cooperation agreement with Rubric and Velan on February 22, 2023 and announced changes to the management team and Board shortly thereafter
- Heron had seen success with the oncology franchise which established the company's commercial footprint, but faced headwinds launching ZYNRELEF® despite clinical differentiation, meaningful patient impact and a compelling value proposition
- Discipline around financial management and spending had been lacking…ACCOUNTABILITY!
- Ultimately, the **people, passion and potential** for this company is why I'm here

Positioned for Success Through Key Accomplishments

New management's strategy promises transformative impact on commercial optimization

2023-2024

New Product Launch

U.S. Commercial launch of APONVIE®

New Executive Team Additions

Ira Duarte as Chief Financial Officer
Bill Forbes as EVP, Chief Development Officer
Ryan Craig, VP of Marketing
David Barozzino, VP of Sales
Kevin Warner, PharmD, VP of Medical Affairs
Melissa Jarel, Executive Director of Legal

Strengthened Financial Position

Gross margin improvement from the 50% range historically to over 70%
Completed capital raise - $30M in Equity and $50M in debt, pulled down $25M ($55M in total)

Expanded Indication for ZYNRELEF

Expanded label almost doubled ZYNRELEF opportunity to ~13M procedures

New CEO and New Chair

Appointment of Craig Collard as CEO. In addition, the Board appointed Adam Morgan as Chairman

Cost-cutting measures in place

Operating expenses (excluding stock compensation and depreciation and amortization) reduced from $182M (2022), $135M (2023), $108-116M (2024)

Signed Deal with CrossLink Life Sciences, LLC

Expanding ZYNRELEF promotion with distributor partnership building to ~650 representatives by the end of 2024

Heron Management Team

Experienced team with a track record of developing and commercializing innovative products

Craig Collard
Chief Executive Officer

Ira Duarte
Chief Financial Officer

Bill Forbes, PharmD
EVP, Chief Development Officer

Kevin Warner, PharmD
Sr. VP, Medical Affairs Strategy and Engagement

Robert Sullivan
Sr. VP, Oncology

Ryan Craig
VP, Marketing

David Barozzino
VP of Sales, Acute Care

Melissa Jarel
Executive Director, Legal

Select Financial Results

In $K	Q1 2024	Q1 2023
Net product sales	34,670	29,615
Cost of product sales	8,444	16,854
Gross profit	**26,226**	**12,761**
Operating expenses:		
Research and development	4,608	8,836
General and administrative	14,974	15,834
Sales and marketing	11,442	21,154
Total operating expense	**31,024**	**45,824**
Loss from Operations	**(4,798)**	**(33,063)**
Cash	**$ 71,524**	**$ 60,022**

Reaffirm 2024 Guidance

$M	2024
Revenues	$138M- $158M
Gross Profit	$94M - $111M
Gross Margin	70%+
Cash OpEx	$108M - $116M
EBITDA (excluding stock compensation)	$(22M) - $3M

Heron, What We Plan to Accomplish Today!

- Clinically differentiate our product portfolio
- Offer a line of site to market potential
- Review the CrossLink advantage and the market impact now, and in the future
- Update for our key development programs for ZYNRELEF, the Vial Access Needle (VAN) and Pre-filled Syringe (PFS)
- Provide insight into our continual consistency of the oncology franchise

More importantly, get to know the special people on this team and how we work as one to drive shareholder value

Delivering on Commitments

Ryan Craig, VP of Marketing, Heron Therapeutics

Our Portfolio Truly Impacts Patient Outcomes

At Heron, we understand what is at stake for patients, their caregivers, and families, which is why we are laser-focused on providing solutions that can address unmet medical needs so they can spend **more time doing the things that matter with the people who matter**.

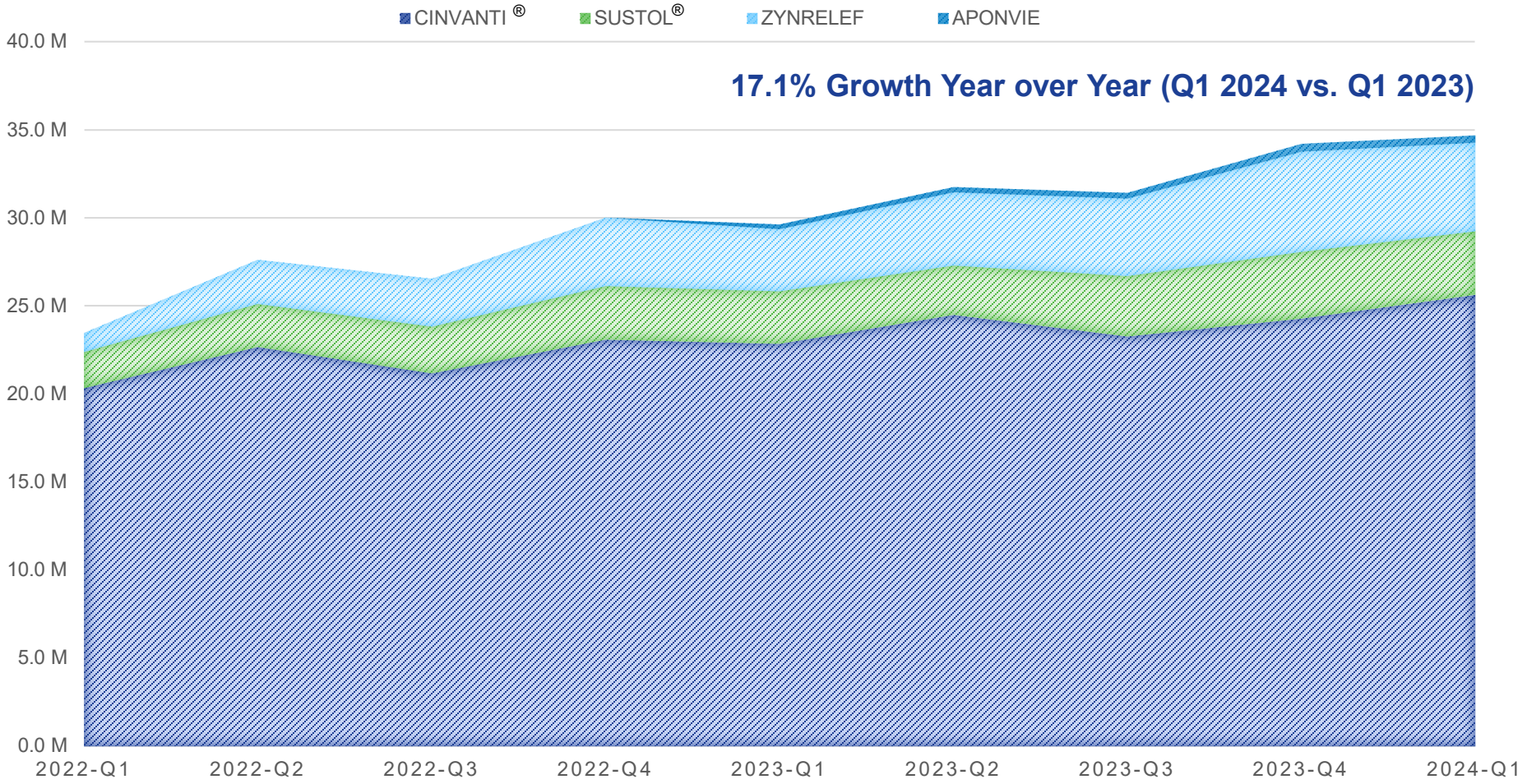
Oncology Care

We’re focused on elevating the standard of care–developing solutions that help patients and enable oncologists to manage and reduce the negative side effects that commonly go along with cancer treatments

Acute Care

In a radically changing healthcare environment, we are currently applying our innovative science and technologies to provide patients and healthcare providers with better ways to reduce postoperative pain and prevent postoperative nausea and vomiting

Revenue Contribution by Brand



Clinical Conversations – A Closer Look at the Improved Patient and Physician Experience with ZYNRELEF and APONVIE

Kevin Warner PharmD, Sr. VP, Medical Affairs Strategy & Engagement, Heron Therapeutics

Randy Robbins MD, Anesthesiologist, Valiant Anesthesia Associates, Dallas, Texas

Alan Rechter MD, Orthopedic Surgeon, Orthopedic Associates LLP, Houston, Texas

HERON THERAPEUTICS®

Heron's Innovative Solutions Provide a Strong Foundation for Postoperative Care and Comfort

Addresses 2 of surgical patients' most concerning side effects[1-3]

ZYNRELEF delivers superior postoperative pain relief, with fewer patients experiencing severe pain and significantly more patients requiring no opioids versus standard-of-care bupivacaine HCl solution[1,4-6]

APONVIE offers superior postoperative nausea and vomiting protection versus standard-of-care IV ondansetron[2,7,8]

Eases HCP burden in the perioperative setting[1,2]

ZYNRELEF is administered via a single, needle-free application that does not require mixing to achieve efficacy[1]

APONVIE is delivered via a single IV push and reaches therapeutic plasma concentrations associated with ≥97% receptor occupancy within 5 minutes[2,9,10]

Committed to novel solutions for long-acting relief from postoperative pain and PONV[1,2]

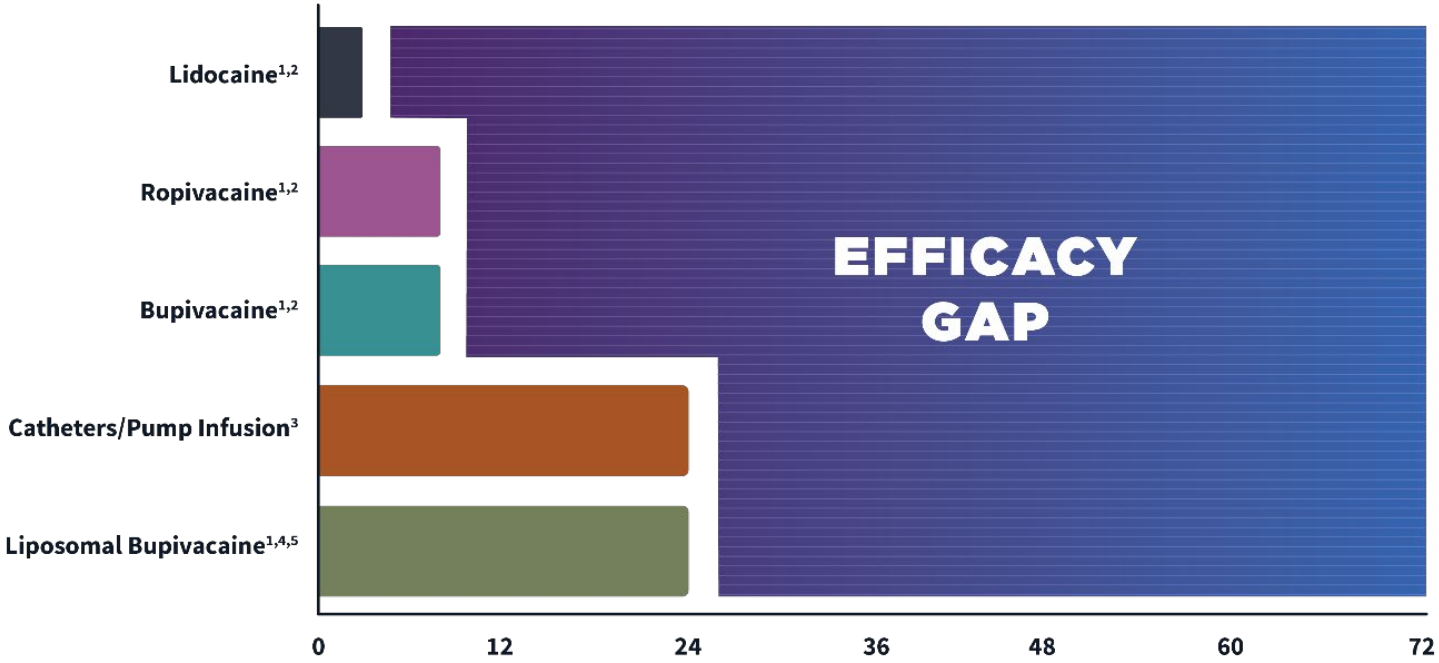
ZYNRELEF, a novel, synergistic combination of bupivacaine and low-dose meloxicam in a proprietary polymer, is the only local anesthetic considered by FDA to be extended-release, based on superiority to bupivacaine through 72 hours[1,11]

APONVIE is the first and only IV NK_1 antagonist for the prevention of PONV, with a 48-hour duration of action[2]

References: **1.** ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics, Inc; 2021. **2.** APONVIE [package insert]. San Diego, CA: Heron Therapeutics Inc; 2022. **3.** Macario A, Weinger M, Carney S, et al. *Anesth Analg.* 1999;89(3):652-658. **4.** Viscusi E, Gimbel JS, Pollack RA, et al. *Reg Anesth Pain Med*. 2019;44(7):700-706. **5.** Viscusi E, Minkowitz H, Winkle P, et al. *Hernia*. 2019;23(6):1071-1080. **6.** Lachiewicz PF, Lee G-C, Pollak R, et al. *J Arthroplasty*. 2020;35(10):2843-2851. **7.** Diemunsch P, Gan TJ, Philip BK, et al. *Brit J Anaesth.* 2007;99(2):202-211. **8.** Gan TJ, Apfel CC, Kovac A, et al. *Anesth Analg*. 2007;104(5):1082-1089. **9.** Data on file. Summary of clinical pharmacology studies. San Diego, CA: Heron Therapeutics Inc; 2021. **10.** Van Laere K, De Hoon J, Bormans G, et al. *Clin Pharmacol Ther.* 2012; 92(2):243-250. **11.** Ottoboni T, Quart B, Pawasauskas J, et al. *Reg Anesth Pain Med*. 2020;45(2):117-123.

HERON THERAPEUTICS

The Efficacy Gap in Postoperative Pain Management[1-5]



Duration of Action by Local Anesthetic With Infiltration[1-4]

- Pain is most severe in the first 72 hours following surgery[1]
- Inflammation peaks around 24 hours postoperatively and remains high through the first 72 hours[2]
- Most local anesthetics inconsistently provide pain relief beyond 12 to 24 hours[3-7]

References: 1. Data on file. DRG physician survey. San Diego, CA: Heron Therapeutics Inc; 2017. **2.** Berde CB, Strichartz GR. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. Vol 1. 8th ed. Philadelphia, PA: Saunders; 2015:1028-1054.e4. **3.** Ali A, Sundberg M, Hansson U, et al. *Acta Orthop*. 2015;86(3):373-377. **4.** Kim J, Burke SM, Kryzanski JT, et al. *World Neurosurg*. 2016;91:460-467. **5.** Exparel [package insert]. San Diego, CA: Pacira Pharmaceuticals Inc; 2021. **6.** Svensson I, Sjöström B, Haljamäe H. *J Pain Symptom Manage*. 2000;20(3):193-201. **7.** Enoch S, Leaper DJ. *Surgery (Oxford)*. 2008;26(2):31-37.

