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): May 13, 2021

Heron Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-33221**	**94-2875566**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

4242 Campus Point Court, Suite 200, San Diego, CA	**92121**
(Address of principal executive offices)	**(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
Common Stock, par value $0.01 per share	**HRTX**	**The Nasdaq Capital Market**

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 May 13, 2021, Heron Therapeutics, Inc. (the "Company") issued a press release announcing that the U.S. Food and Drug Administration has approved ZYNRELEF™ (bupivacaine and meloxicam) extended-release solution for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy and total knee arthroplasty, 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*. The Company does not undertake any obligation to update this presentation.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated May 13, 2021
99.2	Corporate Presentation, dated May 13, 2021
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: May 13, 2021

/s/ David Szekeres
David Szekeres
Executive Vice President, Chief Operating Officer

Heron Therapeutics Announces U.S. FDA Approval of ZYNRELEF™ (HTX-011) for the Management of Postoperative Pain for up to 72 Hours

- ZYNRELEF is the first and only FDA-approved extended-release dual-acting local anesthetic, clinically proven to manage pain and to eliminate the need for opioids for up to 72 hours following surgery better than bupivacaine solution, the current standard-of-care -

- Full U.S. commercial launch of ZYNRELEF is planned for July 2021 -

- Conference call and webcast today at 8:30 am ET -

SAN DIEGO, May 13, 2021 /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 ZYNRELEF (bupivacaine and meloxicam) extended-release solution for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy and total knee arthroplasty. ZYNRELEF, the first and only extended-release dual-acting local anesthetic (DALA), delivers a fixed-dose combination of the local anesthetic bupivacaine and a low dose of the nonsteroidal anti-inflammatory drug (NSAID) meloxicam. The synergy between bupivacaine and meloxicam in ZYNRELEF has resulted in patients experiencing significantly less pain, including severe pain, and significantly more patients requiring no opioids (opioid-free) after surgery as compared to bupivacaine solution, the current standard-of-care.

“The approval of ZYNRELEF marks an exciting milestone for patients, healthcare providers and pain management. Not just because it can reduce postoperative pain for up to 72 hours, but because for many patients it can eliminate the need for opioids after surgery,” said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. “We are in a strong position to launch ZYNRELEF, given our highly successful hospital launch of CINVANTI and our pricing and unprecedented value proposition, which will ensure broad access for patients and healthcare providers. Our existing commercial team will immediately begin working with current accounts to gain formulary access, with full commercial availability expected by July 2021.”

ZYNRELEF is the first and only therapy for postoperative pain management to be rigorously tested in Phase 3 studies and demonstrate superiority to bupivacaine solution. ZYNRELEF demonstrated superior, sustained postoperative pain relief for up to 72 hours and decreased the need for opioids, with more patients opioid-free compared to bupivacaine solution. Clinical studies included over 1,000 patients, with the most common adverse reactions following ZYNRELEF administration being constipation, vomiting, and headache.

“The first three days after surgery are when patients experience the most severe postsurgical pain and are most likely to receive opioids to manage that pain. With the impressive reduction in pain and opioid use demonstrated by ZYNRELEF, we now have an important new option to help many patients achieve an opioid-free recovery,” said Roy G. Soto, M.D., anesthesiologist at Beaumont Health System. “The dramatic increase in opioid-related deaths last year highlights the significant need for safe, effective and non-addictive options to manage pain that decrease opioid exposure and reduce the need for opioid prescriptions after surgery.”

“Approximately 50 million Americans undergo surgery annually, and up to 67 percent of those patients receive opioids,” said Alan Rechter, M.D., Orthopaedic Surgeon at Orthopaedic Associates LLP. “Inadequate postoperative pain management has been associated with poor patient outcomes, causing a substantial burden on public health and contributing to recovery delays. Through today’s approval of ZYNRELEF, we now have a new therapy to offer patients, with the potential to meaningfully impact the postoperative pain management landscape and reduce, and even eliminate, unnecessary exposure to opioids in many patients.”

Conference Call and Webcast

Heron will host a conference call and webcast on May 13, 2021 at 8:30 am ET. The conference call can be accessed by dialing 877-311-5906 for domestic callers and 281-241-6150 for international callers. Please provide the operator with the passcode 3922347 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.herontx.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 for Patients

ZYNRELEF contains an NSAID (non-steroidal anti-inflammatory drug), a type of medicine which:

- **can increase the risk of a heart attack or stroke that can lead to death. This risk increases with higher doses and longer use of an NSAID.**
- **cannot be used during heart bypass surgery.**
- **can increase the risk of gastrointestinal bleeding, ulcers, and tears.**

ZYNRELEF should also not be used if you are allergic to any components of ZYNRELEF, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines; or as a paracervical block, during childbirth.

