

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): September 19, 2022 (September 16, 2022)**

**Heron Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-33221**  
(Commission  
File Number)

**94-2875566**  
(I.R.S. Employer  
Identification No.)

**4242 Campus Point Court, Suite 200, San Diego, CA**  
(Address of principal executive offices)

**92121**  
(Zip Code)

**Registrant's telephone number, including area code (858) 251-4400**

N/A

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
<b>Common Stock, par value \$0.01 per share</b>	<b>HRTX</b>	<b>The Nasdaq Capital Market</b>

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 8.01 Other Events.**

On September 16, 2022, Heron Therapeutics, Inc. (the “Company”) issued a press release announcing that the U.S. Food and Drug Administration has approved APONVIETM (aprepitant) injectable emulsion, for intravenous use for the prevention of postoperative nausea and vomiting in adults, as described in the press release furnished herewith as Exhibit 99.1.

A copy of presentation materials, all or a part of which may be used by the Company in investor or scientific presentations from time to time, is furnished as Exhibit 99.2 hereto. The attached materials have also been posted on the Company’s website at [www.herontx.com](http://www.herontx.com). The Company does not undertake any obligation to update this presentation.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Press Release, dated September 16, 2022</a>
99.2	<a href="#">Corporate Presentation, dated September 19, 2022</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Heron Therapeutics, Inc.

Date: September 19, 2022

/s/ David Szekeres

David Szekeres

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Executive Vice President, Chief Operating Officer



## **Heron Therapeutics Announces U.S. FDA Approval of APONVIE™ (HTX-019) for the Prevention of Postoperative Nausea and Vomiting (PONV)**

- APONVIE is the first and only intravenous (IV) formulation of a substance P/neurokinin-1 (NK1) receptor antagonist indicated for PONV -
- Delivered via a single 30-second IV injection, APONVIE has demonstrated rapid achievement of therapeutic drug levels ideally suited for the surgical setting -

SAN DIEGO, Sept. 16, 2022 /PRNewswire/ -- Heron Therapeutics, Inc. (NASDAQ: HRTX), a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs, today announced that the U.S. Food and Drug Administration (FDA) has approved APONVIE (aprepitant) injectable emulsion, for intravenous use for the prevention of postoperative nausea and vomiting (PONV) in adults.

APONVIE is the first and only IV formulation of aprepitant for PONV prevention. Administered via a single 30-second IV injection, APONVIE reaches drug levels associated with  $\geq 97\%$  receptor occupancy in the brain within five minutes and maintains therapeutic plasma concentrations for at least 48 hours. APONVIE is provided in a single-dose vial that delivers the full 32 mg dose approved for PONV. This ready-to-use, easy to administer, innovative IV formulation ensures rapid and consistent exposure in patients undergoing surgery.

An important component of the FDA approval of APONVIE were results from two multicenter, randomized, double-blind clinical studies comparing oral aprepitant to current standard of care, IV ondansetron, for the prevention of PONV in patients during the 48 hours following open abdominal surgery demonstrating that aprepitant was more effective than ondansetron in preventing vomiting. Treatment with aprepitant resulted in approximately 50% fewer patients vomiting in the first 24 and 48 hours compared to ondansetron. In clinical studies, APONVIE was well-tolerated and presented a safety profile comparable to oral aprepitant.

In a 2020 Cochrane meta-analysis, aprepitant was ranked as the most effective drug approved for PONV prophylaxis, being the most effective for the prevention of vomiting in the first 24 hours post-surgery and the drug with the fewest adverse events.

“With the approval of APONVIE our acute care portfolio now addresses the two most common concerns of patients and clinicians after surgery, postoperative pain and postoperative nausea and vomiting. This marks an important milestone for our expanding acute care portfolio and is a testament to our ongoing commitment to developing innovative solutions to help improve the overall patient experience after surgery,” said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. “With approximately 36 million procedures in the U.S. each year in patients with high to moderate risk for PONV, the approval of APONVIE provides an easy to use, highly effective option for these patients that fits seamlessly into our acute care franchise.”

PONV are common adverse effects of anesthesia and surgery, with an estimated 30 percent of patients receiving general anesthesia and up to 80 percent of high-risk patients experiencing

these symptoms, necessitating more effective preventative agents. PONV is a major cause of patient dissatisfaction after surgery, with patients frequently ranking vomiting as the most undesirable outcome of anesthesia. Additionally, PONV presents a significant risk in outpatient surgeries as patients are often discharged within hours after surgery and no longer have access to highly effective antiemetics.

