Heron Therapeutics Announces FDA Approval of ZYNRELEF® Indication Expansion to Include Additional Orthopedic and Soft Tissue Procedures

January 24, 2024

– Expanded indication for ZYNRELEF now covers approximately 13 million procedures annually –

SAN DIEGO, Jan. 23, 2024 /PRNewswire/ -- Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company, today announced that the U.S. Food and Drug Administration (the "FDA") has approved its supplemental New Drug Application ("NDA") for ZYNRELEF® (bupivacaine and meloxicam) extended-release solution to expand the indication for soft tissue and orthopedic surgical procedures including foot and ankle, and other procedures in which direct exposure to articular cartilage is avoided. ZYNRELEF was previously approved for foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures in adults.

This expanded indication for ZYNRELEF will now cover an estimated 13 million procedures annually, an estimated increase of 86% over prior indicated procedures. To obtain this labeling expansion, Heron successfully conducted studies for cesarean section, spinal surgery, augmentation mammoplasty, and total shoulder arthroplasty. No unique safety issues were identified from the new clinical trials, and the bupivacaine and meloxicam blood concentrations were consistent with previous experience following ZYNRELEF administration.

"The expanded indication is poised to have a transformative impact on patient care, providing healthcare professionals with a versatile and effective solution for managing postoperative pain across an even wider range of surgical procedures. The new label expansion and recent partnership with CrossLink, combined with the potential approval of the Vial Access Needle ("VAN") later this year, are expected to have a significant positive impact for ZYNRELEF and the Company," said Craig Collard, Chief Executive Officer of Heron.

"We're excited for the opportunity to give even more healthcare providers and patients a new, safe and effective option for achieving long-lasting non-opioid pain control after painful surgical procedures," said Bill Forbes, Executive Vice President, Chief Development Officer at Heron. "This new approval further reinforces our commitment to providing meaningful solutions to address unmet medical needs in the acute care and oncology settings."

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, the current standard-of-care. ZYNRELEF demonstrated superiority compared to bupivacaine with lower pain scores, fewer patients experiencing severe pain, and lower opioid consumption. ZYNRELEF was initially approved by the FDA in May 2021 and received approval of the first supplemental NDA for an expanded label in December 2021.

"Patients undergoing orthopedic procedures often experience severe pain, slowing down their recovery time and potentially leading to other complications. Reducing patients' pain within the first three days is critical for patient satisfaction, and having a product like ZYNRELEF now available for additional orthopedic procedures is a great benefit to have in my practice," said Alexander Sah, M.D., orthopedic surgeon at Sah Orthopaedic Associates. "ZYNRELEF helps my patients recover fully, be discharged sooner, and have significantly less pain, with little to no opioid use."

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 component of ZYNRELEF, similar local anesthetics, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines.
- as a paracervical block, during childbirth.

The most common side effects of ZYNRELEF are soft tissue procedures: vomiting and orthopedic procedures: constipation and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) may 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 adverse effects on cartilage; 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).

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.**

About ZYNRELEF for Postoperative Pain
ZYNRELEF is the first and only dual-acting local anesthetic 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 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 initially approved by the U.S. Food and Drug Administration (the "FDA") in May 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. In December 2021, the FDA approved an expansion of ZYNRELEF's indication to include foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures. On January 23, 2024, the FDA approved ZYNRELEF for soft tissue and orthopedic surgical procedures including foot and ankle, and other procedures in which direct exposure to articular cartilage is avoided. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures. ZYNRELEF was granted a marketing authorization by the European Commission in September 2020 and by the United Kingdom Regulatory Authority in January 2021. In August 2023, we cancelled the ZYNRELEF U.K. marketing authorization and, in October 2023, we cancelled the ZYNRELEF European Union (EU) marketing authorization, as we do not plan to commercially launch ZYNRELEF in the U.K. or the EU.

About Heron Therapeutics, Inc.
Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing and commercializing therapeutic innovations that improve medical care. 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, 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 potential additional market opportunity for the approved expanded U.S. label for ZYNRELEF; 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.

Please see full prescribing information, including Boxed Warning, at www.ZYNRELEF.com.

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