The most common side effects of ZYNRELEF are constipation, vomiting, and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) can affect the nervous and cardiovascular system; may cause liver or kidney problems; may reduce the effects of some blood pressure medicines; should be avoided if you have severe heart failure; may cause a rare blood disorder, or life-threatening skin or allergic reactions; may harm your unborn baby if received at 20 weeks of pregnancy or later; and may cause low red blood cells (anemia). **Please see full Prescribing Information, including Boxed Warning.**

About ZYNRELEF™ for Postoperative Pain

ZYNRELEF is the first and only dual-acting local anesthetic (DALA) that delivers a fixed-dose combination of the local anesthetic bupivacaine and a low dose of nonsteroidal anti-inflammatory drug meloxicam. ZYNRELEF is the first modified-release local anesthetic to be classified by FDA as an “extended-release” product because ZYNRELEF is also the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and significantly increased proportion of patients requiring no opioids through the first 72 hours following surgery compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. ZYNRELEF was approved by the U.S. Food and

Drug Administration (FDA) on May 12, 2021 for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy and total knee arthroplasty. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures. In September 2020, the European Commission (EC) granted a marketing authorization for ZYNRELEF for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. As of January 1, 2021, ZYNRELEF is approved in 31 European countries including the countries of the European Union and European Economic Area and the United Kingdom.

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.herontx.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 ZYNRELEF in the U.S.; the timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunity for ZYNRELEF in the US and Europe; the extent of the impact of the ongoing Coronavirus Disease 2019 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

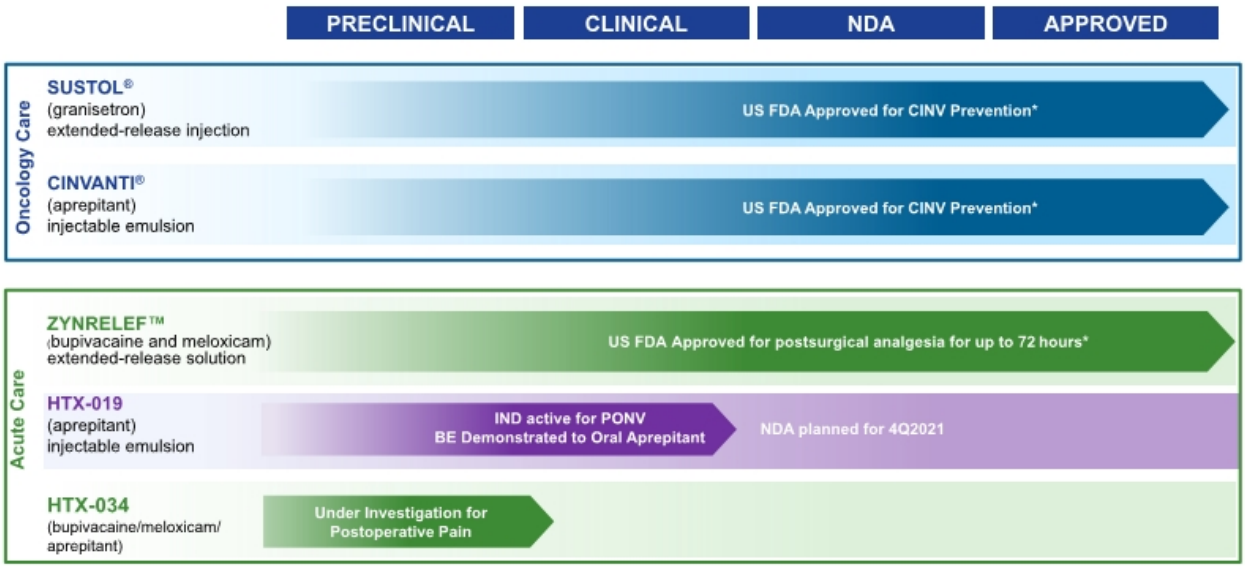
Exhibit 99.2


ZYNRELEF™
(bupivacaine and meloxicam)
extended-release solution
Approval
May 13, 2021
HERON
THERAPEUTICS

Forward-Looking Statements

This presentation contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. We caution investors that forward-looking statements are based on management's expectations and assumptions as of the date of this presentation, and involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, those associated with: risks associated with achieving the full-year 2021 net product sales guidance for the CINV franchise; the timing of the commercial launch of ZYNRELEF in the U.S.; the timing of the commercial launch of ZYNRELEF in Europe; the potential market opportunity for ZYNRELEF in the US and Europe; the timing of Health Canada's NDS review process for HTX-011; whether Health Canada issues a Notice of Compliance for the NDS for HTX-011; the timing and results of studies for HTX-011, the HTX-034 development program, and the HTX-019 development program; the expected future balances of Heron's cash, cash equivalents and short-term investments; the expected duration over which Heron's cash, cash equivalents and short-term investments balances will fund its operations; the extent of the impact of the ongoing Coronavirus Disease 2019 (COVID-19) pandemic on our business; and other risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and we take no obligation to update or revise these statements except as may be required by law.

Heron Pipeline



CINV: Chemotherapy-induced 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 agentsis 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. **ZYRNELEF (bupivacaine and meloxicam) extended-release solution** is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy, and total knee arthroplasty. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures.