“PONV is commonly experienced after surgery and may result in increased hospital stays, prolonged recovery time, and decreased patient satisfaction” said Ashraf Habib, MBBCh, MSc, MHSc, FRCA, Chief, Division of Women’s Anesthesia at Duke University Hospital. “Oral aprepitant has been used to prevent postoperative nausea and vomiting for more than 16 years and it is exciting to see that, with the approval of APONVIE, physicians can now offer patients a more convenient IV injection that delivers the same effective treatment, with a 48-hour duration of effect, in a rapid, consistent and reliable way, ensuring a better experience for patients postoperatively.”

### **Conference Call and Webcast**

Heron will host a conference call and webcast on September 19, 2022 at 8:30 a.m. ET. The conference call can be accessed by dialing (646) 307-1963 for domestic callers and 800-715-9871 for international callers. Please provide the operator with the passcode 4538096 to join the conference call. The conference call will also be available via webcast under the Investor Relations section of Heron's website at [www.heronrx.com](http://www.heronrx.com). An archive of the teleconference and webcast will also be made available on Heron's website for 60 days following the call.

### **Important Safety Information**

APONVIE should not be used:

- if you are allergic to aprepitant or any of the ingredients in APONVIE
- if you are taking pimizide

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.

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](http://www.fda.gov/medwatch).

The information provided here is not comprehensive. **Please see full Prescribing Information.**

#### **About APONVIE for PONV**

APONVIE (aprepitant) injectable emulsion is a substance P/neurokinin-1 (NK1) receptor antagonist, indicated for the prevention of postoperative nausea and vomiting (PONV) in adults. Delivered via a 30-second intravenous (IV) injection, APONVIE 32 mg was demonstrated to be bioequivalent to oral aprepitant 40 mg with rapid achievement of therapeutic drug levels. APONVIE is the same formulation as Heron's approved CINVANTI® (aprepitant) injectable emulsion formulation for prevention of chemotherapy-induced nausea and vomiting (CINV). APONVIE is supplied in a single-dose vial that delivers the full 32 mg dose for PONV. APONVIE was approved by the U.S. Food and Drug Administration (FDA) in September 2022.

#### **About Heron Therapeutics, Inc.**

Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. Our advanced science, patented technologies, and innovative approach to drug discovery and development have allowed us to create and commercialize a portfolio of products that aim to advance the standard-of-care for acute care and oncology patients. For more information, visit [www.heronrx.com](http://www.heronrx.com).

#### **Forward-looking Statements**

This news release contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers 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, the timing of the commercial launch of APONVIE; the potential market opportunity for APONVIE; the extent of the impact of the ongoing COVID-19 pandemic on our business; 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.

**Investor Relations and Media Contact:**

David Szekeres  
Executive Vice President, Chief Operating Officer  
Heron Therapeutics, Inc.  
dszekeres@herontx.com  
858-251-4447

