Heron Therapeutics Announces Publication of Results from HOPE (Helping Opioid Prescription Elimination), Showing ZYNRELEF™ Minimizes the Need for Opioids in a Real-World Setting, With 95% of Patients Experiencing an Opioid-free Recovery

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SAN DIEGO, July 28, 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 the results from the HOPE Hernia-1 study of ZYNRELEF (bupivacaine and meloxicam) in hernia repair surgery have been published online by *Pain and Therapy* in an article entitled, "Opioid-Free Recovery After Hernia Repair With HTX-011 as the Foundation of a Non-Opioid, Multimodal Analgesia Regimen in a Real-World Setting." In this study, ZYNRELEF, used with scheduled over-the-counter oral analgesics (acetaminophen and ibuprofen) and a personalized opioid prescription algorithm in a real-world environment, enabled more than 90% of patients to be discharged without an opioid prescription, with no callbacks for pain management and 95% of patients to recover opioid-free.

ZYNRELEF is an extended-release solution of bupivacaine and meloxicam that 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.

"Despite efforts to combat the nation's growing opioid crisis, recent evidence suggests that clinical practice is lagging and opioids are still overprescribed after inguinal herniorrhaphy," said Jay Redan, M.D., FACS, Chief of Surgery at Advent Health-Celebration in Celebration, Florida and an author of the publication. "The findings from this study demonstrate the ability of ZYNRELEF to serve as the foundation of non-opioid multimodal analgesia. These data also show ZYNRELEF, in conjunction with an algorithm that distinguishes between patients who need or do not need a discharge opioid prescription, could further increase the proportion of opioid-free patients, decrease the amount of opioids required per patient, and decrease the total number of opioid pills prescribed at discharge after surgery."

The study, HOPE Hernia-1, is part of the HOPE project, which is designed to provide surgeons with practical real-world solutions to effectively manage postoperative pain and eliminate the need for opioid prescriptions using ZYNRELEF as the foundation of a scheduled non-opioid multimodal analgesic regimen.

The *Pain and Therapy* article 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 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 Helping Opioid Prescription Elimination (HOPE) Study

The study, Helping Opioid Prescription Elimination Hernia-1 (HOPE Hernia-1), is part of the HOPE project, which is designed to provide surgeons with practical real-world solutions to effectively manage postoperative pain and eliminate the need for opioid prescriptions using a ZYNRELEF-based non-opioid multimodal analgesia (MMA) regimen. All patients received oral ibuprofen 400 mg and acetaminophen 1 g approximately 2 hours before surgery and at the end of surgery all patients received intraoperative ZYNRELEF (300 mg bupivacaine/9 mg meloxicam) administered via needle-free application into the surgical site after final irrigation and suction of fascial layers and prior to suturing. The study randomized patients into two cohorts receiving non-opioid multimodal analgesia regimens – concurrent versus alternating ibuprofen and acetaminophen – following herniorrhaphy. A personalized algorithm determined eligibility for an opioid prescription at discharge: Numeric rating scale (NRS) pain score ≥6 and/or receipt of a postoperative opioid prior to discharge. Key results of the study include the following:

- The majority of patients (85/93; 91.4%) did not receive an opioid prescription at discharge or at any time through 2 weeks

after surgery, and the results were similar between cohorts (alternating MMA, 89.1%; concurrent MMA, 93.6%).
- Overall, 94.6% of patients were opioid-free through the 2-week follow-up period.
- The mean discharge time following surgery was 2.6 hours in the alternating MMA cohort and 2.2 hours in the concurrent MMA cohort.
- Of the 98% of patients who completed the TSQM-9, most patients were "very" or "extremely" satisfied with their MMA regimen.

ZYNRELEF plus acetaminophen and ibuprofen was well tolerated; safety results were similar between concurrent and alternating MMA cohorts.

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) 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. 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 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.

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