First and Only Extended-Release Dual-Acting Local Anesthetic for Pain Relief Up to 72 Hours[1-4]

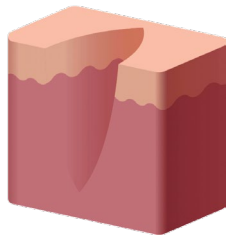
1. **Novel, synergistic combination of bupivacaine and low-dose meloxicam in proprietary polymer[1,4]**
2. **Reduces or eliminates the need for opioids in many patients following surgery[1]**
3. **Single-dose, needle-free application[1]**
4. **Does not require mixing with bupivacaine to achieve efficacy[1]**
5. **Pricing, distribution, and reimbursement designed to maximize access and customer value**

Note: Synergistic increases in analgesia compared with meloxicam or bupivacaine alone shown in preclinical and phase 2 studies.[1,4] Clinical findings were demonstrated in phase 3 trials for bunionectomy with osteotomy and open inguinal herniorrhaphy comparing ZYNRELEF to both placebo and bupivacaine HCl solution.[1-3]

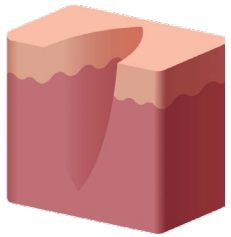
References: 1. ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** Viscusi E, Gimbel JS, Pollack RA, et al. *Reg Anesth Pain Med*. 2019;44(7):700-706. **3.** Viscusi E, Minkowitz H, Winkle P, et al. *Hernia*. 2019;23(6):1071-1080. **4.** Ottoboni T, Quart B, Pawasauskas J, et al. *Reg Anesth Pain Med*. 2020; 45(2):117-123.

HERON THERAPEUTICS

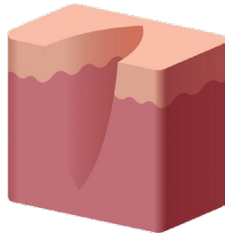
ZYNRELEF Is Applied Without a Needle[1]



ZYNRELEF[1]



Bupivacaine HCl Solution[2]



Liposomal Bupivacaine[3]

Applied by frequent consistent injection technique with 25G needle

ZYNRELEF: Administered via instillation only[2]

- Viscous solution[1]
- Single-dose application[1]
- Directly coats affected tissue following irrigation and suction[1]

Benefits of Needle-Free Administration:

- Reduced risk of intravenous complications
- Expedited medication administration
- Reduced risk of infection
- Eliminates needlestick injuries for clinicians

Surgeons and Physician Assistants require **no specialized training** certification to administer ZYNRELEF[1]

PA: physician assistant.

References: 1. ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2024. **3.** Mont MA, Beaver WB, Dysart SH, et al. *J Arthroplasty*. 2018;33(1):90-96.

HERON THERAPEUTICS

ZYNRELEF Administration: Total Knee Arthroplasty

Clinical Portfolio Development: A Foundation in Efficacy

	Bunionectomy *With Osteotomy* (foot and ankle)	*Open Inguinal* **Herniorrhaphy** *With Mesh* (small-to-medium open abdominal)	**Total Knee Arthroplasty** (lower extremity total joint arthroplasty)
Phase 2a Studies Demonstrating Synergy	**Phase 2a** (Synergy vs ER bupivacaine and ER meloxicam alone) *Study 208*[1,2]	**Phase 2a** (Synergy vs ER bupivacaine and ER meloxicam alone) *Study 202*[1,3]	
RCT Studies Included in PI • Did not include non-opioid MMA regimen • Included 72-hour, in-hospital postoperative monitoring	EPOCH 1 Evaluation of Pain Relief and Opioid Control **Phase 3** (vs placebo and bupivacaine) *Study 301*[1,4]	EPOCH 2 Evaluation of Pain Relief and Opioid Control **Phase 3** (vs placebo and bupivacaine) *Study 302*[1,5]	EPOCH TKA Evaluation of Pain Relief and Opioid Control **Phase 2b** (vs placebo and bupivacaine) *Study 209*[1,6]
Follow-On Studies • Open-label, single-arm, uncontrolled • Included non-opioid MMA regimen • Included 72-hour, in-hospital postoperative monitoring	**EPOCH 1 Single-Arm Follow-On** *Study 218*[7]	**EPOCH 2 Single-Arm Follow-On** *Study 215*[8]	**EPOCH TKA Single-Arm Follow-On** *Study 306*[9]
Real-World Setting • Open-label • Included non-opioid MMA regimen • Discharged per site practice (2.41 hours on average after surgery)		HOPE **HOPE Hernia 1** *Study 304*[10,11]	

ZYNRELEF achieved statistically significant reductions in pain scores, percentage of patients experiencing severe pain, and opioid use vs placebo and bupivacaine HCL through 72h. [1,4,5,6]

HERON THERAPEUTICS

ZYNRELEF May Serve as a Foundation for Postoperative Pain Management

Synergistic Mechanism of Action

- First and only extended-release, dual-acting, local anesthetic[1-4]
- Overcomes inflammation at surgical site[1]
- Biochronomer® polymer for controlled diffusion[1,5]
- Only FDA approved extended-release local anesthetic[1]

Superior 72-Hour Pain Relief

- Significant pain reduction[2,3]
- Less severe pain[2,3]
- No pain callbacks with OTC regimen among HOPE hernia patients discharged without an opioid prescription[6]

Opioid Reduction & Elimination

- More opioid-free patients through 72 hours, and 28-day period[2,3]
- Reduced overall opioid consumption[2,3]
- Fewer opioid-related adverse events (ORAEs)[2,3]
- Opioid elimination and reduction in opioid discharge prescriptions in the real-world setting of The HOPE Project[6]

Needle-Free & No Mixing

- Unique needle-free application[1]
- No mixing with bupivacaine required to achieve efficacy[1]
- No specialized training for NPs/PAs[7]

Customer Value

- 2 SKUs, priced to achieve broad access; GPO, 340B, and sub-WAC pricing available
- Favorable reimbursement
- Available through wholesalers and specialty distributors; prime vendor discounts apply
- Potential to increase procedure throughput[7,8]

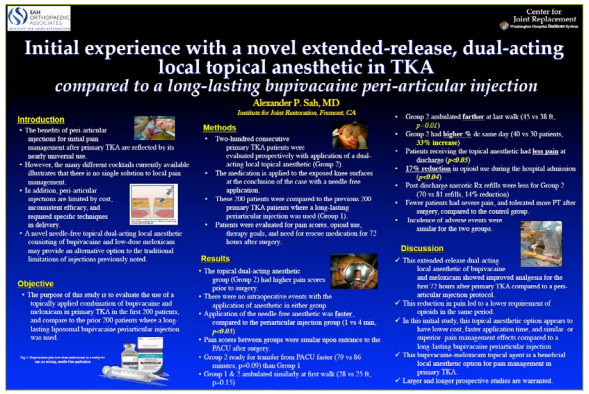
NP: nurse practitioner; **PA:** physician assistant.

References: 1. ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** Viscusi E, Minkowitz H, Winkle P, et al. *Hernia*. 2019;23(6):1071-1080. **3.** Viscusi E, Gimbel JS, Pollack RA, et al. *Reg Anesth Pain Med*. 2019;44(7):700-706. **4.** Lachiewicz PF, Lee G-C, Pollak R, et al. *J Arthroplasty*. 2020;35(10):2843-2851. **5.** Ottoboni T, Quart B, Pawasauskas J, et al. *Reg Anesth Pain Med*. 2019; 45:117-123. **6.** Minkowitz H, Soto R, Fanikos J, et al. *Pain Ther*. 2021;10(2):1295-1308. **7.** ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2021. **8.** Mont MA, Beaver WB, Dysart SH, et al. *J Arthroplasty*. 2018;33(1):90-96.

HERON THERAPEUTICS

ZYNRELEF vs. Competitors in TKA Real World Evaluation Studies

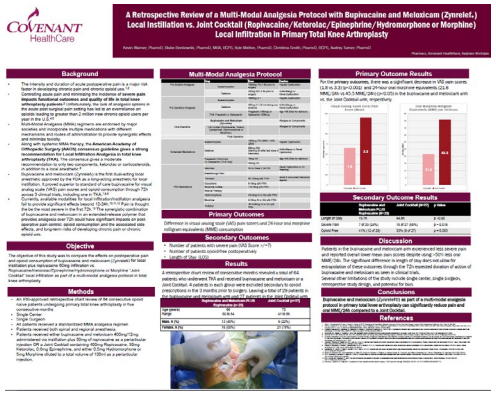
ZYNRELEF vs. LIPOSOMAL BUPIVACAINE: Dr. Sah[1]



Pain Management-

- TKA (N=200):
- All but 4 patients received spinal anesthesia (2 patients in each group received general anesthesia).
- Adductor canal block with ropivacaine 0.5% 10 to 15 mL
- Standardized multimodal analgesic regimen
- Quicker transfer to PACU
- Farther ambulation
- Higher same day discharge, less pain at discharge
- Less opioids used in hospital and post-discharge
- Less severe pain, better able to tolerate PT

ZYNRELEF vs. Generic Cocktail: Dr. Warner[2]



Blocks Used-

- TKA (N=64) with all patients received spinal and regional anesthesia (adductor canal block of bupivacaine 0.5% 50 mg to 150 mg), and both groups were given a standardized multimodal analgesic regimen.

Outcomes-

- Pain and oral MME/24h significantly reduced compared to a joint cocktail
  - Less severe pain (24% vs 55%)
  - More opioid free (41% vs 33%)
  - ~1 day LOS savings (25.1 hrs)

References: 1. Sah AP. Initial experience with a novel extended release, dual-acting local topical anesthetic in TKA compared to a long-lasting bupivacaine peri-articular injection. Poster presented at: Orthopedics Today Hawaii; January 8-12, 2023; Koloa, HI. **2.** Warner K, Bonkowski B, Melton K, Smith C, Turner A. A retrospective review of a multi-modal analgesia protocol with bupivacaine and meloxicam (Zynrelef) local instillation vs. joint cocktail (ropivacaine/ketorolac/epinephrine/hydromorphone or morphine) local infiltration in primary total knee arthroplasty. Poster presented at: Orthopedics Today Hawaii; January 8-12, 2023; Koloa, HI.

HERON THERAPEUTICS

ZYNRELEF Offers Unprecedented Clinical and Economic Value

Clinical Features	ZYNRELEF	EXPAREL®[a]
Designed to Overcome Challenges of Inflammation at Surgical Site[1]	✓	✗
Greater Pain Reduction Through 72 Hours vs Bupivacaine HCl[1-4]	✓	✗
Superior Pain Reduction vs Bupivacaine HCl[1-3]	✓	✗
Greater Reduction in Severe Pain vs Bupivacaine HCl[2,3]	✓	✗
Significant Increase in Opioid-Free Patients vs Bupivacaine HCl[1-3]	✓	✗
Greater Decrease of Opioid-Related AEs vs Bupivacaine HCl[2,3]	✓	✗
Needle-Free Instillation[1]	✓	✗

Pharmacy Collaboration and Cost Savings	ZYNRELEF	EXPAREL
Lower Acquisition Cost and Average Cost	✓	✗
2 SKUs and 340B Pricing at Launch	✓	✗
340B Pricing	✓	✓
GPO Contracting	✓	✗
Full-Line Wholesaler Distribution (Prime Vendor Discount Will Apply)	✓	✗
Separate Reimbursement in HOPD (Medicare)[b,c]	✓	✗
Separate Reimbursement in ASC (Medicare)[b,c]	✓	✓

[a]Exparel (bupivacaine liposome injectable suspension) is a trademark of Pacira Pharmaceuticals, Inc.
[b]ZYNRELEF will be separately reimbursed under pass-through status through March 2025. Separate reimbursement will continue through December 2027 under legislation calling for coverage of certain non-opioid treatments for pain relief (HR 2617 §4135).
[c]From January 1, 2025 through December 31, 2027, Medicare will reimburse separately in HOPDs and ASCs for certain non-opioid drugs without pass-through status, per HR 2617 §4135.
Note: ZYNRELEF and Exparel have not been studied in a head-to-head trial. Cost comparisons do not imply safety or efficacy.
SKU: stock keeping unit. **GPO:** group purchasing organization. **HOPD:** hospital outpatient department. **ASC:** ambulatory surgical center.
References: 1. ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** Viscusi E, Minkowitz H, Winkle P, et al. *Hernia*. 2019;23(6):1071-1080. **3.** Viscusi E, Gimbel JS, Pollack RA, et al. *Reg Anesth Pain Med*. 2019;44(7):700-706. **4.** Lachiewicz PF, Lee G-C, Pollak R, et al. *J Arthroplasty*. 2020;35(10):2843-2851.

HERON THERAPEUTICS®

APONVIE: Enhancing Recovery After Surgery with Appropriate PONV Prophylaxis

The Burden of PONV

From adverse events to increased financial cost. PONV can challenge patients and surgical facilities.

Patient Dissatisfaction

Vomiting ranked as the most undesirable complication and the most common reason for dissatisfaction in the perioperative experience[3,4]

Longer PACU Stays

Extended recovery times in the PACU can result in **delayed operating room availability** and decreased throughout for surgical procedures[5]

Risk for Re-Admissions

Re-admissions from PONV may lead to costly inpatient stays and **threaten institutional quality measures**[6]

63 MINUTE INCREASE in PACU time for patients with PONV[5]

How Can You Manage PONV Effectively?

