Heron Therapeutics Announces Publication Showing Reduction of Pain and Opioid Use Compared to Bupivacaine in Patients 65 and Older with ZYNRELEF™

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SAN DIEGO, July 21, 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 online publication of new analysis evaluating the efficacy and safety of ZYNRELEF (bupivacaine and meloxicam) extended-release solution in adults aged 65 years and older undergoing bunionectomy and hernia repair from the Phase 3 EPOCH 1 and EPOCH 2 studies. The analysis, published in the peer-reviewed journal *Pain Management*, showed that 58% of bunionectomy and 87% of hernia repair patients aged 65 years and older receiving ZYNRELEF required no opioids to manage their postoperative pain through 72 hours following surgery. Further, throughout the 72-hour period, the mean pain intensity never rose above the mild range.

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.

In this post-hoc analysis, those 65 years and older who were administered ZYNRELEF used fewer opioids in bunionectomy and herniorrhaphy compared with bupivacaine (7.7 morphine milligram equivalents (MME) vs 15 MME, and 1.7 MME vs 3.5 MME, respectively). Importantly, a greater proportion of patients 65 years and older required no opioids (i.e., opioid-free) through 72 hours (58% vs 25%, and 87% vs 64%, respectively).

ZYNRELEF was well tolerated in patients 65 years and older, with a safety profile similar to that for bupivacaine. The safety was also similar to patients aged younger than 65 years and to the overall populations in the Phase 3 studies. No local anesthetic systemic toxicity events occurred and serious adverse events were rare with none considered related to ZYNRELEF.

"Adults ages 65 and over account for approximately half of all surgeries in the United States each year and are commonly prescribed opioids to treat pain following surgery," said Gary M. Oderda, Pharm.D., MPH, Professor, Director Utah Medicaid Drug Regimen Review Center & Director, Pharmacotherapy Outcomes Research Center, and an author of the publication. "In addition, as people age, medications affect them more strongly and are slower to leave their systems, so the side effects of opioids can be severe. This analysis shows ZYNRELEF demonstrated reduction in both pain and the need for opioids in those 65 years and older, which could eliminate the risks of taking opioids without compromising patient care."

ZYNRELEF is the first and only local anesthetic that has been clinically shown to significantly reduce pain, including severe pain, better than bupivacaine, the current standard-of-care, for up to 72 hours and to significantly reduce or eliminate opioid use in many patients following surgery.

The *Pain Management* 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 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 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 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. For more information visit ZYNRELEF.com

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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