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

May 13, 2021

- 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.

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