**APONVIE™ (HTX-019)  
FDA Approval**

**September 19, 2022**

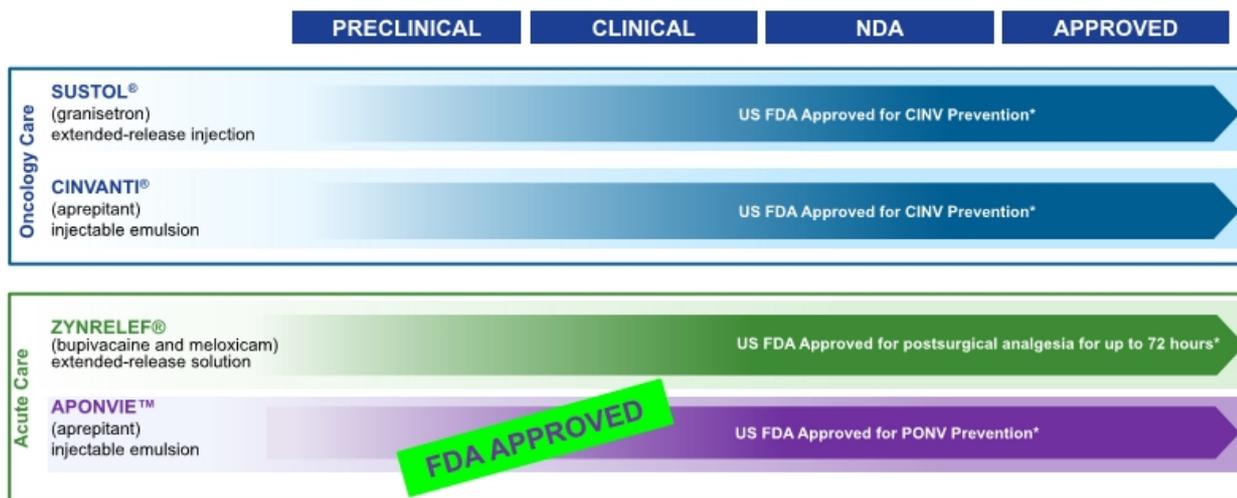


# Forward-Looking Statements

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: the timing of the commercial launch of APONVIE; the potential market opportunity for APONVIE; 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.



# Heron Pipeline



**FDA APPROVED**

**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 periarthicular 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.

Please See IMPORTANT SAFETY INFORMATION at the end of this presentation



## Is Heron's 4<sup>th</sup> Drug Approval and an Ideal Strategic Fit

### INDICATIONS AND USAGE

APONVIE is indicated for the prevention of postoperative nausea and vomiting (PONV) in adults.

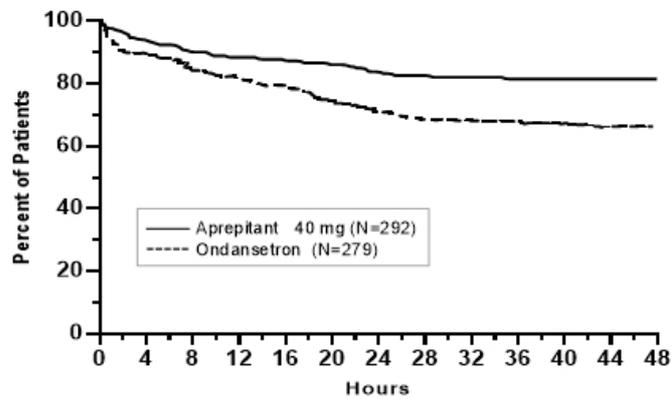
#### Limitations of Use

APONVIE has not been studied for the treatment of established nausea and vomiting.

The recommended dose in adults of APONVIE is 32 mg (4.4 ml) administered as a 30 second intravenous injection prior to induction of anesthesia.

APONVIE will be available as a ready-to-use 32 mg single-dose vial.

# Aprepitant Reduced the Proportion of Patients Vomiting Through 48 hours by 15.2% ( $p < 0.001^*$ ) vs. IV Ondansetron (SOC)



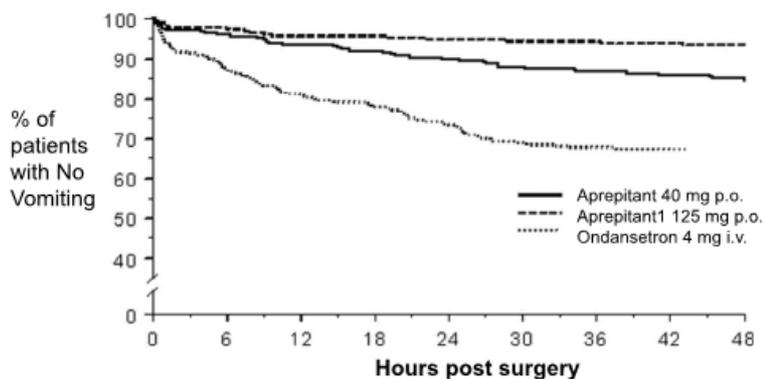
Aprepitant also significantly delayed the time to first vomiting episode compared with ondansetron