HTX-034 and HTX-019 are investigational new drugs and are not approved by the FDA

Why Approval of ZYNRELEF is so Important
Postoperative Opioids Can Be a Doorway to Addiction

More than 50 million
surgical procedures happen in the United States.[1]

67% of patients
filled an opioid prescription between 30 days before through 14 days after surgery.[2*]

> 2 million Americans
may become persistent opioid users annually after surgery. [1]

In 2020, drug overdoses were linked to more than
90,000 deaths
the highest number ever recorded in a single year.[3]

In addition, most patients take fewer opioids than the amount prescribed after surgery, resulting in excess opioid pills that are accessible to others.[4]

80%
of patients report unused opioid tablets[4]

Up to **77%**
of opioid pills remain inside the home in unsecured locations[4]

51%
of nonmedical users of opioids received them from friends and family[5]

More than
$23.4 billion
in annual healthcare costs associated with persistent opioid users can be attributed to postoperative pain management.[1,6]

* This was determined using a 20% national sample of Medicare claims among beneficiaries aged 65 and older with Medicare Part D claims who underwent a major or minor surgical procedure between January 1, 2009 and June 30, 2015.

References: 1. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults [published correction appears in *JAMA Surg*. 2018 Mar 1;154(3):272]. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504. **2.** Santosa KB, Hu HM, Brummett CM, et al. New persistent opioid use among older patients following surgery: A Medicare claims analysis. *Surgery*. 2020;167(1):732-742. doi:10.1016/j.surg.2019.04.014 **3.** NCHS, National Vital Statistics System. Estimates for 2020 are based on provisional data. Estimates for 2011–2019 are based on final data (available from https://www.cdc.gov/nchs/nvss/vsrr/mortality_publ_use_data.htm). **4.** Vickerman MC, Long JJ, Pranowo PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surg*. 2017;152(11):1066–1071. doi:10.1001/jamasurg.2017.3931 **5.** Substance Abuse and Mental Health Services Administration. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; Rockville, MD; 2019. Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf. Accessed April 19, 2021. **6.** Brummett CM, Evans-Shreve J, England C, Kong AM, Lew CR, Henriques C, Zimmerman NM, Sun EC. Increased health care costs associated with new persistent opioid use after major surgery in opioid-naive patients. *J Manag Care Spec Pharm*. 2021 Feb 26:1-12. doi: 10.18553/jmcp.2021.20567. Epub ahead of print. PMID: 33624534.

HERON THERAPEUTICS

ZYNRELEF Approved Indications and Limitations of Use

Indication

- ZYNRELEF is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy, and total knee arthroplasty.

Limitations of Use

- Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures.

Unique Labeling Attributes for ZYNRELEF Extended-Release Solution

- ZYNRELEF is first modified-release local anesthetic to be classified by FDA as an “extended-release” product
  - ZYNRELEF only product to demonstrate superiority to immediate release bupivacaine HCL for 72 hours
- 72-hour duration in the indication statement
  - Registrational studies in clinical data section in indicated procedures include pain curves showing 72-hour duration of activity and superiority to standard of care
- Focus is on opioid-free results in clinical data section as both statistically superior and clinically meaningful
- Standard NSAID class warnings included, with modifications due to single-dose local application allowing for additional NSAID use in multimodal analgesia (MMA) with monitoring

HERON THERAPEUTICS

FDA Approach to Modified-Release Local Anesthetics Changed Following Withdrawal of Guidance on Analgesic Indications

- Rather than approving a broad indication based on 1 soft tissue and 1 bony surgical model, FDA approved other modified-release local anesthetics for specific indications based on positive randomized, controlled trials in specific surgical procedures starting in 2020.
- Heron sought advice from FDA throughout development to discuss requirements for a broad label for ZYNRELEF, the only modified-release local anesthetic to demonstrate superiority to bupivacaine solution
- Based on these discussions with FDA, Heron believed that the studies submitted in the ZYNRELEF NDA would be sufficient to obtain a broad indication
- One week prior to PDUFA, FDA informed Heron more PK and safety data would be required to support additional surgical procedures
  - Heron has multiple studies in process intended to support expanded labelling

The Commercialization of ZYNRELEF

Advancing Postoperative Pain Management

May 2021

HERON THERAPEUTICS®

Developing Best-in-Class Medicine. Improving Lives.™

Executive Summary: Go-to-Market Strategy

Vision

ZYNRELEF is the **foundation** of acute postoperative pain management

Strategy

Establish ZYNRELEF as the market leader in indicated launch targets by replacing other local anesthetics, creating a positive user experience and strong base for expansion

Strategic Imperatives

1. Establish ZYNRELEF as a new class and best choice for postoperative pain
2. Raise the bar with ZYNRELEF's superior value proposition to expedite access
3. Highly focused targeting strategy to convert usage and accelerate sales

Strategic Imperative #1

Establish ZYNRELEF as a new class and best choice for postoperative pain

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

Positioning

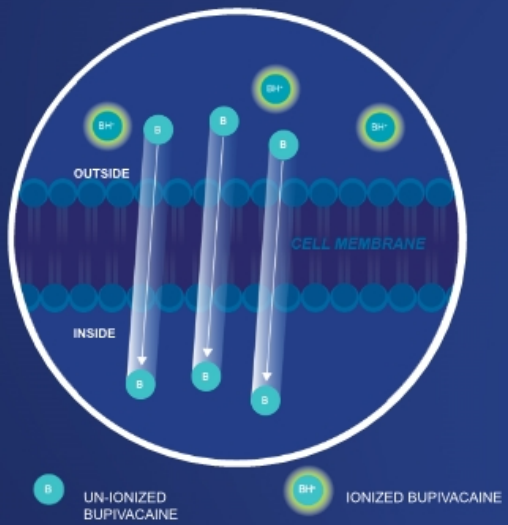
The first and only extended-release, dual-acting local anesthetic (DALA), keeping more patients out of severe pain and opioid-free for 72 hours after surgery[1-3]

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.