High Unmet Need Exists in Managing PONV

More than 30% of patients still experience PONV within the first 48 hours after surgery, even when treated with ondansetron or other antiemetics[7]

Multimodal PONV Management is Recommended

Multimodal prophylaxis should be considered for patients who have one or more risk factors, according to the latest guidelines[1]

Aprepitant Was Ranked #1

As part of the most effective multimodal PONV regimen, aprepitant is also the most effective single agent with a high certainty of evidence among drugs with PONV prophylactic indication, and with the lowest rate of vomting[8]

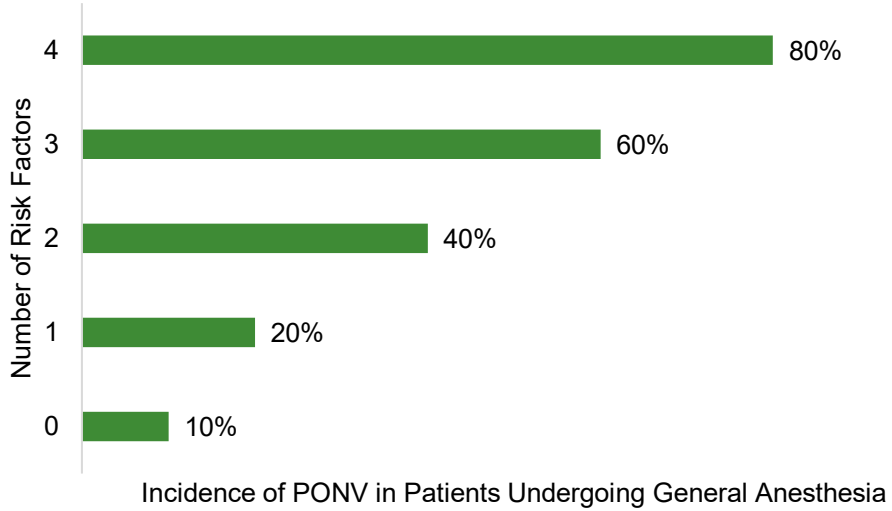
Emerging Preoperative Management Concerns with GLP-1 Agonists

The introduction of glucagon-like peptide-1 (GLP-1) agonists has led the American Society of Anesthesiologists to introduce new guidelines for effective surgical procedures. GLP-1 agonists have raised concerns around delayed gastric emptying and the associated high risk of regurgitation and aspiration of gastric contents

HERON THERAPEUTICS

Prevalence of Postoperative Nausea and Vomiting (PONV)

Apfel Score[5]:



- PONV is a common adverse effect associated with anesthesia, surgery, and postoperative opioid use, with an estimated incidence of 30% in the general surgical population and **up to 80% in high-risk patients**[1,2]
- Ondansetron, one of the most commonly used antiemetics, has a relatively short half-life (3 to 6 hours). Even when treated with ondansetron or other antiemetics, more than 30% of patients still experience postoperative nausea and vomiting.[3,4]

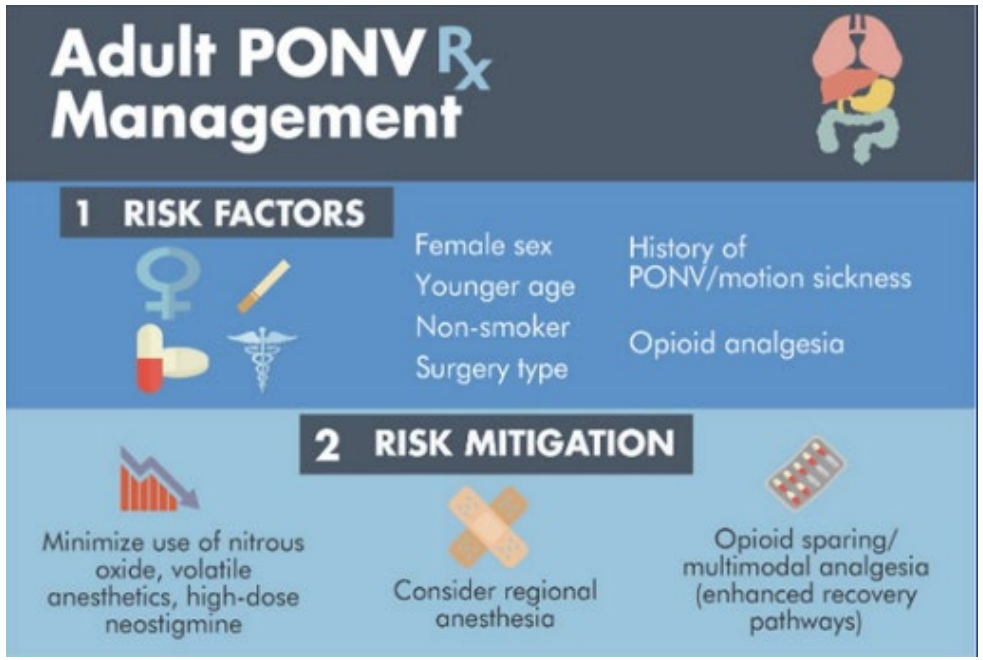
APFEL SCORE:
Risk Level Per # of Traits
- 0-1 Low Risk
- 2 Medium Risk
- 3+ High Risk

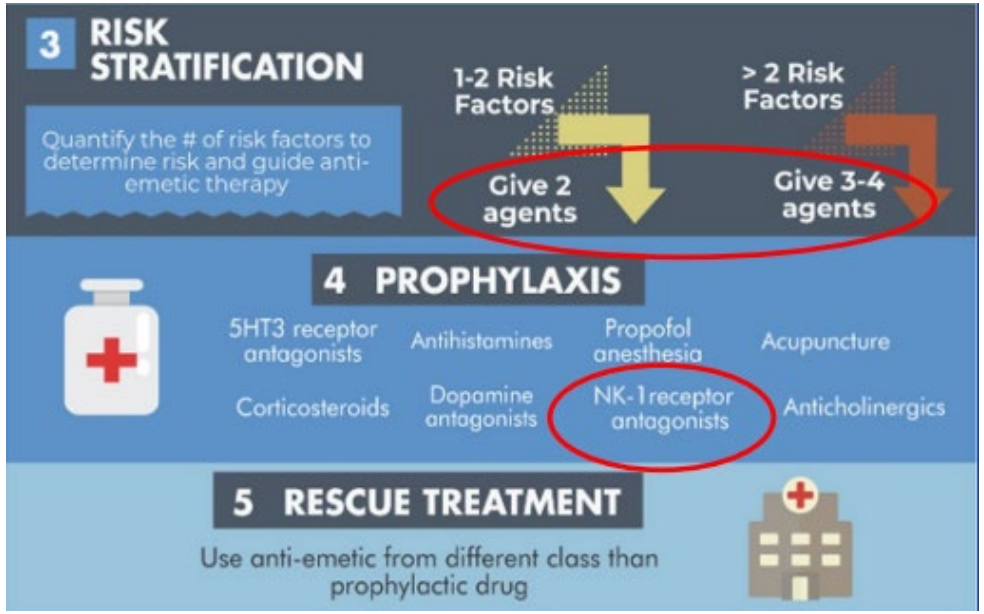
Patients at moderate-to-high risk of PONV exhibit the following traits[3]:			
Females	Non-smokers	A history of PONV or motion sickness	Patients who are treated with opioids

References: 1. Weibel S, Schaefer MS, Raj D, et al. *Anaesthesia.* 2021;76(7):962-973. **2.** Gan TJ. *CNS Drugs*. 2007;21(10):813-833. **3.** Diemunsch P, Gan TJ, Philip BK, et al. *Brit J Anaesth.* 2007;99(2):202-211. **4.** Zofran [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2017. **5.** Gan TJ, Belani KG, Bergese S, et al. *Anesth Analg.* 2020;131(2):411-448.

HERON THERAPEUTICS

2020 PONV Consensus Guidelines





APONVIE Overview

- The **first and only intravenous (IV) NK_1 antagonist** for prevention of PONV[1]
- **Superior vomiting prevention** versus IV ondansetron through 48 hours[1-3,a]
- The active ingredient in APONVIE was ranked as the **most effective agent** among drugs with a PONV prophylactic indication[4]
- Administered via a **single 30-second IV injection** prior to induction of anesthesia and reached therapeutic plasma concentrations associated with ≥97% receptor occupancy within 5 minutes[1,5,6,b]
- Offers a **comparable safety profile** to standard-of-care IV ondansetron without QT prolongation[1]
- Ideally suited to be the first-line foundation of a multimodal protocol **for patients at moderate-to-high risk for PONV**[1,7]
- **Priced to support broad access** with convenient packaging and distribution

[a]Unadjusted *P* value.
[b]The relationship between receptor occupancy and efficacy has not been established.

References: 1. APONVIE [package insert]. San Diego, CA: Heron Therapeutics Inc; 2022. **2.** Diemunsch P, Gan TJ, Philip BK, et al. *Brit J Anaesth.* 2007;99(2):202-211. **3.** Gan TJ, Apfel CC, Kovac A, et al. *Anesth Analg.* 2007;104(5):1082-1089. **4.** Weibel S, Schaefer MS, Raj D, et al. *Anaesthesia.* 2021;76(7):962-973. **5.** Data on file. Summary of clinical pharmacology studies. San Diego, CA: Heron Therapeutics Inc. **6.** Van Laere K, De Hoon J, Bormans G, et al. *Clin Pharmacol Ther.* 2012; 92(2):243-250. **7.** Gan TJ, Belani KG, Bergese S, et al. *Anesth Analg.* 2020;131(2):411-448.

HERON THERAPEUTICS®

Aprepitant Real World Clinical Efficacy

Single Studies	Vomiting Incidence
Aprepitant Plus Ondansetron VS. Ondansetron (Plastic Surgery)[1]	**9.3**% vs 29.7%
Aprepitant Plus Dexamethasone VS. Ondansetron Plus Dexamethasone (Craniotomy) [2]	**16**% vs. 38%
Aprepitant VS. Ondansetron plus Dexamethasone Plus either metoclopramide, diphenhydramine, or prochlorperazine every 6 hours for the 48h study period. (TKA) [3]	**25**% (PONV) vs. 75% (PONV)

The efficacy of aprepitant for the prevention of postoperative nausea and vomiting. (A meta-analysis)[4]

- March 20, 2022. Seventeen RCTs were identified, with 3299 patients
- Aprepitant Combined with Ondansetron and Dexamethasone
- PONV incidence was significantly reduced among those receiving aprepitant (odds ratio [OR]: **0.34**; 95% confidence interval [CI]: 0.26, 0.44; P < .0001), with a more complete response (OR: 1.35; 95% CI:1.14, 1.59; P = .0004)
- Aprepitant was better at preventing vomiting than nausea (OR: 8.6; 95% CI: 3.84, 19.29; P < .00001)

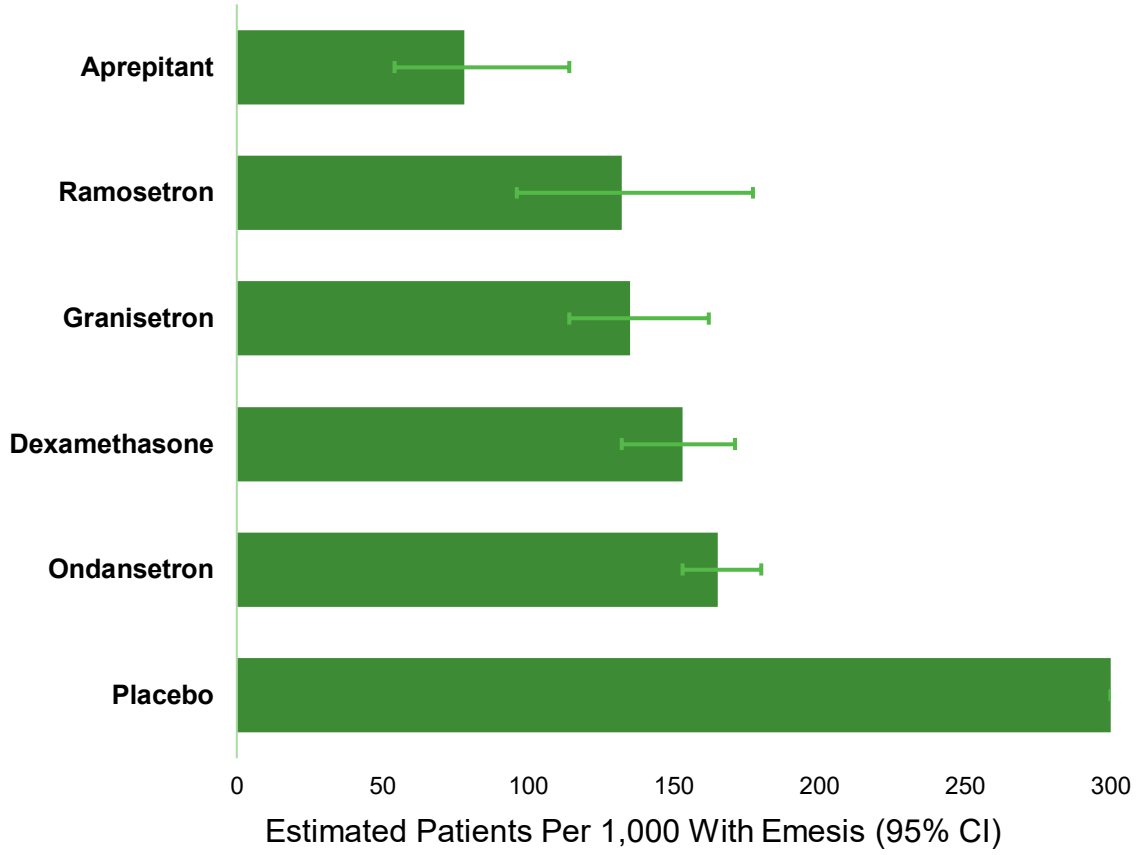
Conclusion: Our study revealed that aprepitant effectively reduces the incidence of PONV among high-risk patients. Further, vomiting was more significantly prevented by aprepitant than nausea. **The use of dexamethasone and ondansetron combined with aprepitant may be most effective for preventing PONV.**

References: 1. Vallejo MC, Phelps AL, Ibinson JW, Barnes LR, Milord PJ, Romeo RC, Williams BA, Sah N. Aprepitant plus ondansetron compared with ondansetron alone in reducing postoperative nausea and vomiting in ambulatory patients undergoing plastic surgery. Plast Reconstr Surg. 2012 Feb;129(2):519-526. doi: 10.1097/PRS.0b013e31822b6932. PMID: 21987042 **2.** Habib AS, Keifer JC, Borel CO, White WD, Gan TJ. A comparison of the combination of aprepitant and dexamethasone versus the combination of ondansetron and dexamethasone for the prevention of postoperative nausea and vomiting in patients undergoing craniotomy. Anesth Analg. 2011 Apr;112(4):813-8. doi: 10.1213/ANE.0b013e3181ff47e2. Epub 2010 Nov 16. PMID: 21081776**. 3**. Hartrick CT, Tang YS, Hunstad D, et al. Aprepitant vs. multimodal prophylaxis in the prevention of nausea and vomiting following extended-release epidural morphine. *Pain Pract*. 2010;10(3):245-248. doi:10.1111/j.1533-2500.2010.00364.x**. 4.** Liu Y, Chen X, Wang X, Zhong H, He H, Liu Y, Liao Y, Pan Z, Hu W, Liu W, Zheng F. The efficacy of aprepitant for the prevention of postoperative nausea and vomiting: A meta-analysis. Medicine (Baltimore). 2023 Jul 21;102(29):e34385. doi: 10.1097/MD.0000000000034385. PMID: 37478247; PMCID: PMC10662847.