Diemunsch P. *Br J Anesth.* 2007;202-11. \*Unadjusted p-value

Please See IMPORTANT SAFETY INFORMATION at the end of this presentation



# 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

Please See IMPORTANT SAFETY INFORMATION at the end of this presentation



# 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
IV Aprepitant**	0.06	18

## 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
- Aprepitant had a favorable safety profile versus placebo

\*Based on high-certainty evidence

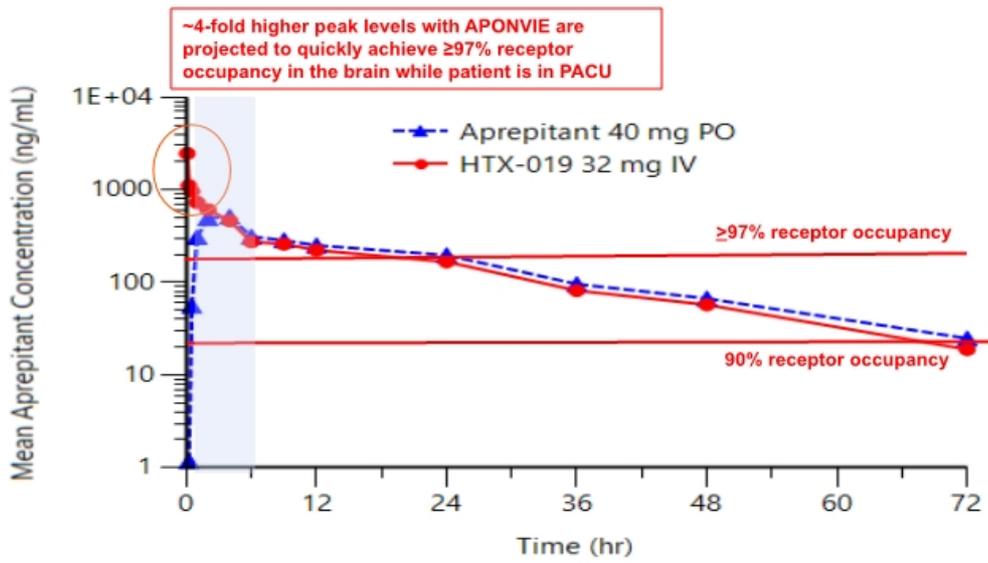
\*Weibel S, Rucker G, Eberhart LHJ, Pace NL, Hartl HM, Jordan OL, et al. *Cochrane Database of Systematic Reviews*. 2020

\*\*High dose aprepitant prodrug

Please See **IMPORTANT SAFETY INFORMATION** at the end of this presentation



# Drug Levels Associated with $\geq 97\%$ Receptor Occupancy Occur Much Faster With APONVIE 30-Second IV Push Than with Oral Aprepitant



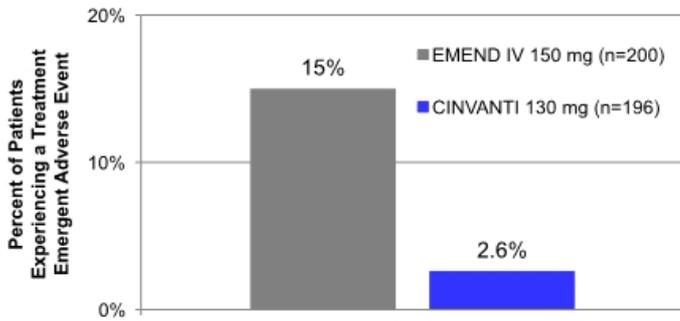
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Please See IMPORTANT SAFETY INFORMATION at the end of this presentation

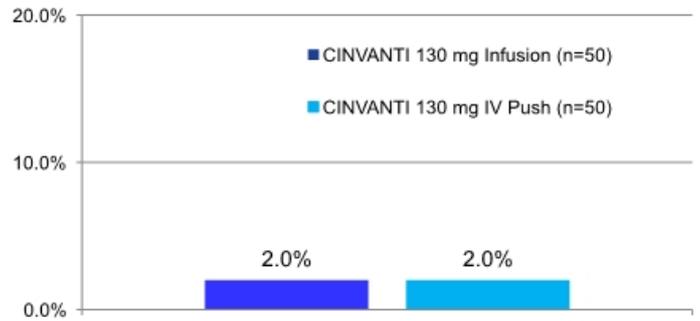
# Why Generic Fosaprepitant is not Used for PONV

- Fosaprepitant is poorly tolerated when administered through peripheral veins with up to 40% infusion site reactions reported<sup>1</sup>, so it was never developed nor approved for PONV
- The 20-30 minute infusion required for fosaprepitant is inconvenient for PONV
- The aprepitant emulsion used in APONVIE is significantly better tolerated than fosaprepitant infusion at equivalent doses (CINVANTI has been used >2.5 million times since launch)

