Heron Therapeutics Presents ZYNRELEF® Data at the Society for Obstetric Anesthesia and Perinatology 54th Annual Meeting

May 16, 2022

- New interim data from Phase 2 study suggests ZYNRELEF was well-tolerated and may effectively manage postpartum pain and minimize postoperative opioid use in women undergoing Caesarean sections -

SAN DIEGO, May 16, 2022 /PRNewswire/ -- Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on improving the lives of patients by developing and commercializing therapeutic innovations that improve medical care, today presented at the Society for Obstetric Anesthesia and Perinatology (SOAP) 54th Annual Meeting results from a Phase 2 open-label, multi-cohort study evaluating interim safety and efficacy of ZYRNELEF (bupivacaine and meloxicam) extended-release solution administered postpartum to women undergoing a planned Caesarean section (C-section). ZYNRELEF is currently approved by the U.S. Food and Drug Administration (FDA) for use in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.

The primary objective of this 25-patient study was to characterize the pharmacokinetics (PK) of the active ingredients and excipients of ZYNRELEF in breast milk and/or plasma following postpartum administration of ZYNRELEF 300 mg/9 mg in Cohort 1 and 400 mg/12 mg in Cohort 2 to women undergoing a planned C-section who did not intend to breastfeed. Overall, a single postpartum dose of ZYNRELEF resulted in very low (microgram) levels of bupivacaine and meloxicam in breast milk. Levels of the well-known excipient dimethyl sulfoxide (DMSO) were barely detectable by 48 hours.

The secondary objective was to assess the safety of ZYNRELEF and an exploratory objective was to characterize its efficacy in women undergoing C-section. Results from the study indicate that ZYNRELEF was well-tolerated across both the 300 mg/9 mg and 400 mg/12 mg doses tested. The data also suggest that ZYNRELEF 400 mg/12 mg may effectively manage postpartum pain and minimize postoperative opioid use. In the study, patients given ZYNRELEF 400 mg/12 mg with a scheduled postoperative oral non-opioid multimodal analgesia (MMA) regimen had pain scores in the mild range and 27% had an opioid-free recovery. These patients also requested 69% less opioid rescue medication for pain compared to the lower dose group and reported fewer opioid-related adverse events.

"Managing pain after surgery has always been a passion of mine and I actively teach other surgeons techniques to decrease or completely eliminate the use of opioids after surgery. This is especially important after C-sections in women who need to take care of their newborns very soon afterwards," said Craig Saffer, M.D., an OB-GYN at West Coast OB/GYN, Inc. "Because of this concern, opioids are commonly overprescribed for managing pain following C-sections, and this excess opioid exposure has risks for both mothers and their newborns. More non-opioid postpartum analgesic therapies are needed."

In this study, all patients underwent ropivacaine spinal anesthesia (≤20 mg). In Cohort 1, additional intraoperative anesthesia was managed by institutional practice, and in Cohort 2 patients received intrathecal morphine sulfate 50 µg and fentanyl 20 µg plus scheduled postoperative oral acetaminophen and ibuprofen. Rescue analgesia was available upon request. The poster presentation with this interim data can be found here.

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 constipation, vomiting, 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).

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 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. ZYNRELEF is now indicated in the U.S. in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures. Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel spinal, and head and neck procedures. In September 2020, the European Commission 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. In March 2022, Health Canada issued a Notice of Compliance for ZYNRELEF for instillation into the surgical wound for postoperative analgesia after bunionectomy, open inguinal herniorrhaphy, and total knee arthroplasty surgical procedures.

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

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, the potential market opportunity for ZYNRELEF in the U.S.; 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.

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