HERON THERAPEUTICS

Aprepitant Is the Most Efficacious Compound for the Prevention of Vomiting After Surgery[1]

Cochrane Meta-Analysis: Ranking of most effective single-agent prophylactic with high-confidence evidence through 24 hours



In an **independent 2020 Cochrane meta-analysis** of 585 studies and 97,516 patients:

- Aprepitant was ranked as most effective among drugs with a PONV prophylactic indication, with the lowest rate of vomiting
- Among agents with a high certainty of evidence, aprepitant was ranked as the most effective single agent

References: 1. Weibel S, Schaefer MS, Raj D, et al. *Anaesthesia.* 2021;76(7):962-973.

HERON THERAPEUTICS

APONVIE Appropriate Incorporation into ERAS (A Formulary Review Perspective)

Pros	Cons
Safety Profile (No QT Prolongation, EPS, or Anticholinergic Effects)	Cost
Superior to Ondansetron, Aprepitant Ranked Most Effective Agent per Cochrane Meta-Analysis	Drug interactions with oral-contraceptives and warfarin
Synergistic in a multimodal approach	Emulsion contains alcohol, usp, egg phospholipids (egg lecithin), soybean oil
48h Duration of Action (Prevent Post Discharge Nausea and Vomiting)	
Rapid Onset (97% Receptor Occupancy within 5 min) vs Oral (1-5h) or Oral may be contraindicated.	
30 Second IV Push	

Formulary Recommendation

Add Aponvie to formulary for prevention of post-operative nausea and vomiting for moderate to high-risk patients.

Per 2020 fourth consensus guidelines patients with moderate to high-risk of PONV should receive 3-4 agents for prophylaxis. Aprepitant (Aponvie) will allow for an appropriate multi-modal approach incorporating the most efficacious single and in combination agent with low risk of additive side effects and enhanced safety profile.

Moderate to High-Risk Patients include those patients with ANY 3(three) OR MORE of the following risk factors:

Patient Specific Risk Factors	Anesthetic Risk Factors	Surgical Risk Factors
Female Sex	Use of Volatile Anesthetics	Head & Neck
Non-Smoker	Opioid Analgesia (Post-Operatively)	Abdominal
Age <50	Duration of Anesthesia >3h	Gynecological
History of PONV/Motion Sickness		Breast

The Adoption Tailwinds for ZYNRELEF and APONVIE

ZYNRELEF® (bupivacaine and meloxicam) extended-release solution, for instillation use 29.25 mg/mL and 0.88 mg/mL

- Significant Label Expansion (New Indications/Providers/Formulary Substitutions)
- Crosslink Partnership (Awareness/Adoption/Implementation)
- Opioid Stewardship (Accrediting Bodies ex. Joint Commission Require)
- Opioid Settlement ($53 Billion to be Spent on Opioid Awareness/Treatment/Prevention)
- NOPAIN Act (Non-Opioids Prevent Addiction in the Nation Act)
  - NOPAIN goal is the reduce opioid consumption by promoting alternative pain management options for surgical patients.
  - Establishes separate Medicare Reimbursement for non-opioid treatments in HOPD and ASC. (Commercial Payors Typically Follow CMS)
  - Separate Payment applies to pain management treatments that can replace or reduce opioid use, as demonstrated through clinical trials or data.
  - 2025-2027 (Extension Beyond Likely)

APONVIE™ (aprepitant) injectable emulsion

- Education and Awareness of the safety and efficacy. (Leverage Cochrane Meta-Analysis #1 most effective agent.)
- PONV Guideline Update
- GLP-1 Usage (High Risk for PONV, Poor Absorption of Oral Medications)

Transition from Inpatient to Outpatient Surgical Models and Need for Enhanced Recovery After Surgery

HERON THERAPEUTICS®

Q&A

Kevin Warner PharmD, Sr. VP, Medical Affairs Strategy & Engagement, Heron Therapeutics

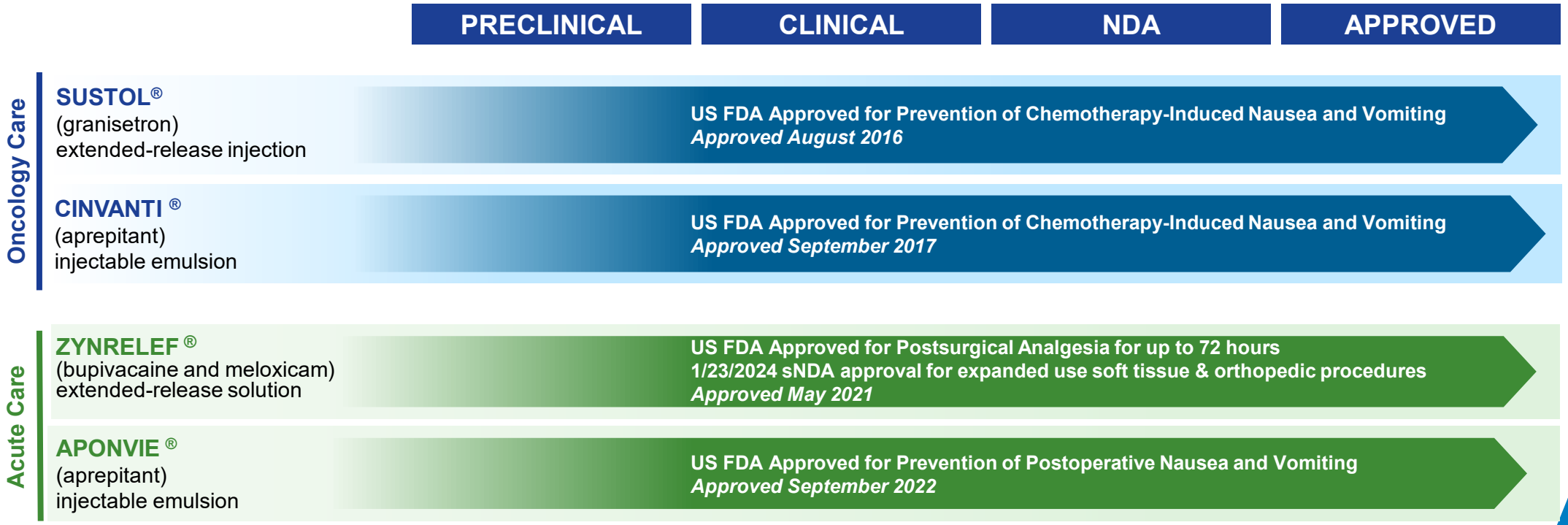
Randy Robbins MD, Anesthesiologist, Valiant Anesthesia Associates, Dallas, Texas

Alan Rechter MD, Orthopedic Surgeon, Orthopedic Associates LLP, Houston, Texas

Research & Development

Bill Forbes, PharmD, EVP and Chief Development Officer,
Heron Therapeutics

Product Portfolio Overview



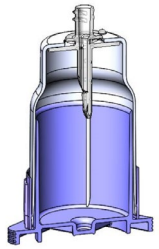
ZYNRELEF Regulatory and Development Offer Continued Expansion of Opportunity

2024-2026 Milestones

sNDA Approval

Expanded label almost doubled ZYNRELEF opportunity to ~13M procedures

January 23, 2024



Anticipated Vial Access Needle (VAN) Approval

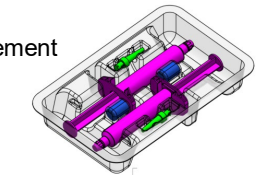
VAN reduces withdrawal time from >1 minute to 20-30 seconds

Q4 2024

Anticipated Prefilled Syringe (PFS) Approval

Perceived as the most meaningful improvement given potential to more rapidly administer intra-operatively in market research

Q4 2026



ZYNRELEF is indicated in adults for instillation to produce postsurgical analgesia for up to 72 hours after soft tissue and orthopedic procedures including foot and ankle, and other procedures in which direct exposure to articular cartilage is avoided.

VAN is on track for a Prior Approval Supplement submission in Q2 2024 and an anticipated launch in late 2024

HERON THERAPEUTICS

Vial Access Needle (VAN) vs. Vented Vial Spike (VVS)

External Surface Completely Sterile

Drug Product Readable through VAN (Prototype in Photo, commercial is better)

Surface held by both Sterile and non-sterile nurses

Sterile = White adapter

Non-sterile – Glass Vial & Vial label

HERON THERAPEUTICS

VAN Withdrawal Time is Faster than Currently Marketed VVS

Comparison of VVS and VAN Withdrawal Times as a Function of Temperature

Bupivacaine (mg)/ Meloxicam (mg)	VVS Withdrawals (seconds)			VAN Withdrawals (seconds)		
	16°C	19°C	25°C	15°C	18°C	25°C
60/1.8	149	104	55	41	31	14
200/6	275	167	106	58	38	18
300/9	412	264	149	88	54	27
400/12	470	355	186	112	85	45

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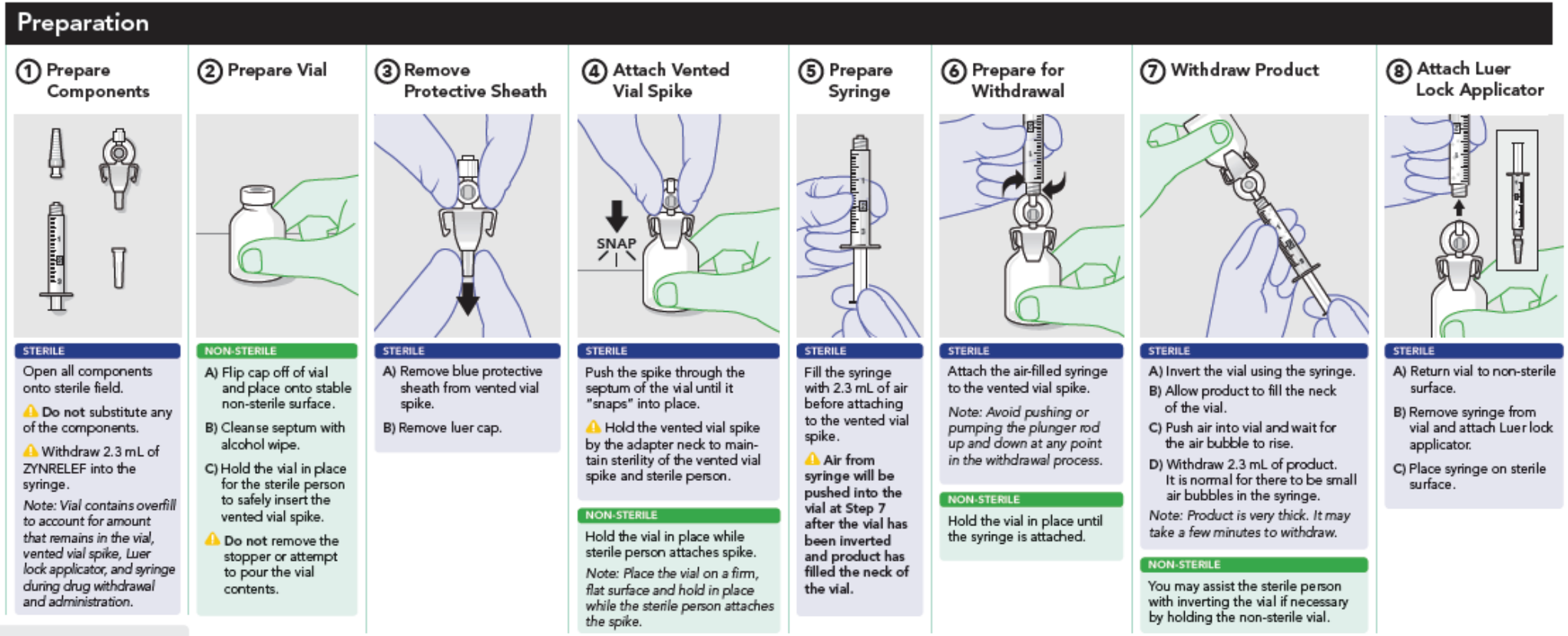
VVS Instructions for Use

Non-sterile nurse:
1) Opens packaging and places sterile components onto the sterile field
2) Holds the non-sterile vial, while the sterile nurse attaches the VVS to the vial
3) Holds the non-sterile vial while the sterile nurse connects the sterile syringe
4) Holds the non-sterile vial while the sterile nurse draws up drug product
5) Holds the non-sterile vial while the sterile nurse removes the filled sterile syringe

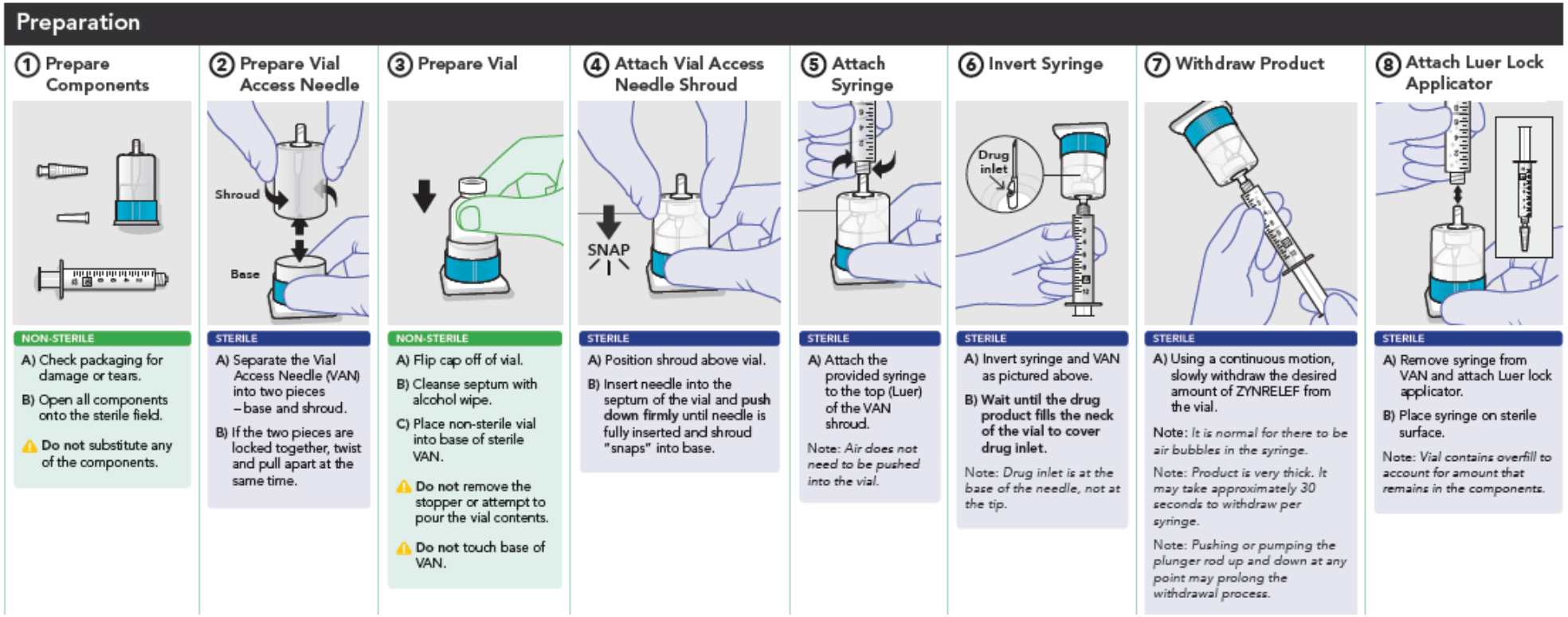
Repeat: Do it all over again if a second syringe is needed.