CINVANTI Produced Fewer TEAEs Within 30 Minutes of Infusion Than EMEND IV<sup>2</sup>



CINVANTI Was Well Tolerated When Given by Both 30-minute Infusion and 2-minute IV Push<sup>3</sup>



1. Goncalves, et al. Art and Science of Infusion Nursing 2017;40(6):380-383 2. Ottoboni, et al. Future Oncol. 2018;14(27):2849-2859 3. Ottoboni, et al. Future Oncol. 2019;15(8):865-874.



**AONVIE™**  
(aprepitant) injectable emulsion



## Postoperative Nausea and Vomiting (PONV) Market Opportunity

**HERON**  
THERAPEUTICS  
Developing Best-in-Class Medicine. Improving Lives.™

# APONVIE – The Next Big Opportunity at Heron



Brand Name Conveys  
“Aprepitant for PONV”

- **Large market potential**
  - Addressable market = 69M procedures\*
- **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

Please see **IMPORTANT SAFETY INFORMATION** at the end of this presentation



## Robust Market Research was Conducted with > 700 HCPs

Respondent Type	Quantity
<b>Surgeons</b>	<b>411</b>
<i>Bariatric</i>	30
<i>Cardiothoracic</i>	50
<i>Colorectal</i>	31
<i>ENT</i>	51
<i>General</i>	41
<i>Neuro</i>	35
<i>OB/GYN</i>	52
<i>Orthopedic</i>	39
<i>Plastic</i>	52
<i>Spine</i>	30
<b>Anesthesiologists</b>	<b>151</b>
<i>Anesthesiologist</i>	101
<i>CRNA Nurse</i>	50
<b>Nurses</b>	<b>50</b>
<i>PACU Nurse</i>	50
<b>Pharmacy</b>	<b>100</b>
<i>Pharmacy Directors</i>	70
<i>Clinical Pharmacists</i>	30
<b>Total</b>	<b>712</b>

- Leading 3<sup>rd</sup> party conducted a comprehensive survey on the PONV opportunity and APONVIE Demand
- This market research along with other surveys serve as the basis for:
  - Market size and anti-emetic usage
  - Segmentation strategy
  - HCP preference share
  - Formulary access
  - Pricing strategy
  - Forecasts

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

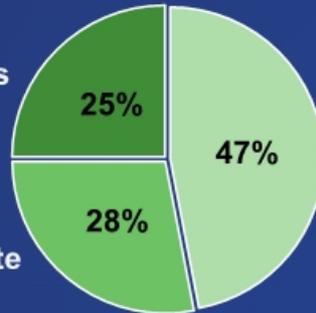
# APONVIE Target Market Opportunity ~ 36 Million Procedures in Patients at Moderate to High Risk for PONV\*

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

~ 17M High Risk Patients

~ 19M Moderate Risk Patients

% PONV Patient Risk



■ Low ■ Moderate ■ High

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)

\* 2023 Procedure projections

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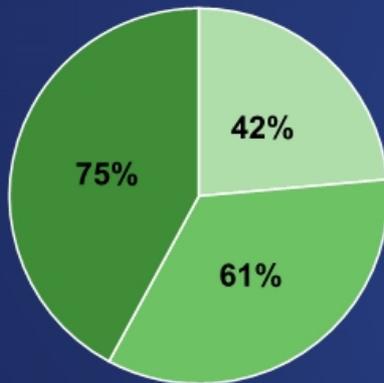
Please see **IMPORTANT SAFETY INFORMATION** at the end of this presentation



# APONVIE Opportunity ~ 38M Annual Procedures\* Receive Prophylaxis for PONV

~12M High to Moderate Risk Patients Currently Not Receiving Prophylaxis\*

## % Prophylaxis by PONV Patient Risk

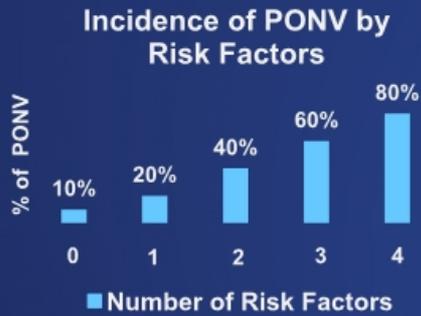


■ Low ■ Moderate ■ High

- Overall, prophylaxis for PONV is currently administered in **56%** of patients\*
- Inadequate prophylaxis for CINV existed when CINVANTI was launched; total NK<sub>1</sub> use increased by **33%** within a year of launch
- **20.7M** annual administrations of rescue treatment for PONV clearly demonstrates the need for better prophylaxis\*

Source: DRG / Clarivate PONV Demand Study (Dec. 2021)  
\* 2023 Procedure projections

# Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting<sup>1</sup>



“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”.