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

HERON THERAPEUTICS

Differentiating ZYNRELEF and Establishing A Reason to Believe for Clinicians: A Novel Mechanism of Action



ZYNRELEF is the first and only extended-release dual-acting local anesthetic (DALA).[1-3]

The synergistic combination of bupivacaine with low-dose meloxicam is designed to reduce local inflammation, thereby normalizing the pH and allowing considerably more bupivacaine to penetrate the cell membrane.[1,4]

Market Research[5]

- The majority of physicians found ZYNRELEF's novel mechanism of action to be clinically relevant
- It was viewed as a valuable differentiator when compared to Exparel, which does not target the local inflammatory process

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. **5.** LSSG Mechanic, 2018

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

ZYNRELEF Offers Superior Clinical Value Over Bupivacaine, Not Demonstrated with Exparel

Exparel Share is an early opportunity for ZYNRELEF

- > $400M in sales
- Exparel has never demonstrated head-to-head superiority to bupivacaine
- Exparel has efficacy challenges beyond 24 hours
- Surveyed pharmacy directors state that they would provide better access to ZYNRELEF than to Exparel[6]

	ZYNRELEF	Exparel
Extended-Release Local Anesthetic[1]	✓	✗
Overcomes Challenges of Inflammation at Surgical Site[2]	✓	✗
Pain Reduction Through 72 Hours vs Bupivacaine[1,3-5]	✓	✗
Superior Pain Reduction vs Bupivacaine[1,3,4]	✓	✗
Greater Reduction in Severe Pain vs Bupivacaine[3-4]	✓	✗
Significant Increase in Opioid-Free Patients vs Bupivacaine[1,3,4]	✓	✗
Greater Decrease of Opioid-Related AEs vs Bupivacaine[3]	✓	✗
Needle-free Application[1]	✓	✗

References: 1. ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** Ottoboni T, Quart B, Pawasauskas J, et al. *Reg Anesth Pain Med*. 2020;45(2):117-123. **3.** Viscusi E, Minkowitz H, Winkle P, et al. *Hernia*. 2019;23(6):1071-1080. **4.** Viscusi E, Gimbel JS, Pollack RA, et al. *Reg Anesth Pain Med*. 2019;44(7):700-706. **5.** Lachiewicz PF, Lee G-C, Pollak R, et al. *J Arthroplasty*. 2020;35(10):2843-2851. **6.** DRG Pharmacy Director Surveys.

HERON THERAPEUTICS

An Extensive Body of Peer-reviewed Data will be Available for Launch

MANUSCRIPTS

EPOCH 1 (301), *RAPM*—May 2019
EPOCH 2 (302), *Hernia*—Aug 2019
MOA (Inflammation and PK/PD), *RAPM—Jan 2020*
TKA (209), *JoA—Oct* 2020
Truven HEOR–opioid naive, *JMCP*—July 2019
Hernia (215), *Surgery* – Sept 2020
Bunion (218), *JAPMA*—Jan 2021
Truven HEOR, persistent users, *JMCP*—Feb 2021