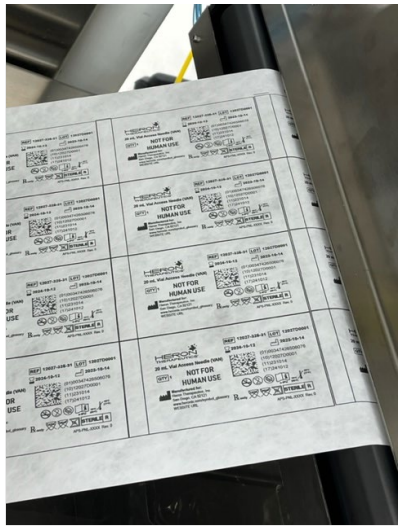
VAN Instructions for Use

Non-sterile nurse:
1) Opens packaging and places sterile components onto the sterile field
2) Places the vial into the VAN base

Non-sterile nurse is not involved if a second pull from the vial is needed

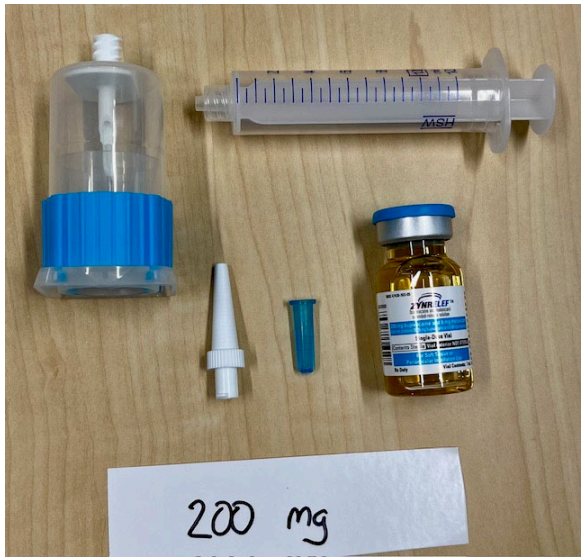


Heron R&D VAN Development: Designed, Manufactured & Tested; Heron Regulatory Scheduled to Submit PAS to FDA in Q2



VAN Kit


400 mg


200 mg


HERON
THERAPEUTICS
REF 12027-325-31
LOT 12027D0001
2024-10-12
2023-10-14
20 mL Vial Access Needle (VAN)
QTY 1
NOT FOR
HUMAN USE
(01)00347426506076
(10)12027D0001
(11)231014
(17)241012
Manufactured for:
Heron Therapeutics, Inc
San Diego, CA 92121
www.herontx.com/symbol_glossary
WEBSITE URL
Rx only
STERILE R
APS-PNL-XXXX Rev. 0

Prototype Prefilled Syringe Kit

1. Prefilled syringe (PFS) is sealed in moisture barrier foil pouch
2. Tray is sealed with a TYVEK film (not shown) and includes:
3. PFS filled with 200mg bupivacaine and 6 mg meloxicam (7 mL)
4. Luer lock applicator
   - PFS tray is terminally sterilized, contents of TYVEK sealed tray (**2**) are sterile.
5. Desiccant attached to bottom of tray then sealed into foil pouch (**1**)

Break In Progress

Acute Care Current Strategic Focus and Forward Progress

Ryan Craig, VP of Marketing, Heron Therapeutics

David Barozzino, VP of Sales and National Accounts, Heron Therapeutics

Total Target Opportunity for Acute Care Franchise

~65M US Surgical Procedures per Year

APONVIE™ (aprepitant) injectable emulsion

- ~50% of these patients are at high risk of PONV, or **~32.5M**

ZYNRELEF® (bupivacaine and meloxicam) extended-release solution, for instillation use 29.25 mg/mL and 0.88 mg/mL

- **~13M** of these surgeries indicated for ZYNRELEF

HERON THERAPEUTICS

APONVIE Strategy

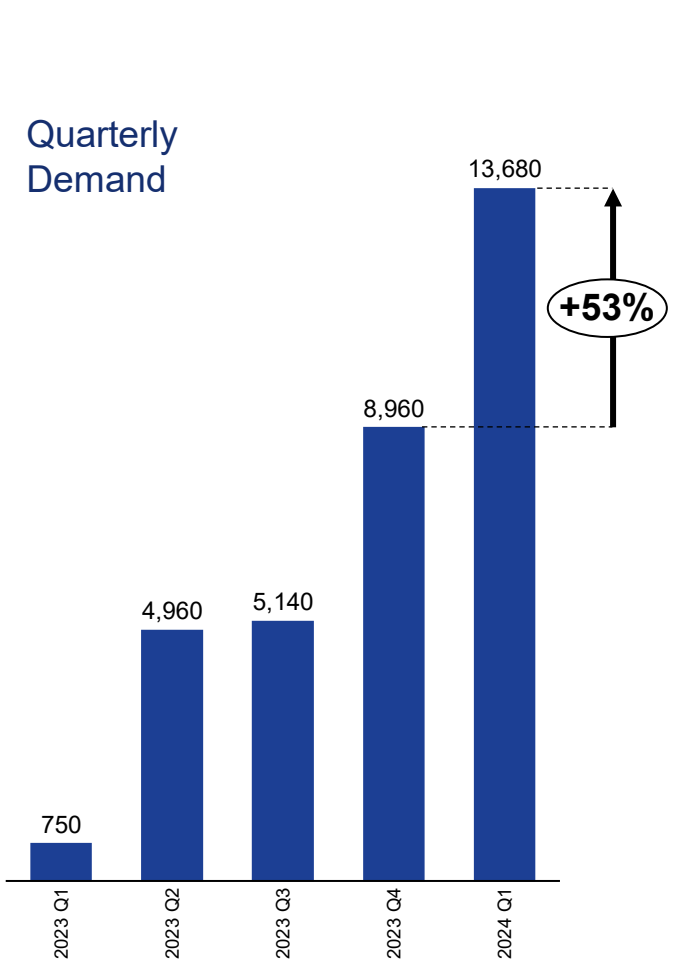
Establish APONVIE as the foundation of multimodal PONV management through specialties that align with the PONV conversation and expand from there

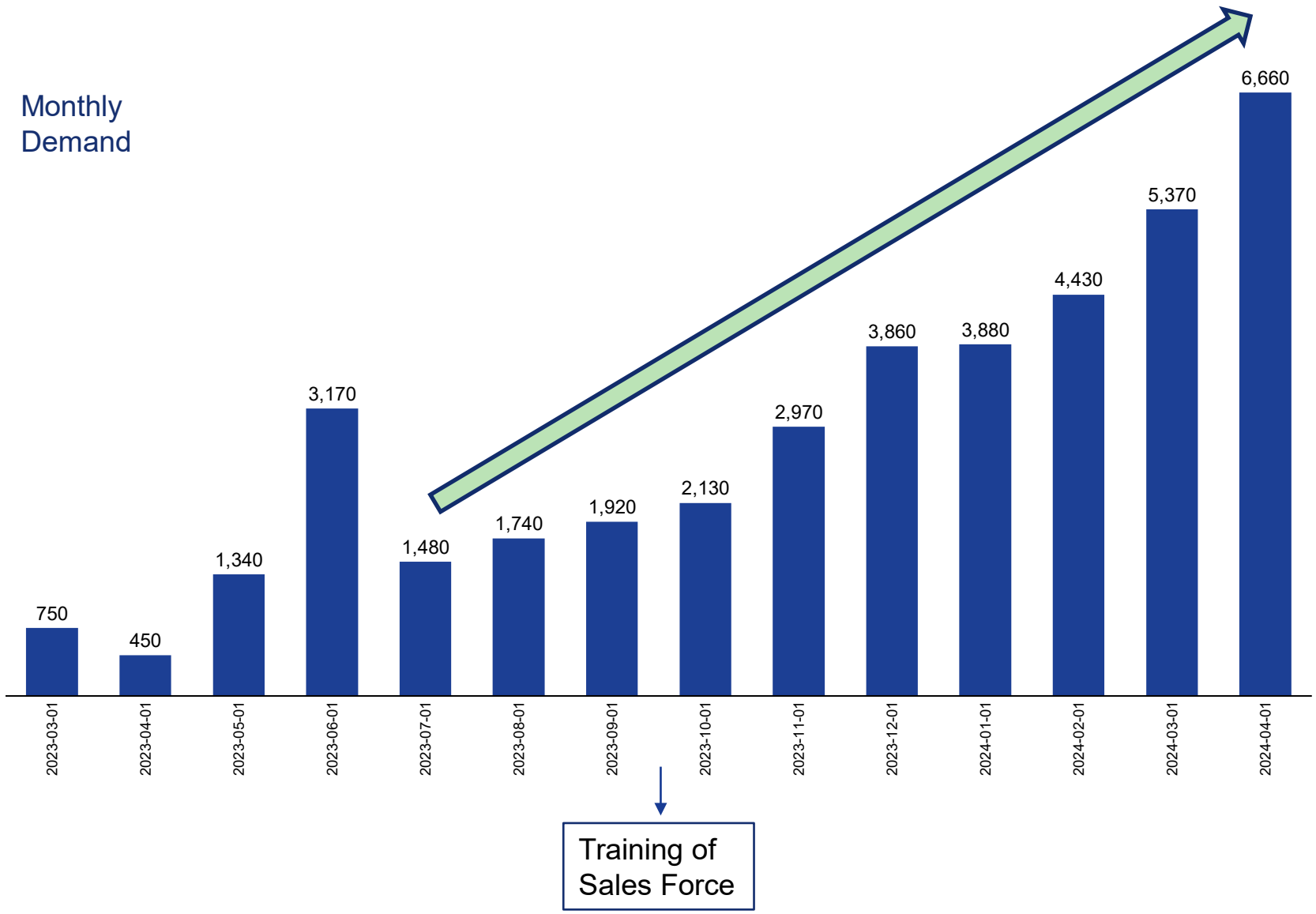
"Above the waist" target

- Significant burden of PONV is well understood by Bariatric, ENT, Neuro and Plastics specialties
- Targeted focus for field team, proven ability to expand to other surgical lines
- Establish APONVIE as the foundation of multi-modal PONV prevention

High Risk Patients	32,500,000	32,500,000	32,500,000
Procedure Share	**1%**	**5%**	**10%**
APONVIE Units	325,000	1,625,000	3,250,000
Net Price	$44	$44	$44
Net Sales	$14.3M	$71.5M	$143M

APONVIE – Unit Demand





APONVIE Pipeline Continues to Build

109 P&T wins since training in Q4 2023

305 Ordering accounts

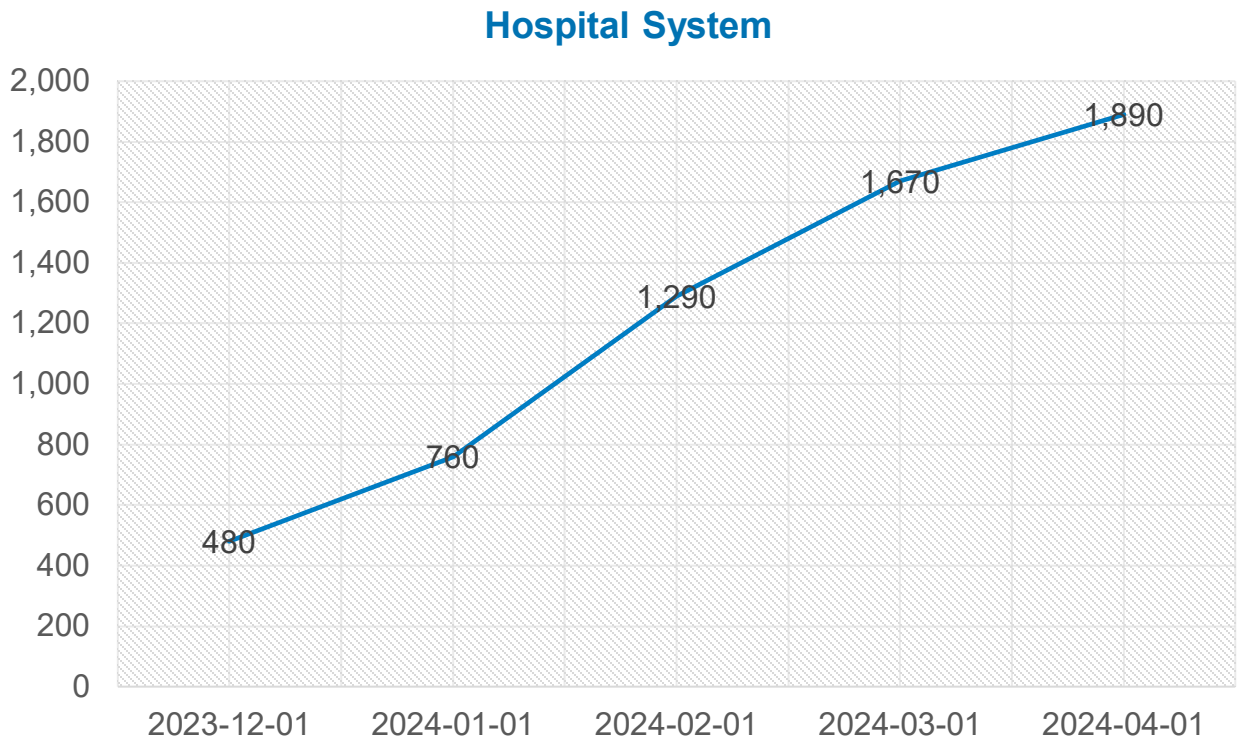
Driving to Peak Performance

Tiering	Procedure Volume	# of Hospitals/Clinics	Annual Procedure Counts	Driving to Peak Performance (20%)	Net Revenue Potential
Tier 1	**High** 33% of total procedures	31	887,737	177,547	$7,812,086
Tier 2	**Medium** 33% of total procedures	64	636,939	127,388	$5,605,063
Tier 3	**Low** 33% of total procedures	210	202,493	40,499	$1,781,938
Total		**305**	**1,727,169**	**345,434**	**$15,199,087**