<sup>1</sup> Gan TJ, Belani KG, Bergese S, et al. Anesth Analg. 2020;131(2):411-448.

## Adult PONV<sub>Rx</sub> Management

**1 RISK FACTORS**

- Female sex
- Younger age
- Non-smoker
- Surgery type
- History of PONV/motion sickness
- Opioid analgesia

**2 RISK MITIGATION**

- Minimize use of nitrous oxide, volatile anesthetics, high-dose neostigmine
- Consider regional anesthesia
- Opioid sparing/multimodal analgesia (enhanced recovery pathways)

**3 RISK STRATIFICATION**

Quantify the # of risk factors to determine risk and guide anti-emetic therapy

- 1-2 Risk Factors: Give 2 agents
- > 2 Risk Factors: Give 3-4 agents

**4 PROPHYLAXIS**

- 5HT<sub>3</sub> receptor antagonists
- Antihistamines
- Propofol anesthesia
- Acupuncture
- Corticosteroids
- Dopamine antagonists
- NK-1 receptor antagonists**
- Anticholinergics

**5 RESCUE TREATMENT**

Use anti-emetic from different class than prophylactic drug

THERAPEUTICS™  
Dexamethasone, Ondansetron, Aprepitant, NK-1 Antagonists



# One Push to Prevent PONV

## APONVIE Key Attributes



**First and only IV NK<sub>1</sub> antagonist for the prevention of PONV<sup>3</sup>**



**Superior vomiting prevention versus ondansetron through 48 hours<sup>1-3,a</sup>**



**Administered via a single 30-second IV push<sup>3</sup>**



**Comparable safety profile to IV ondansetron without QT prolongation<sup>3,4</sup>**



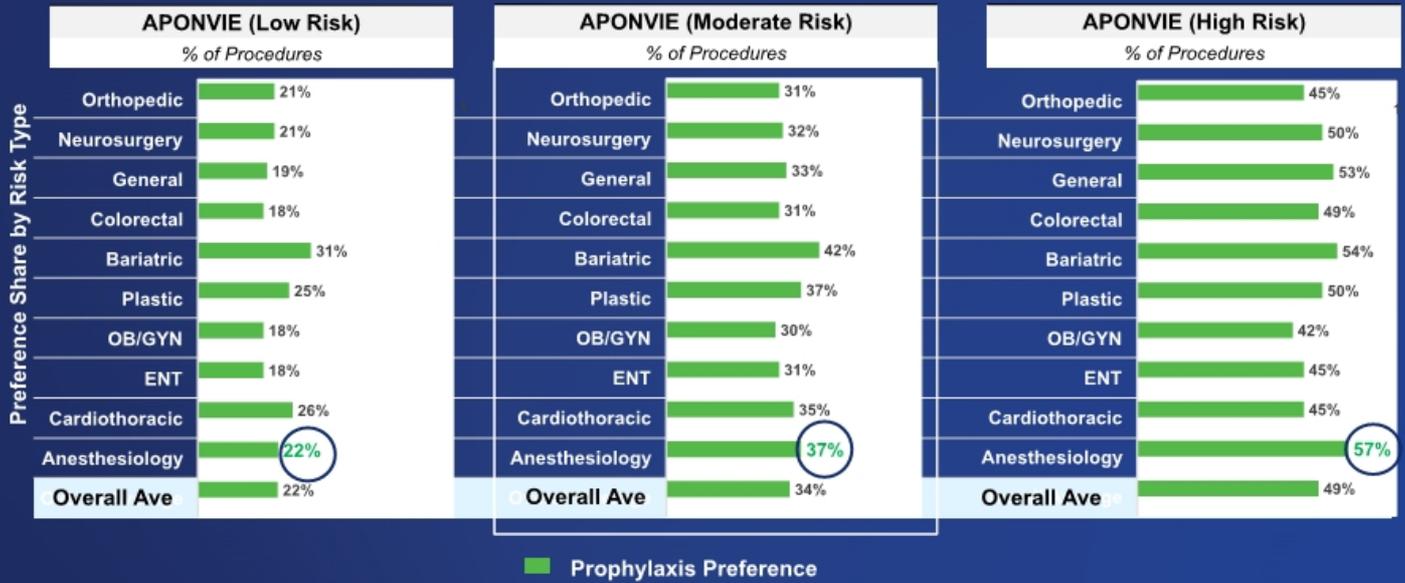
**Reaches therapeutic plasma concentrations associated with ≥97% receptor occupancy within 5 minutes<sup>3,5,6,b</sup>**