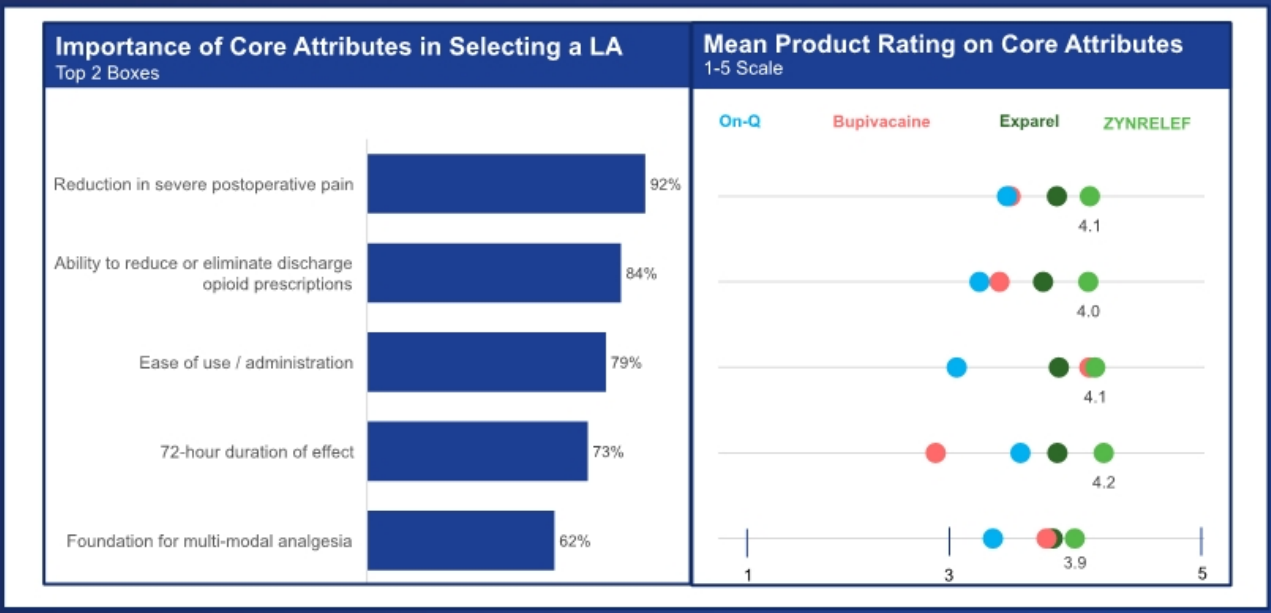
POSTERS & ABSTRACTS

Bunion (202, 208, 301, 218)
HOPE Hernia 1
Hernia (215, 302)
TKA (209, 306)
MOA PK/PD
Truven HEOR
502/PK
211 (Augmentation Mammoplasty)
220 (PK in breast milk and plasma concentrations)
Healthagen TKA/THA opioid use
All Studies—Lack of LAST (C_{max})
All Studies—Max Dose and Release Rates
HOPE Algorithm, HOPE Regimen and Patient Satisfaction

Accepted for 2021 Congresses:
Bone Healing
Safety with NSAID containing MMA
Safety with NSAID containing MMA in the elderly
HOPE Part 1 and 2 Combined

HERON THERAPEUTICS

ZYNRELEF Is Well Positioned on Core Drivers to Create Fast Access and Early Uptake



Source: Company-sponsored ATU Study July 2020 – Survey of 386 surgeons, anesthesiologists, pharmacists, NP/Pas of potential use of an approved product with the attributes for which ZYRELEF was developed

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

Targeting ~2.1M Procedures at Launch With Unprecedented Data Supporting Fast Uptake with Influential Specialties

Indicated Launch Targets		
Inguinal Hernia 617,100	**Bunion** 481,300	**TKA** 1,051,000
Closely-Related Procedures Without Promotion		
Other Hernia 831,000	Other Foot & Ankle 197,900	THA 630,000
Potential Combined Opportunity		
Total 1,448,100	**Total 679,200**	**Total 1,681,000**

- Orthopedic and general surgeons account for 10.6M procedures or 76% of the 14M high value market procedures
- Orthopedic and general surgeons account for 82% of Exparel market utilization
- Orthopedic surgeons are heavy influencers (P&T, new drugs, profitability) across all settings of care

Reference: DRG Claims Analysis, 2019 / May 2021 DRG USPI Market Research. High value market procedures selected on severity and duration of pain and opioid use validated thorough medical review

HERON THERAPEUTICS

$91M of Exparel 2019 Usage was in Our 3 Indicated Procedures

Procedure	Exparel Share	Procedure Volume	Exparel Annual WAC
TKA	25%	263,920	$78M
Hernia	8%	23,212	$7M
Bunion	4%	20,087	$6M
Total Launch	**17%**	**307,219**	**$91M**

References: 1. DRG Claims Analysis. **2.** Exparel Sales – SHA Symphony Health – FY2019.

HERON THERAPEUTICS

Strategic Imperative #2

Raise the bar with ZYNRELEF's superior value proposition to expedite access

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

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

ZYNRELEF's Unprecedented Value Proposition

ZYNRELEF Go-to-Market Strategy Comparison

	ZYNRELEF	Exparel
Lower Acquisition and Average Cost to Support Broad Access	✓	✗
340B Pricing	✓	✗
Pass-Through Status: Separate Reimbursement in HOPD*	✓	✗
Positive Net Cost Recovery	✓	✗
Full-Line Wholesaler Distribution	✓	✗
GPO Contracting	✓	✗

*Medicare Reimbursement only, pass-through status is for 3 years.
GPO = Group Purchasing Organization. **HOPD** = Hospital Outpatient Department.

HERON THERAPEUTICS

ZYNRELEF Reimbursement & Pricing Creates Economic Benefits Across All Settings of Care

Medicare: ZYNRELEF Is Reimbursed Separately in HOPD and ASC

Setting of Care	At Launch *C9399*	3-Year Pass-Through[a] *Product-specific C-code /J-code*
Inpatient	Diagnosis-Related Group (DRG) Payment	
HOPD	95% of AWP	ASP + 6%[c]
HOPD (304B)	95% of AWP	ASP + 6%[c]
ASC	95% of AWP	ASP + 6%[c,d]

Heron will apply for a C-Code with expected grant date of October 1, 2021

Commercial Reimbursement Varies by Payer

- Heron will apply for a J-code to facilitate separate reimbursement with expected grant date of January 1, 2022
- Like all new products, until CMS assigns a permanent code, commercial payers will require a miscellaneous code (J3490 or C9399) for ZYNRELEF
- Heron Connect helps customers navigate coding and reimbursement for ZYNRELEF

a. Heron will apply for transitional pass-through status for ZYNRELEF. Typically, pass-through status is for 3 years. **b.** Exparel (bupivacaine liposome injectable suspension) is a trademark of Pacira Pharmaceuticals, Inc. **c.** ZYNRELEF will be reimbursed at WAC + 3% until ASP is established. **d.** Effective January 1, 2019, ASCs are reimbursed at ASP + 6% for non-opioid postoperative pain management drugs, like ZYNRELEF, when administered during a surgical procedure.
HOPD: hospital outpatient department. **AWP:** average wholesale price. **ASP:** average selling price. **ASC:** ambulatory surgical center. **WAC:** wholesale acquisition cost.

