Heron Therapeutics Announces Approval of ZYNRELEF® by Health Canada for the Management of Postoperative Pain

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- ZYNRELEF is the first and only extended-release local anesthetic approved by Health Canada -

SAN DIEGO, March 17, 2022 /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 Health Canada has issued a Notice of Compliance (NOC) to commercialize ZYNRELEF (bupivacaine and meloxicam extended-release solution) for instillation into the surgical wound for postoperative analgesia after bunionectomy, open inguinal herniorrhaphy, and total knee arthroplasty surgical procedures. Based on prior agreements with the U.S. Food and Drug Administration (FDA), Heron already has clinical studies underway, which we plan to submit to Health Canada to expand the indication statement.

ZYNRELEF is the first and only extended-release bupivacaine product approved in Canada. It is a dual-acting fixed-dose combination of the local anesthetic bupivacaine and a low dose of the nonsteroidal anti-inflammatory drug (NSAID) meloxicam. The meloxicam in ZYNRELEF is associated with an increase in the analgesic effect of bupivacaine, resulting in patients experiencing significantly less pain, including severe pain, after surgery as compared to bupivacaine solution, the current standard-of-care.[1]

"The approval of ZYNRELEF in Canada marks another important regulatory milestone for Heron in our plans for increased global adoption of the product. With the continuing opioid crisis in Canada, we are well positioned with the only approved non-opioid, locally applied analgesic demonstrated to significantly reduce postoperative pain and opioid use," said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. "With this approval, Heron will move forward with partnering discussions and submitting manufacturing supplements to Health Canada for large-scale suppliers of ZYNRELEF to significantly reduce ZYNRELEF's cost of goods. These manufacturing supplements have already been approved in the U.S. We will also work closely with Health Canada to expand the indications for ZYNRELEF in a similar fashion to what we have done with the FDA."

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. The most common adverse event following ZYNRELEF administration in clinical trials was dizziness, which was reported at a similar incidence for bupivacaine solution.

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 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 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 (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. 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 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 Canada; the potential market opportunity for ZYNRELEF in Canada; the timing and results of studies for the expansion of the Canadian label for ZYNRELEF; 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.

[1] Viscusi E, Minkowitz H, Winkle P, Ramamoorthy S, Hu J, Singla N. HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCl in herniorrhaphy: results from the phase 3 EPOCH 2 study. *Hernia*. doi: 10.1007/s10029-019-02023-6.

Viscusi E, Gimbel JS, Pollack RA, Hu J, Lee G-C. HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCl in bunionectomy: Phase 3 results from the randomized EPOCH 1 study. *Reg Anesth Pain Med*. 2019;44:700-706.

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