<sup>a</sup>Not adjusted for multiplicity.

<sup>b</sup>The relationship between receptor occupancy and efficacy has not been established.

**References:** 1. Diemunsch P, Apfel C, Gan TJ, et al. Preventing postoperative nausea and vomiting: post hoc analysis of pooled data from two randomized active-controlled trials of aprepitant. *Curr Med Res Opin.* 2007;23(10):2559-2565. doi:10.1185/030079907X233115. 2. Gan TJ, Apfel CC, Kovac A, et al. A randomized, double-blind comparison of the NK<sub>1</sub> antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. *Anesth Analg.* 2007;104(5):1082-1089. doi:10.1213/01.ane.0000263277.35140.a3. 3. APONVIE [package insert]. San Diego, CA: Heron Therapeutics Inc; 2022. 4. EMEND [package insert]. Whitehouse Station, NJ: Merck & Co Inc; 2019. 5. Data on file. Summary of clinical pharmacology studies. San Diego, CA: Heron Therapeutics Inc; 2021. 6. Van Laere K, De Hoon J, Bormans G, et al. Equivalent dynamic human brain NK<sub>1</sub>-receptor occupancy following single-dose i.v. fosaprepitant vs. oral aprepitant as assessed by PET imaging. *Clin Pharmacol Ther.* 2012;92(2):243-250. doi:10.1038/clpt.2012.62.

# 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)

# Initial APONVIE Target of > 500k Oral Aprepitant Units

Oral Aprepitant Volume is Growing Rapidly at Premium Price  
(WAC ~ \$88) without Promotion

Oral Aprepitant – 40mg Units<sup>1</sup>



- APONVIE is a 30-second IV push with therapeutic levels associated with  $\geq 97\%$  receptor occupancy achieved within 5 minutes and lasts for 48 hours
- Oral aprepitant was taken 1 to 3 hours prior to induction of general anesthesia in clinical trials and does not reach maximum concentration until 3 hours after administration<sup>2</sup>

<sup>1</sup> Source IQVIA DDD Non-Retail data 2017 – July 2022

<sup>2</sup> Source Oral Aprepitant USPI



## Is the Ideal Strategic Fit for Heron

- PONV is a large market opportunity with **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 Advantages with Unmet Needs
  - Aprepitant is the most effective approved antiemetic, alone or in combination, for vomiting prevention<sup>1</sup>
  - Administered via a single 30-second IV push with rapid onset of action
  - Safety profile comparable to ondansetron without QT prolongation
- Synergies with Heron commercial organization
- Rapid uptake converting oral aprepitant business based on more convenient IV formulation with much less variable absorption and faster onset of action
- Leverage existing CINVANTI manufacturing capabilities to meet COGS target

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

Please see **IMPORTANT SAFETY INFORMATION** at the end of this presentation



# Establish Heron as a Leader in Acute Care

Portfolio of Two Best-in-Class Products Addressing Significant Unmet Needs



The first and only extended-release, dual-acting local anesthetic (DALA), keeping more patients out of severe pain and opioid-free for 72 hours after surgery<sup>1-3</sup>



The first and only IV NK1 approved with a rapid onset of action and demonstrated superiority to the standard-of-care for prevention of vomiting for 48 hours after surgery<sup>4</sup>

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. APONVIE [package insert]

# 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.

## Important Safety Information for Patients (cont.)

- 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](http://www.fda.gov/medwatch).
- The information provided here is not comprehensive. **Please see full Prescribing Information.**