HERON THERAPEUTICS

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

ZYNRELEF	WAC	340B
400 mg/12 mg	$267.50	$203.57
200 mg/6 mg	$135.50	$103.12

Exparel	WAC	340B
266 mg (20 mL)	$344.20	$344.20
133 mg (10 mL)	$189.37	$189.37

ZYNRELEF Savings vs Exparel

WAC $/unit	WAC %	340B $/unit	340B %
~ $77	22%	~$141	41%
~ $54	28%	~$86	46%

Medicare NCR By Site of Care**

	NCR 340B	NCR HOPD	ASC
ZYNRELEF 400 mg/12 mg	$71.53	$10.37	ASP +6%
Exparel 266 mg	($344.20)	($344.20)	ASP +6%
ZYNRELEF 200 mg/6 mg	$34.50	$3.45	ASP +6%
Exparel 133 mg	($189.37)	($189.37)	ASP + 6%

ZYNRELEF Economic Benefit vs. Exparel*

- 340B accounts: >$415 (400 mg to 266 mg) and >$223 (200 mg to 133 mg)
- HOPD accounts: >$354 (400 mg to 266 mg) and >$192 (200 mg to 133 mg)
- Research has shown all customer segments were more sensitive to and favored acquisition cost over reimbursement**

Does not include additional cost of bupivacaine to admix with Exparel to achieve efficacy

*Comparing WAC acquisition cost to NCR reimbursement under Medicare/Exparel NCR assumes ASCs purchasing at WAC.
†Medicare NCRs are shown based on estimated ASP reimbursement for ZYNRELEF and Exparel Q2'21 published ASP reimbursement.
WAC: wholesale acquisition cost. NCR: net cost recovery. HOPD: hospital outpatient department. ASC: ambulatory surgical center.
**DRG Research Pricing Research 2018 and Mock P&T Research 2019

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

HERON THERAPEUTICS

Ease of Use and Implementation

The needle-free application[1]

- Avoids risks of inadvertent venous punctures and eliminates accidental needle sticks with local anesthetics[1]
- Eliminates the need for up to 120 injections (as in total knee arthroplasty)[2] and the time needed for aspiration and application

No specialized training or certification required to administer ZYNRELEF via needle-free application[1]

Launching with 2 SKUs for different surgery requirements[1]

- Reducing cost per procedure
- Minimizing waste

Room temperature storage[1,3]

Kits fit standard OR medication carts (eg, Pyxis™) and include all components

400 mg bupivacaine
12 mg meloxicam
20-mL vial

200 mg bupivacaine
6 mg meloxicam
10-mL vial

Note: Kit components include single-dose glass vial, Luer lock syringe(s), vented vial spike, Luer lock applicator(s), and tip cap(s).
SKU: stock keeping unit.
References: 1. ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** Mont MA, Beaver WB, Dysart SH, et al. *J Arthroplasty*. 2018;33(1):90-96. **3.** ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021.

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

HERON THERAPEUTICS

Strategic Imperative #3

Highly focused targeting strategy to convert usage and accelerate sales

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

High Performing and Focused Organization: Established Platform With Experienced Teams in Place

We are prepared for the launch of ZYNRELEF. Our critical teams are already in place, with extensive experience in successful hospital launches.

Existing Platform Advantages

- Strong KOL relationships
- Successful hospital and Pain Management launch experience
- IDN/hospital/ASC expertise and relationships
- Reimbursement infrastructure in place
- GPO contracts, Full-line wholesaler agreements and 3PL in place
- **89 New Hospital Sales Reps**
  - P&T Experience
  - Pain Experience
  - OR Experience
  - Pull-Through Experience

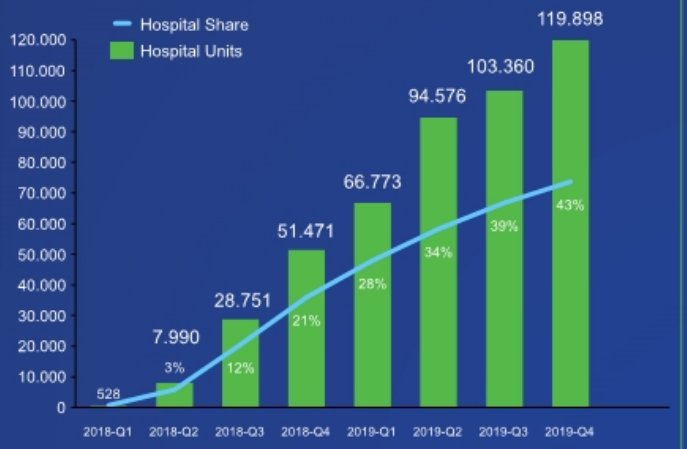
Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

A Proven Track Record of Hospital Launch Success

- Heron launched CINVANTI in January 2018
- In a very short time period, we quickly achieved significant market share
- Flawless execution:
  - Superior pricing and contracting
  - Providing 340B discount
  - Differentiated product attributes
  - Rapid formulary adoption
  - Accelerated account pull-through
  - Trade and reimbursement expertise