Future Opportunity	**12,000**	**30,772,831**	**6,154,566**	**$270,800,913**

HERON THERAPEUTICS

Potential of a Fully Adopted Account



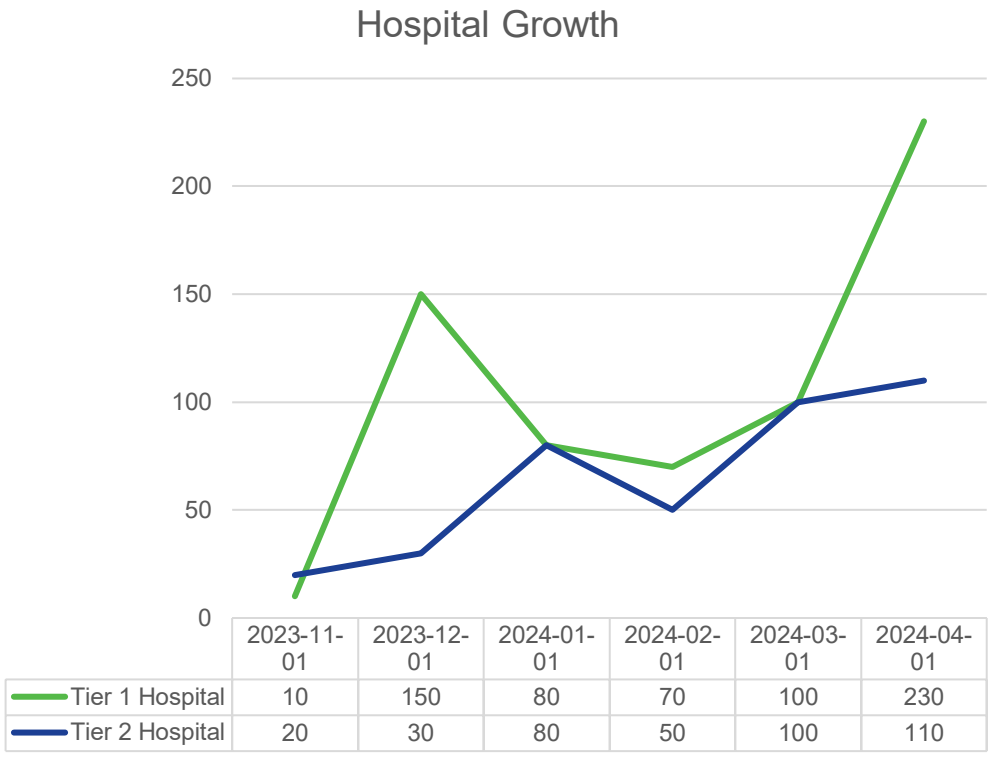
Summary:

- 7 campuses
- 49,700 procedures per year
- 24,850 High-Risk patients
- Fully Adopted - 2,070 vials per month

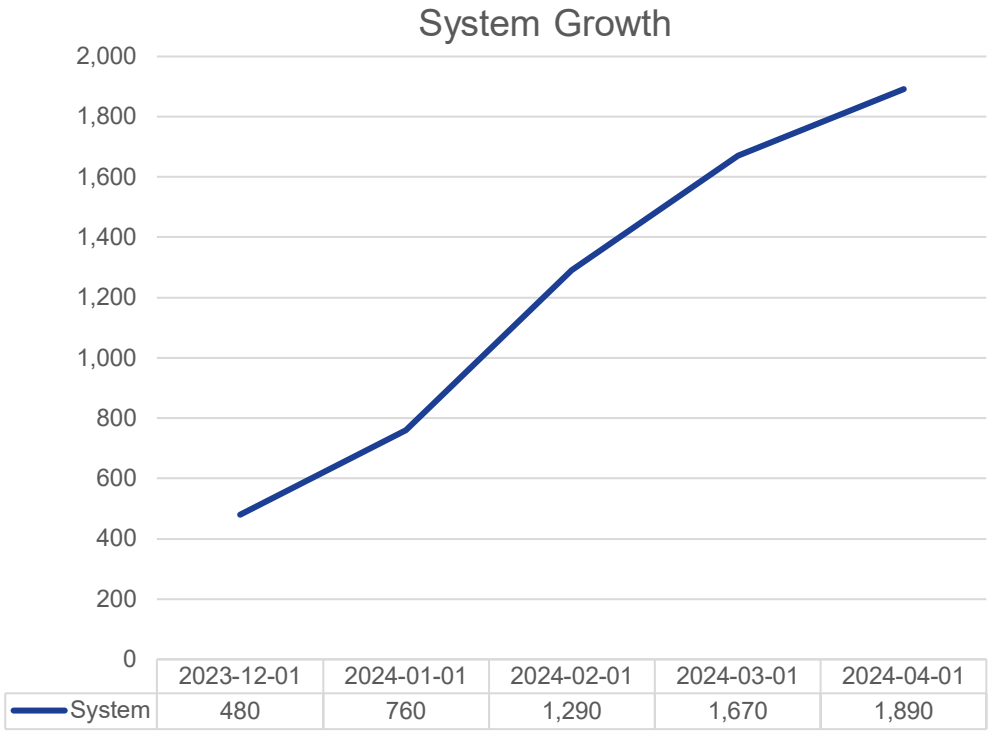
- Potential Net Revenue

$1 million-dollar IDN

Ramp-up with APONVIE



	2023-11-01	2023-12-01	2024-01-01	2024-02-01	2024-03-01	2024-04-01
Tier 1 Hospital	10	150	80	70	100	230
Tier 2 Hospital	20	30	80	50	100	110



	2023-12-01	2024-01-01	2024-02-01	2024-03-01	2024-04-01
System	480	760	1,290	1,670	1,890

ZYNRELEF Strategy

Drive ZYNRELEF volume by leveraging its superior clinical profile through orthopedic surgeon focus and expanding promotional presence via distributor partnership

Powerful and precise follow through

- Most significant pain is experienced in orthopedic procedures
- Higher volume of procedures by specialty
- Aligns to sNDA approval and launch
- Distributor partnership will amplify awareness and impact

Total Indicated Procedures	**13,017,847**[1]
sNDA2 – Ortho	**1,352,710**
Hip + Knee	**1,681,000**
C-Section	1,185,138
sNDA1 – Other	5,728,253
sNDA2 – Other	3,070,746

$558M* Opportunity in Orthopedics Alone

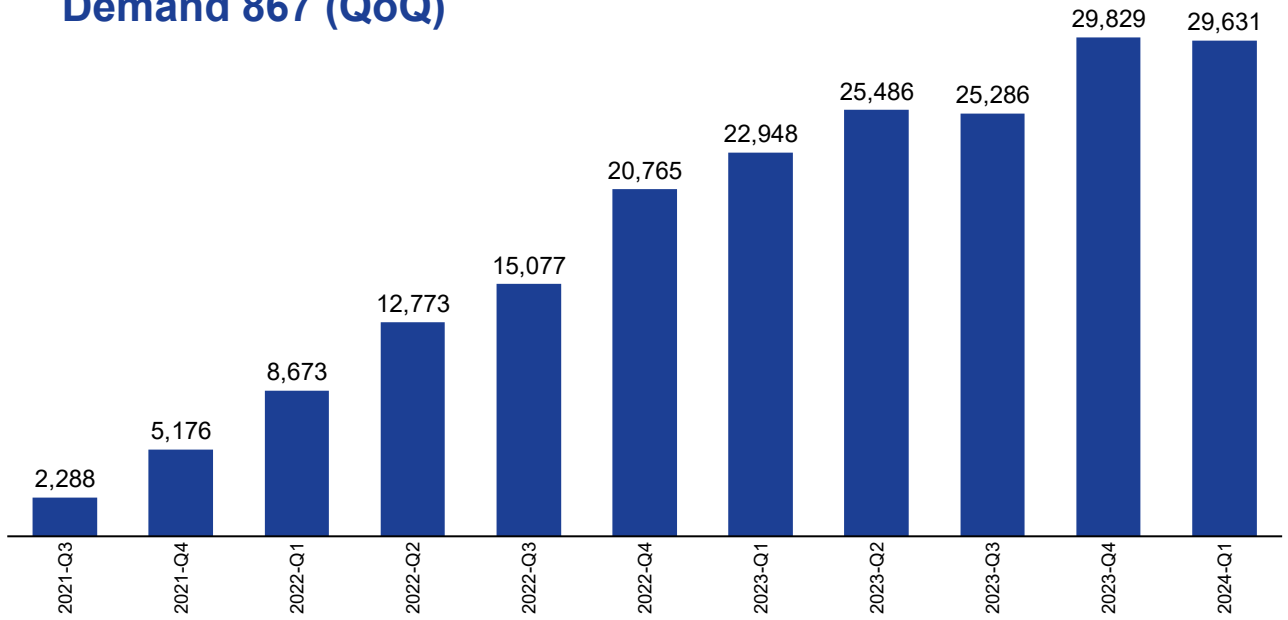
$2.39B* Opportunity in All Labeled Indications

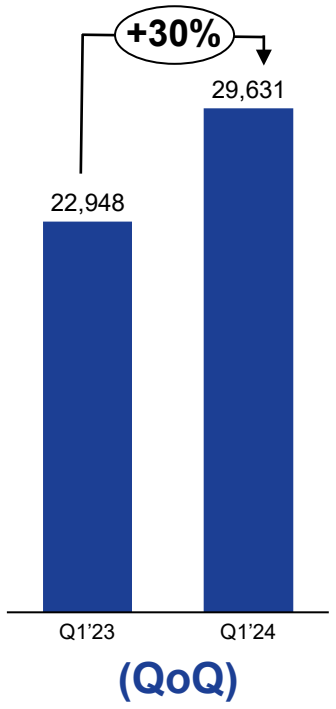
1. 2019 DRG Procedure Data Set

* Blended net price of $184

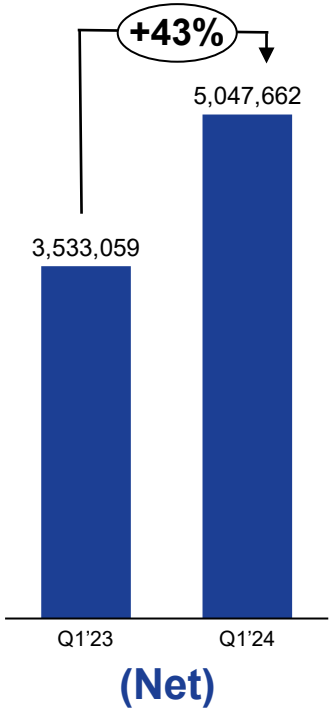
ZYNRELEF – Demand 867 (units)

Demand 867 (QoQ)



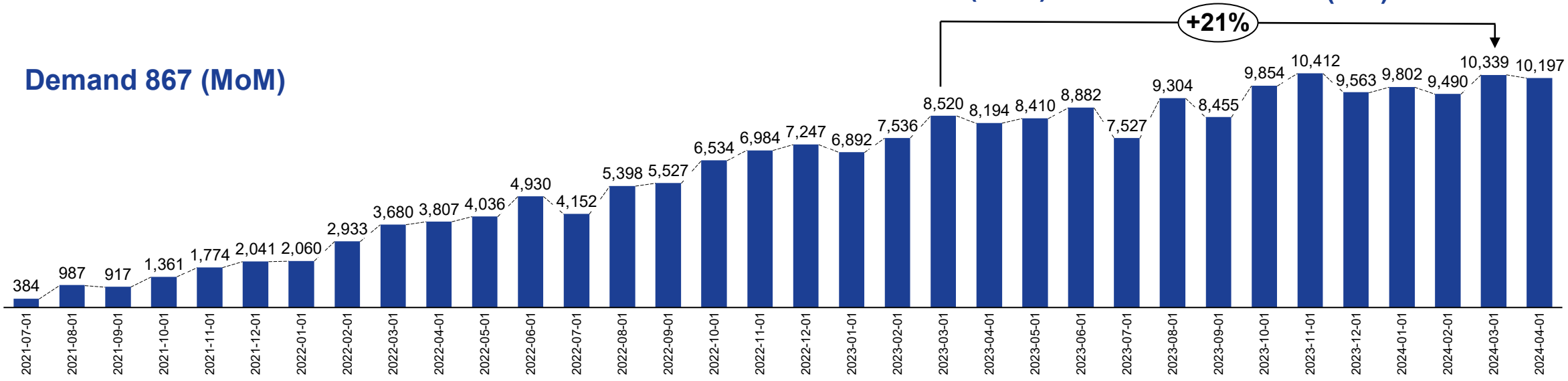


(QoQ)



(Net)

Demand 867 (MoM)



Partnership with CrossLink

Strategic, Methodical and Precise!

