Heron Therapeutics Announces Publication of the Mechanism of Action Data for HTX-011, a Dual-Acting Local Anesthetic Being Developed for Management of Postoperative Pain

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SAN DIEGO, Dec. 16, 2019 /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 data supporting the novel mechanism of action for the investigational agent HTX-011 have been published online by the *Regional Anesthesia & Pain Medicine* (RAPM) journal, in an article entitled "Mechanism of action of HTX-011: a novel, extended-release, dual-acting local anesthetic formulation for postoperative pain."

HTX-011 is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam in a proprietary Biochronomer® polymer. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control.

The synergistic mechanism of action of HTX-011 was demonstrated in preclinical and clinical studies. Preclinical research in a validated postoperative pig model demonstrated the ability of the low-dose of meloxicam combined with bupivacaine in HTX-011 to address local tissue inflammation at the surgical site, as demonstrated by a less acidic tissue pH level. This maintenance of the physiologic pH level within the surgical site microenvironment was associated with potentiated and prolonged analgesic activity of bupivacaine. The synergy of the low-dose meloxicam combined with bupivacaine in HTX-011 was further confirmed in a Phase 2 bunionectomy study, where HTX-011 achieved superior and sustained pain relief through 72 hours after surgery compared to the Biochronomer polymer formulation of bupivacaine alone, while the Biochronomer polymer formulation of meloxicam alone produced no appreciable pain relief.

"The inability of local anesthetics, including current extended release formulations, to demonstrate consistent postoperative pain relief beyond 24 hours creates challenges for both physicians and patients. This may lead them to use opioids to fill the analgesic gap following surgery," said Eugene Viscusi, M.D., Professor of Anesthesiology and Chief of Pain Medicine in the Department of Anesthesiology at the Sidney Kimmel Medical College of Thomas Jefferson University in Philadelphia, Pennsylvania. "By normalizing pH levels within the inflamed tissue, more bupivacaine is able to penetrate the nerve membrane, prolonging the analgesic activity of HTX-011. The extended delivery of effective pain relief over the course of 72 hours following surgery may allow physicians to manage pain with less reliance on opioids."

The *Regional Anesthesia and Pain Medicine* article can be found here.

About HTX-011 for Postoperative Pain

HTX-011, an investigational agent, is a dual-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam. It is the first and only extended-release local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use through 72 hours compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control. HTX-011 was granted Fast Track designation from the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2017 and Breakthrough Therapy designation in the second quarter of 2018. Heron submitted a New Drug Application (NDA) to the FDA for HTX-011 in October of 2018 and received Priority Review designation in December of 2018. A Complete Response Letter (CRL) was received from the FDA regarding the NDA for HTX-011 on April 30, 2019 relating to chemistry, manufacturing and controls and non-clinical information. No issues related to clinical efficacy or safety were noted. Heron resubmitted an NDA to the FDA for HTX-011 in September 2019 and the FDA set a Prescription Drug User Fee Act (PDUFA) goal date of March 26, 2020. A Marketing Authorisation Application (MAA) for HTX-011 was validated by the European Medicines Agency (EMA) in March 2019 for review under the Centralised Procedure. Heron's New Drug Submission (NDS) for HTX-011 for the management of postoperative pain was granted Priority Review status by Health Canada in October 2019 and accepted by Health Canada in November 2019.

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. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer. 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, those associated with: whether the United States Food and Drug Administration (FDA) approves the New Drug Application (NDA) for HTX-011; the timing of the commercial launch of HTX-011; the timing of the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) review process for HTX-011; whether the European Commission authorizes the Marketing Authorization Application (MAA) for HTX-011; the timing of Health Canada's New Drug

Submission (NDS) review process for HTX-011; whether Health Canada issues a Notice of Compliance for the NDS for HTX-011; 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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