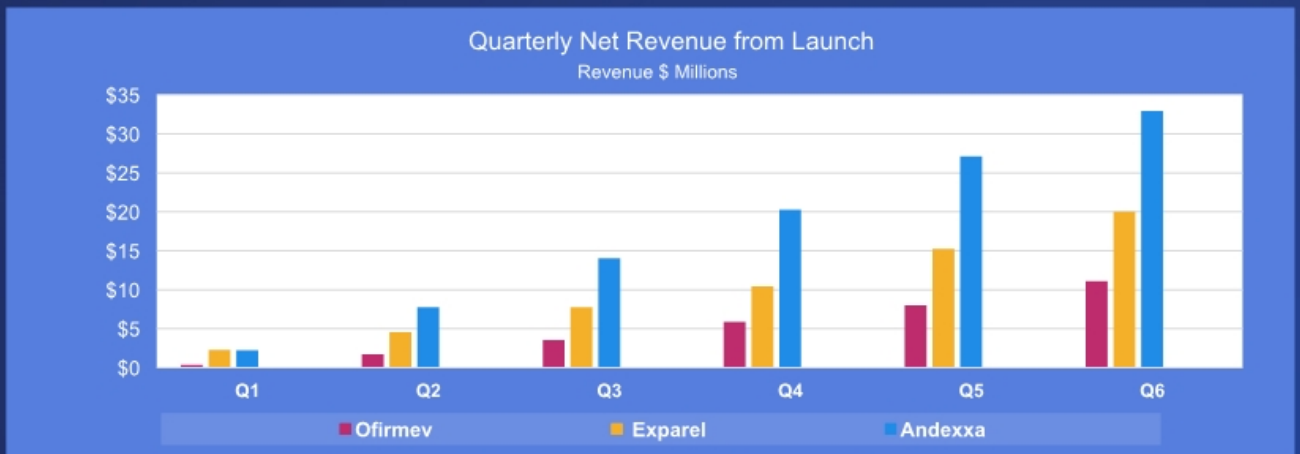
We will leverage the success and experience gained from CINVANTI as we enter the postoperative pain management landscape with ZYNRELEF.

CINV Hospital Share/Units



Reference : Chargeback/867 5.5.2020, IMS DDD 5.1. 2020.

Comparison of Successful Hospital Launches



Product	Launch Date	Q1	Q2	Q3	Q4	Q5	Q6	Q1-Q6 TOTAL
Andexxa	**May-Jun 2018**	$2.2	$7.7	$14.0	$20.3	$27.1	$33.0	**$104.3**
Exparel	**May 2012**	$2.3	$4.6	$7.8	$10.4	$15.2	$20.0	**$60.4**
Ofirmev	**Jan 2011**	$0.4	$1.7	$3.5	$5.9	$8.0	$11.1	**$30.60**

Source: Net product revenue & launch dates based on SEC filings

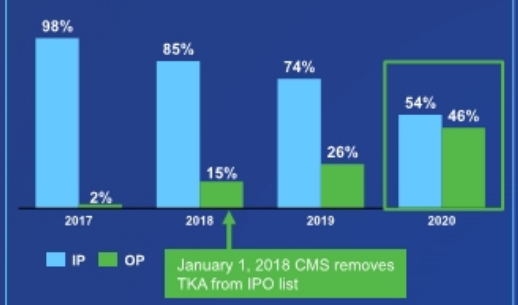
HERON THERAPEUTICS

Outpatient Growth is Anticipated to Accelerate Over the Next 3 Years

- CMS will eliminate the Inpatient Procedure Only (IPO) list over 3 years starting in CY 2021
- CMS has expanded the ASC-Covered Procedures List including Total Hip Arthroplasty
- CMS has eliminated their exclusion criteria leaving the determination of appropriate site of care to the physician

Launch Procedure Outpatient Shift in 2020

TKA Outpatient Shift



Reference: Surgical procedure volume data, 2017-2020. New York, NY: LexisNexis; 2021.

HERON THERAPEUTICS

ZYNRELEF Competitive Position Across Settings of Care

~14M
High Value Market Procedures[1]

Hospital Inpatient 46% (6.5M procedures)

- Bundled in DRG
- 57% (3.7M) of inpatient procedures are done in 340B hospitals

Hospital Outpatient 39% (5.4M procedures)

- 17% (0.9M) have Medicare reimbursement (3-year pass-through)
- 58% (3.1M) eligible for 340B discount
- Multiple SKUs – lower average costs

Ambulatory Surgical Centers 15% (2.1M procedures)

- 18% (0.4M) eligible for Medicare reimbursement at ASP + 6%
- Multiple SKUs – lower average costs

54% of the opportunity lends itself to favorable reimbursement and access

76% of ~2.1M indicated launch procedures opportunity lends itself to favorable reimbursement and access