Q1 and Q2 - 2024

Sign Contract

Jan 7th, 2024 – signed 5-year agreement with CrossLink. CrossLink is the largest private orthopedic with over 45 years experience

January - Built Training Program

During the month of January, we built out a robust but comprehensive training program both online and in person virtual workshops

February - Rolled out Training to CrossLink Legacy & Co Leads put in Place

Assigned 10 hours of virtual training to entire joint legacy team and started scheduling live events for March (163 reps)

March - Live ZYNRELEF Training

Conducted and facilitated 5 live in persons team joint trainings. Had virtual guests provide insights and feedback around product as well. Did hands on demos and verbalized core messages

March - Co Leads Started Signing Up Distributors

Identified and prioritized strategic roll out across the US outside of key legacy states (NC, SC, GA)

April – May
More Live ZYNRELEF Trainings

Trained groups in Michigan, Kansas, St. Louis, Houston and Dallas

Over Next Several Months - Continue Expansion

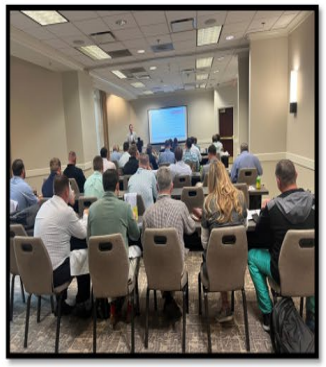
Staggering calendar build out around training, expanding across the country with a strategic measured approach

Robust Training

Crosslink Training-Tier 1

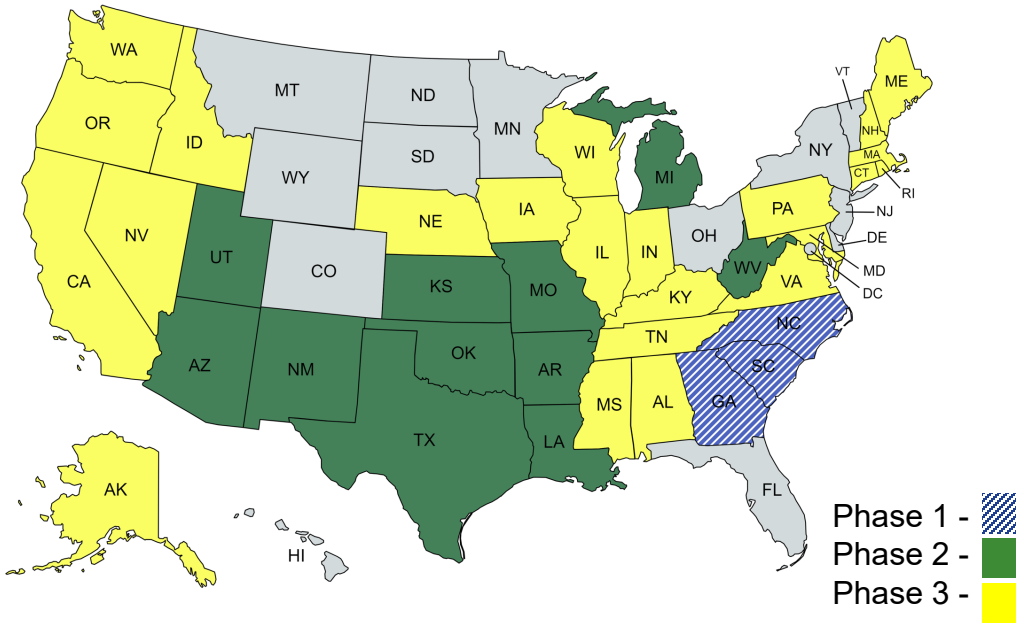
Category	Details
MOA	Mechanism of Action Clinical Study Explorer
MOA	VIDEO - How does ZYNRELEF work? (MOA)
MOA	MOA Quiz
Category	**Details**
Core Messages	ZYNRELEF Module 4 - Product Rationale
Core Messages	Zynrelef Fact Sheet
Core Messages	Dr. Warner On Demand Postoperative Pain Management Dr Warner
Core Messages	Reimbursement Overview Q4 23
Core Messages	Zynrelef FAQs and Objection Handlers
Category	**Details**
Prep & Admin	Total Knee Arthroplasty Clinical Study Explorer
Prep & Admin	VIDEO - Dr. Broome TKA
Prep & Admin	VIDEO- Dr. Noble THA
Prep & Admin	VIDEO - ZYNRELEF 14 ML Prep
Prep & Admin	Total Knee Arthroplasty (TKA) Clinical Study Explorer Assessment
Category	**Details**
Anesthesia Optional Resources	Release Rates (need pdf upload)
Anesthesia Optional Resources	Upload Warner Poster
Anesthesia Optional Resources	Upload Sah Poster
Anesthesia Optional Resources	Upload Warner Fact Sheet
Anesthesia Optional Resources	Upload Sah Fact Sheet
Anesthesia Optional Resources	PI Section 12.3 Table 7 for Cmax
Anesthesia Optional Resources	Upload PK Slide Deck
Category	**Details**
Compliance	AE and PQC Training (prerequisite to ID 24)
Compliance	Adverse Event and Product Quality Compliant Training Assessment
Compliance	Roles and Responsibilities of Sales Representatives - Commercial Field
Compliance	Responding to Requests for Medical Information
Compliance	Field sales compliance overview

“Great things in business are never done by one person. They’re done by a team of people.” – Steve Jobs


CrossLink Implementation Continues to Progress

- **CL Legacy/Southeast Region**
  - Joint Team ~150 Reps
  - Trauma Team ~50 reps
- **National Expansion**
  - 11 Signed ~200 reps
  - 13 Under Review ~335 reps
  - 8 Discovery Phase



Training

- 216 CrossLink representatives have completed ZYNRELEF product training to date

CrossLink Partnership Making an Early Impact

~10 new Orthopedic surgeons generated per month by Heron team prior to CrossLink partnership

+20 new Orthopedic surgeons (NC, SC, and GA) in first month of promotion with CrossLink; anticipating another 80 new Orthopedic surgeons in the next thirty days

12-fold increase in sales within the initial rollout states (NC, SC and GA) versus the rest of the country

+3 unit increase in non-CrossLink states

+36 unit increase in NC, SC and GA

CrossLink Impact - Legacy

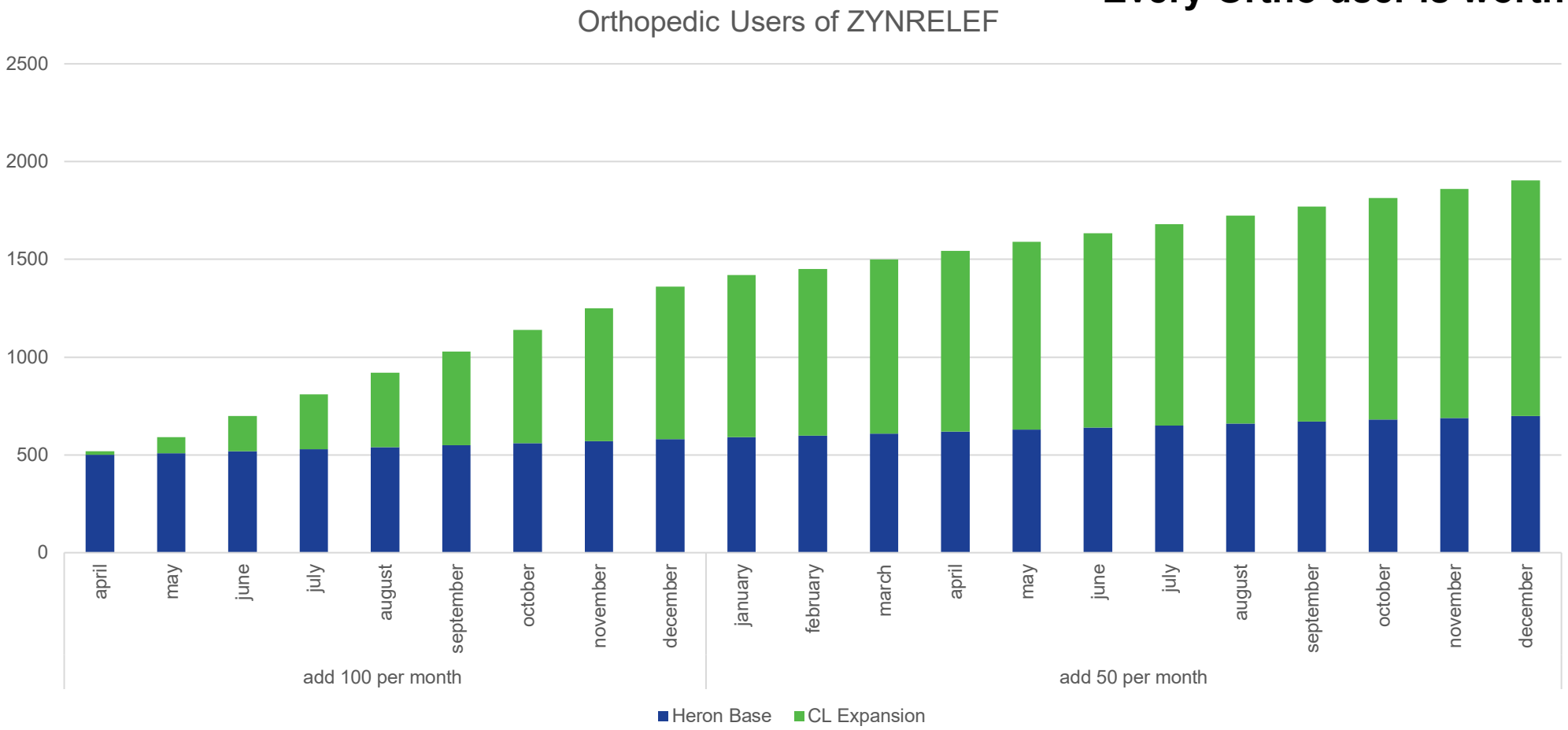
180 Unique interactions

80 Expected users over next 30 – 45 days

80 Programs, in-services and clinical touches

Anticipating Doubling our Orthopedic Users in 2024

Every Ortho user is worth ~$50k/year



Keys to Success in 2024

APONVIE

- Continue to fill pipeline with P&T's by establish the unmet clinical need and the cost of burden
- Leverage the Cochrane meta-analysis – Aprepitant as #1 agent
- Pull throw utilization within the hospitals and close the feedback loop

ZYNRELEF

- Own and dominate the total joint market
- Capitalize on the new broad label as CrossLink frees our reps time up to focus on additional procedures outside of orthopedics
- Build out the CrossLink partnership which sets us up for success in the second half of the year and into the future

Drive adoption and expand use by
Owning the perioperative space!!!!

HERON THERAPEUTICS

Future is Bright!

- Our products address the top 2 concerns with surgeries (PONV and PAIN)
- APONVIE is growing steady, and we continue to fill the pipeline with future P&T's
- CrossLink partnership will help grow ZYNRELEF sales across the country while freeing up our rep's time to sell elsewhere
- VAN helps shorten the preparation time and bridges to future
- PFS (pre-filled syringe) is the Holy Grail

HERON THERAPEUTICS

Oncology Care Current Strategic Focus and Forward Progress

Rob Sullivan, Sr. VP of Oncology Care Franchise and Commercial Operations

HERON THERAPEUTICS®

Business Highlights

- Chemotherapy Induced Nausea and Vomiting (CINV) is a substantial and growing market opportunity with ~5mm moderately and highly-emetogenic chemotherapy cycles requiring treatment annually
- SUSTOL and CINVANTI are established, differentiated CINV products that target complementary 5-HT3 and NK1 pathways
- CINVANTI retains a ~27% market share 4 years post generic fosaprepitant entry
- CINVANTI sales performance is driven by a focused commercial strategy and strong execution
- Oncology Portfolio has generated > $630M since Inception and $107.9 in 2023
- Highly profitable franchise with a small, cost-efficient, highly effective commercial footprint
- Robust IP Estate with patent protection through 2035

HERON THERAPEUTICS

CINVANTI Highlights

PS80-free IV NK1 RA approved for acute & delayed CINV due to both HEC and MEC

Portfolio Overview

Indication	• indicated in adults, in combination with other antiemetic agents, 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.
Mechanism of Action	• NK1 receptor antagonist
Description	• Intravenous formulation of aprepitant (approved for administration via 30-minute infusion or 2-minute IV push)
Distinguished Product Variable	• Free of synthetic surfactant polysorbate-80, which has been associated with infusion-site reactions and hypersensitivity in Emend IV patients
Launch	• January 2018
Primary Competitors	• Emend IV / fosaprepitant genericized in September 2019
Patent Expiration	• September 2035
Generic Entry	• CINVANTI maintains ~27% NK1 market share 4 years post generic entry

Positioning

- Differentiated clinical profile supporting ~27% NK1 market share despite generic fosaprepitant entry
  - Demonstrated fewer AEs within 30 minutes of infusion vs. fosaprepitant in healthy subjections (~2.6% AE rate vs. 15% AE rate)[1]
- Synthetic-surfactant-free formulation (no polysorbate 80) reduces risk of hypersensitivity and anaphylaxis reactions
- Patent protection through September 2035

	CINVANTI® (aprepitant) injectable emulsion	EMEND® (aprepitant) for oral suspension 125 mg	Akynzeo® fosnetupitant 235 mg/palonosetron 0.25 mg injection
Indicated for acute & delayed CINV caused by MEC & HEC	✓	✗	✗
Proven efficacy (aprepitant)	✓	✓	✗
Clinical flexibility of a single agent NK_1	✓	✓	✗
Approved for administration via 2-minute IV push	✓	✗	✗
Polysorbate 80-free formulation	✓	✗	✓
Emulsion formulation requiring no reconstitution	✓	✗	✓
Vials storable for 60-days at room temperature	✓	✗	✓

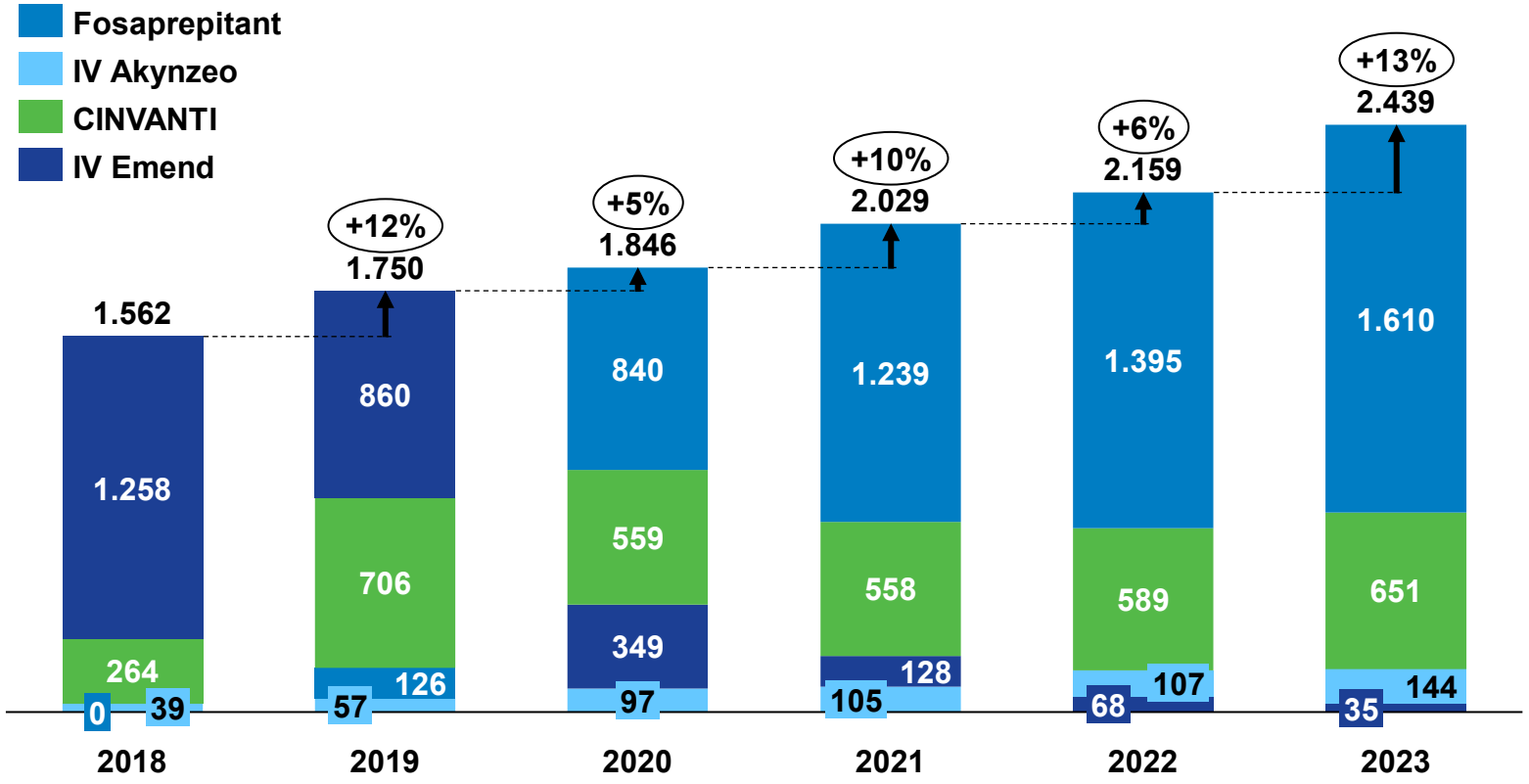
1. Data on file, Heron Therapeutics, San Diego, CA

