Heron Therapeutics Announces Publication of Results from Study 209, a Phase 2b Study of HTX-011 in Patients Undergoing Total Knee Arthroplasty

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SAN DIEGO, June 4, 2020 /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 results from Study 209, a Phase 2b study of the investigational agent HTX-011 in primary unilateral total knee arthroplasty (TKA), have been published online by *The Journal of Arthroplasty* in an article entitled "HTX-011 Reduced Pain and Opioid Use After Primary Total Knee Arthroplasty: Results of a Randomized Phase 2b Trial." All primary and key secondary endpoints in Study 209 were achieved, with HTX-011 demonstrating statistically significant reductions in pain intensity following surgery.

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. 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.

In Study 209, patients undergoing primary unilateral TKA who received a single, needle-free application of HTX-011 demonstrated superior pain reduction when compared to patients receiving placebo or bupivacaine solution through 48 and 72 hours. In addition, patients receiving HTX–011 consumed fewer opioids when compared to patients receiving placebo or bupivacaine solution. Fewer patients receiving HTX-011 had severe pain through 72 hours, and more patients receiving HTX-011 were deemed ready for discharge at 8, 12 and 24 hours, both as compared to patients receiving placebo or bupivacaine solution. HTX-011 was well tolerated in Study 209, with a safety profile comparable to placebo and bupivacaine solution.

"Effective pain management is crucial after TKA to permit earlier mobilization, maximize patient satisfaction and facilitate outpatient surgery," said Alan J. Rechter, M.D., an orthopedic surgeon at Orthopaedic Associates, LLP. "Based on my experience in Study 209, the fast and easy needle-free administration of HTX-011 provided patients with effective and improved pain control despite taking fewer opioids."

The Journal of Arthroplasty article can be found here.

About Study 209

Study 209 was a randomized, placebo- and active-controlled, double-blind, Phase 2b clinical study in patients undergoing primary unilateral total knee arthroplasty to evaluate the analgesic efficacy, safety and pharmacokinetics of HTX-011 locally administered into the surgical site. Following a dose-escalation phase, 232 patients were randomized, and 222 patients received treatment with: (1) HTX-011 400 mg bupivacaine/12 mg meloxicam administered via instillation into the surgical site; (2) HTX-011 400 mg bupivacaine/12 mg meloxicam administered via instillation into the surgical site plus a low dose of ropivacaine solution injected into the posterior capsule; (3) bupivacaine solution 125 mg administered via multiple injections into the surgical site; or (4) placebo. Ropivacaine solution and bupivacaine solution are generically available standard-of-care local anesthetics used in the management of postoperative pain. This study included a pre-specified hierarchical testing strategy for the primary and key secondary endpoints for the HTX-011 400 mg bupivacaine/12 mg meloxicam treatment groups. The primary endpoint was pain intensity as measured by the Area Under the Curve (AUC) from 0 to 48 hours post-surgery (AUC 0-48) for HTX-011 compared to placebo. The primary and key secondary endpoints were achieved:

- HTX-011 alone and in combination with ropivacaine solution resulted in reductions of 19% and 22%, respectively, in pain intensity through 48 hours when compared to placebo ($p=0.0002$ and $p<0.0001$, respectively).
- HTX-011 alone and in combination with ropivacaine solution resulted in reductions of 18% and 22%, respectively, in pain intensity through 72 hours when compared to placebo ($p=0.0004$ and $p<0.0001$, respectively).
- Sensitivity analyses using patient-reported pain scores without adjustment for opioid use confirmed that HTX-011 alone and in combination with ropivacaine solution resulted in reductions of 29% and 27%, respectively, in pain intensity through 48 hours, and 28% and 26%, respectively, in pain intensity through 72 hours when compared to placebo ($p\leq0.0002$ for both comparisons).
- Sensitivity analyses using patient-reported pain scores without adjustment for opioid use confirmed that HTX-011 alone and in combination with ropivacaine solution resulted in reductions of 19% and 17%, respectively, in pain intensity through 48 hours, and 17% and 16%, respectively, in pain intensity through 72 hours when compared to bupivacaine solution ($P<0.05$ for both comparisons).
- Total opioid consumption for HTX-011 alone or in combination with ropivacaine solution was lower over 24, 48 and 72 hours when compared to placebo or bupivacaine solution.

HTX-011 was well tolerated in Study 209, with a safety profile comparable to placebo and bupivacaine solution.

About HTX-011 for Postoperative Pain

HTX-011, an investigational non-opioid, 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. The Prescription Drug User Fee Act (PDUFA) goal date is June 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 U.S. 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's (EMA) Committee for Medicinal Products for Human Use (CHMP) review process for HTX-011; whether the European Commission (EC) authorizes the Marketing Authorisation 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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View original content:http://www.prnewswire.com/news-releases/heron-therapeutics-announces-publication-of-results-from-study-209-a-phase-2b-study-of-htx-011-in-patients-undergoing-total-knee-arthroplasty-301070514.html

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