OVERALL TOTAL

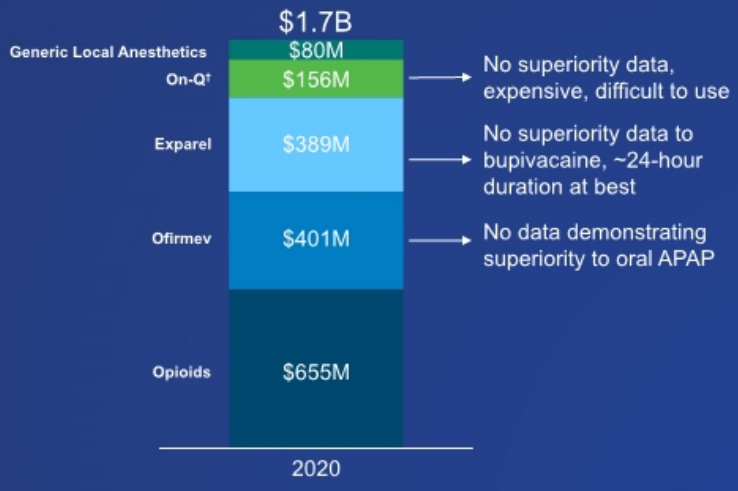
- **ZYNRELEF has lower acquisition cost benefit versus Exparel**
- **ZYNRELEF will have HOPD reimbursement – 3-year pass-through**
- **ZYNRELEF will offer 340B pricing**

SKU: stock keeping unit. **HOPD:** hospital outpatient department. 1. **Reference:** 2019 DRG Claims Data: Procedures selected on severity and duration of pain and opioid use validated thorough medical review

HERON THERAPEUTICS

Branded Product Utilization and Spending is ~$1B Despite Limitations of Current Products

Units	2020	YOY%
Local Anesthetics	16.8M	12%
Exparel	1.3M	-4%
Ofirmev*	8.5M	-23%
Opioids	151.9M	-2%
TOTAL	**178.4M**	**-2%**



*Ofirmev sales decline with generic entries.
†On-Q sales are estimated at ~$150M (down mid-single digits) 2019.
Reference: SHA Symphony Health – FY2019-2020.

58% of Prioritized Target Accounts are Fast Moving

	Accts	340B %	high value market Procedures	Indicated Launch Procedures	Branded Utilization
Hospitals	705	53%	4.6M	1.2M	$309M
ASC	398	0%	414K	144K	$13M

0-3 Months
When will the account order post commercial availability of ZYNRELEF

4-8 Months
When will the account order post commercial availability of ZYNRELEF

*Includes Exparel and Offirmev. **ASC:** ambulatory surgical center. **WAC:** wholesale acquisition cost.
References: 1. Symphony Drug Market – 2020. **2.** LexisNexis Procedure Data August 2019 YTD.

Please see **IMPORTANT SAFETY INFORMATION** on pages 32 to 33 and accompanying full Prescribing Information, including **Boxed Warning**.

HERON THERAPEUTICS

Heron Is Positioned to Execute a Blockbuster Launch for ZYNRELEF

- Proven track record with hospital launch success
- Existing platform and highly experienced team to execute launch
- Shaped market on significant unmet need and opportunity
- Unprecedented clinical and customer value proposition, with significant cost savings
- Highly focused go-to-market launch strategy to accelerate sales

Important Safety Information for Patients

Important Safety Information

ZYNRELEF contains an NSAID (non-steroidal anti-inflammatory drug), a type of medicine which:

- **can increase the risk of a heart attack or stroke that can lead to death. This risk increases with higher doses and longer use of an NSAID.**
- **cannot be used during heart bypass surgery**
- **can increase the risk of gastrointestinal bleeding, ulcers, and tears.**

ZYNRELEF should also not be used:

- if you are allergic to any components of ZYNRELEF, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines.
- as a paracervical block, during childbirth.

Important Safety Information for Patients (cont)

The most common side effects of ZYNRELEF are constipation, vomiting, and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) can affect the nervous and cardiovascular system; may reduce the effects of some blood pressure medications; should be avoided if you have severe heart failure; may cause liver or kidney problems, a rare blood disorder or life-threatening skin or allergic reactions; may harm your unborn baby if received at 20 weeks of pregnancy or later; and may cause low red blood cells (anemia).

Tell your healthcare provider about all your medical conditions and about all the medicines you take including prescription or over-the-counter medicines, vitamins, or herbal supplements to discuss if ZYNRELEF is right for you.

Talk to your healthcare provider for medical advice about side effects. Report side effects to Heron at 1-844-437-6611 or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The information provided here is not comprehensive.

Please see full Prescribing Information, including Boxed Warning.

HERON THERAPEUTICS

Financial Summary

Heron expects that its cash, cash equivalents and short-term investments of $166.5 million as of March 31, 2021 will be sufficient to fund its operations into 2022.

Summary Statement of Operations and Net Cash Used in Operations (In thousands, except per share amounts)	Three Months Ended March 31, 2021
Net product sales	$ 20,018
Operating expenses[1]	72,132
Other income (expense)	(500)
Net loss[1]	$ (52,614)
Net loss per share[2]	$ (0.58)
Net cash used in operations	$ (41,938)
Condensed Balance Sheet Data (In thousands)	**March 31, 2021**
Cash, cash equivalents and short-term investments	$ 166,466
Accounts receivable, net	$ 38,525
Total assets	$ 310,932
Total stockholders' equity	$ 196,225

Common shares outstanding as of March 31, 2021 totaled 91.4 million.

[1] Includes $11.5 million of non-cash, stock-based compensation expense for the three months ended March 31, 2021.
[2] Based on 91.4 million weighted-average common shares outstanding for the three months ended March 31, 2021.