HERON THERAPEUTICS

Market and Competition

Recent Sales Performance

Units ('000s)



Commentary

- Market Basket:
  - CINVANTI (aprepitant injectable emulsion) – **Heron Therapeutics**
  - Branded IV Emend (fosaprepitant) – **Merck**
  - Generic IV fosaprepitant (multiple entrants) – **Multiple Generic Companies**
  - IV Akynzeo – fosnetupitant (NK1) + palonosetron (5HT3) fixed dose combination – **Helsinn**
- IV NK1 RA Market: ~66% generics
- ~56.2% market growth from 2018-2023
- ~ 32.2% market growth form 2020-2023

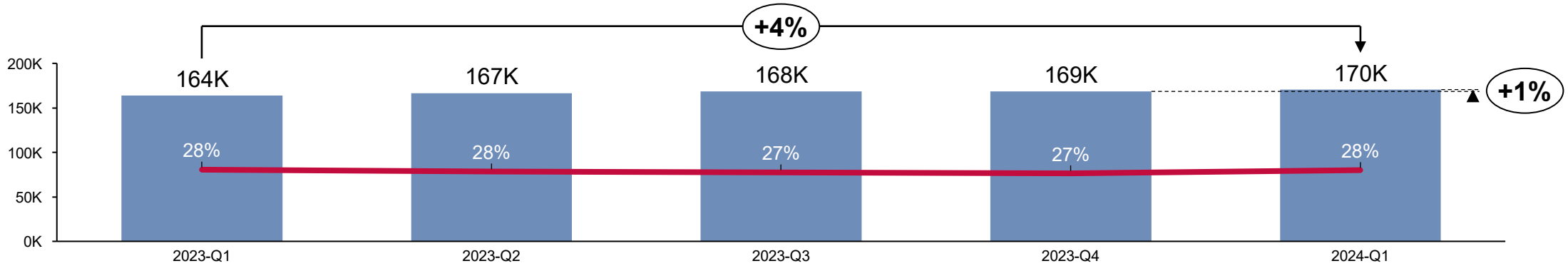
CINVANTI has maintained a 27% market share >4 years post generic entry

Source: IMS DDD 4.1.24

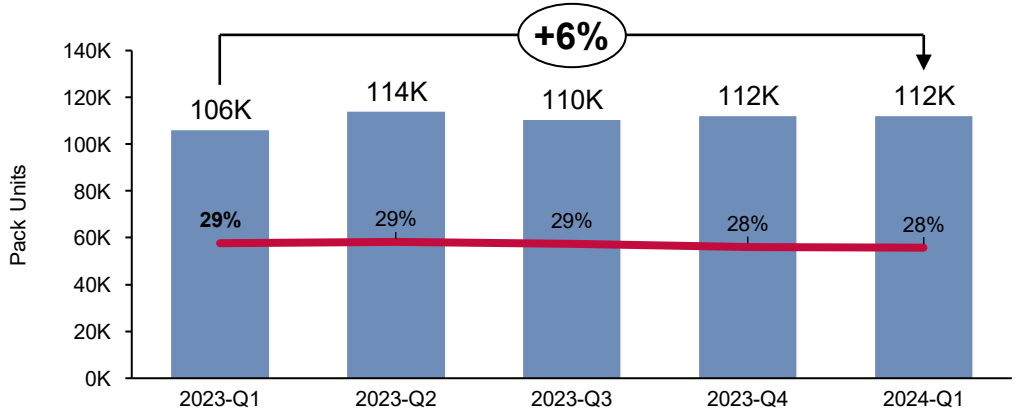
CINVANTI – Steady Growth in Unit Volume

Held Market Share at ~27%

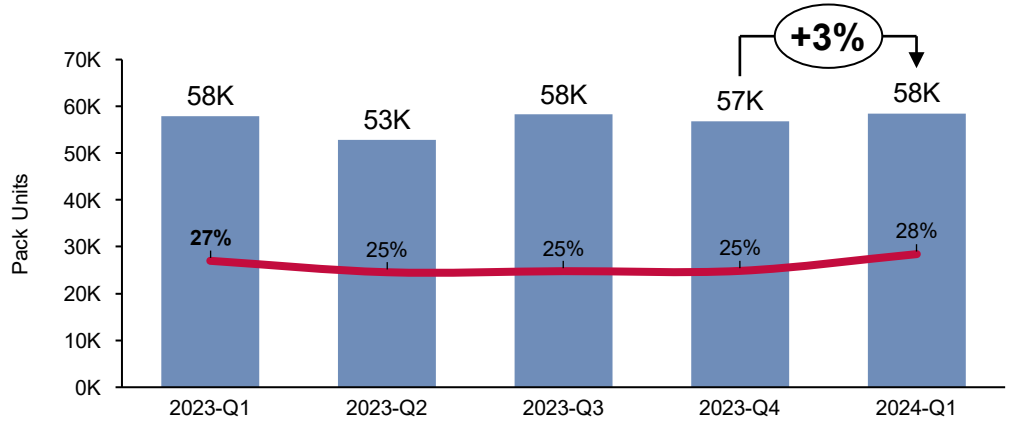
CINVANTI National Unit Sales/share%



CINVANTI Hospital Unit Sales / Share%



CINVANTI Clinic Unit Sales / Share%



Source: IMS DDD 4.12.24 .23, 867 4.23.24

CINVANTI Used by Top NCCN® Cancer Centers Since 2018

NCCN Cancer Center	Q1'24 Share
Memorial Sloan-Kettering Cancer	98%
Dana-Farber Cancer Institute	99%
Duke Cancer Institute	78%
City of Hope	85%
Fred Hutchinson Cancer Center (U of Washington Health)	88%
The Ohio State University Comprehensive Cancer Center	52%
Roswell Park Comprehensive Cancer Center	69%
Vanderbilt Ingram Cancer Center	91%
O'Neal Comprehensive Cancer Center at UAB	67%

National Comprehensive Cancer Network® (NCCN®) CATEGORY 1 RECOMMENDED OPTION

Aprepitant injectable emulsion (CINVANTI) is a Category 1 recommended option in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis for the prevention of acute and delayed emesis due to HEC and MEC.[2]

The American Society of Health-System Pharmacists (ASHP) recommends switching from IV infusion to IV push whenever possible[1]

1. ASHP fluid shortages. Accessed March 28, 2022. https://www.ashp.org/drug-shortages/shortage-resources/publications/fluid-shortages-suggestions-for-management-and-conservation# . **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2023. **3.** Share: IMS DDD data 4.26.24 **4.** Market Basket for Share Calculation: CINVANTI, IV Akynzeo, Fosaprepitant, Emend

HERON THERAPEUTICS

SUSTOL Highlights

Only IV/SC 5-HT$_3$ RA able to control and sustain therapeutic levels of granisetron over ≥5 days

Portfolio Overview

Indication	• SUSTOL 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) and anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.
Mechanism of Action	• 5-HT3 receptor antagonist
Description	• Subcutaneous, extended release granisetron leveraging proprietary biochronomer polymer- based drug delivery system
Distinguished Product Variable	• Only 5-HT3 receptor antagonist approved in delayed CINV associated with highly-emetogenic anthracycline and cyclophosphamide (AC) based chemotherapy
Launch	• October 2016
Primary Competitors	• Palonosetron genericized in March 2018, IV Akynzeo (branded)
Patent Expiration	• September 2024
Generic Entry	• Extremely high bar for generic entry given polymer manufacturing

Positioning

- Engineered using unique polymer technology to enable controlled, sustained release of granisetron for ≥5 days
  - Demonstrated superiority vs. ondansetron IV in the prevention of delayed CINV in a trial of over 900 patients receiving HEC regimens[1]
  - Unscheduled mean CINV-related hydrate rate was lower for SUSTOL than palonosetron in 2 real-world retrospective studies[2,3]
  - Sub-analysis suggests efficacy in patients in patients who previously failed palonosetron treatment[4,5]
- Patent protection through September 2024 with high bar for generic entry given polymer manufacturing

SUSTOL Proprietary Polymer Technology

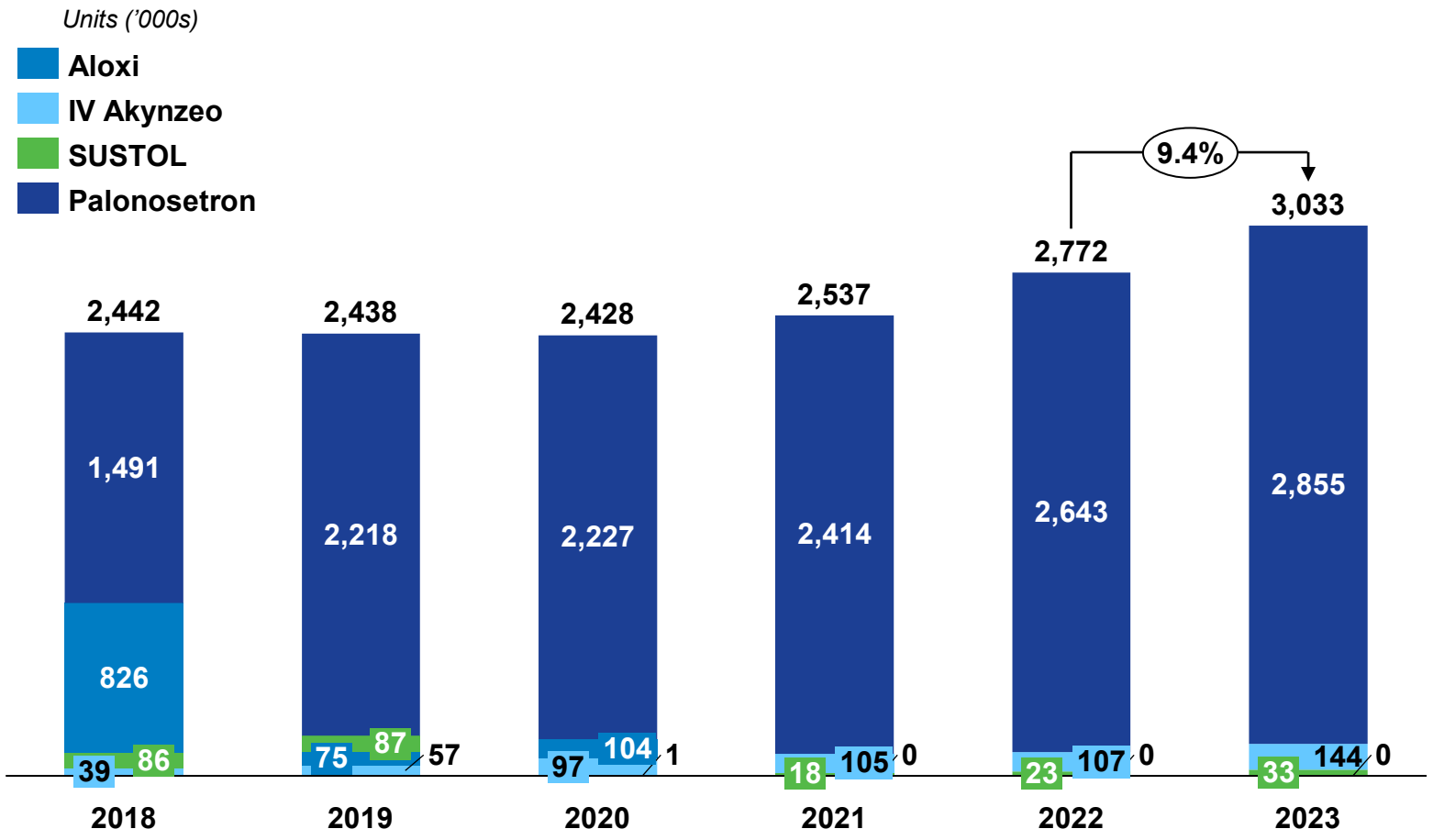
1. SUSTOL is engineered using a unique polymer technology that enables a controlled release of the otherwise shorter-acting granisetron
2. After subcutaneous injection, the polymer undergoes hydrolysis and delivers granisetron in a controlled, sustained release for ≥5 days
3. After the granisetron has been released, the polymer hydrolyzes and is eliminated from the body

1. Schnadig et al. *Future Oncol*. 2016.
2. Vacirca et al. *Future Oncol*. 2018.
3. Erickson et al. *Future Oncol*. 2019.
4. Smith C et al. *Cancer Nursing*. 2019.
5. Arevalo-Araujo et al. *J. Clin Oncol*. 2013.

HERON THERAPEUTICS

Market and Competition

Recent Sales Performance



Commentary

- Market Basket:
  - Generic **palonosetron – *Multiple generic companies***
  - Branded **SUSTOL** (SC extended release granisetron) **– *Heron Therapeutics***
  - **IV Akynzeo** – fosnetupitant (NK1) _ palonosetron (5HT3) fixed dose combination – **Helsinn**
  - *Note: Market basket excludes ultra low priced generic ondansetron and IR granisetron*
- IV 5HT3 Market: 98% of volume are generics (or generic level pricing)
- 5HT3's are the backbone of all antiemetic regimens – used in ~90+% of all patients receiving HEC or MEC
- SUSTOL launched in **Q3 2016** focused on **clinic segment only**
- Branded Aloxi LOE was Q1 2018 (after legal process delayed generic entry

Executive Panel Q&A and Closing Remarks