Heron Announces Positive Topline Results from Phase 2b Clinical Studies of HTX-011 in Total Knee Arthroplasty and Breast Augmentation

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-HTX-011 Significantly Reduced Both Pain Intensity and Opioid Use in Patients Undergoing Total Knee Arthroplasty-

-HTX-011, Administered via Either Instillation or Nerve Block, Significantly Reduced Both Pain Intensity and Opioid Use in Patients Undergoing Breast Augmentation-

-Conference Call and Webcast Today at 8:30 a.m. ET-

SAN DIEGO, Calif.--(BUSINESS WIRE)--Jun. 21, 2018-- 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 positive topline results from two completed Phase 2b studies of HTX-011: Study 209 (local administration in total knee arthroplasty) and Study 211 (instillation or pectoral pocket nerve block in breast augmentation). HTX-011 achieved the primary endpoints in both studies.

Total Knee Arthroplasty (Study 209) Results

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, 222 patients were randomized to receive: (1) HTX-011 400 mg administered via instillation into the surgical site (HTX-011 alone); (2) HTX-011 400 mg administered via instillation into the surgical site with a low dose of ropivacaine injected into the posterior capsule (HTX-011 combination); (3) bupivacaine 125 mg administered via multiple injections into the surgical site; and (4) placebo. Ropivacaine and bupivacaine 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 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 key secondary endpoint was pain intensity as measured by the AUC from 0 to 72 hours post-surgery (AUC 0-72) for HTX-011 compared to placebo. The primary and key secondary endpoints were achieved:

- The HTX-011 combination and HTX-011 alone resulted in reductions of 23% and 19%, respectively, in pain intensity measured at rest through 48 hours when compared to placebo ($p<0.0001$ and $p=0.0002$, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine ($p=0.0212$).
- The HTX-011 combination and HTX-011 alone resulted in reductions of 22% and 19%, respectively, in pain intensity measured at rest through 72 hours when compared to placebo ($p<0.0001$ and $p=0.0004$, respectively). These pain reductions from HTX-011 were also approximately double that of bupivacaine, which resulted in a reduction of 11%. The HTX-011 combination reduction was significantly better than that of bupivacaine through 72 hours ($p=0.0325$).
- With the more conservative assessment of pain with activity, the HTX-011 combination and HTX-011 alone resulted in reductions of 16% and 12%, respectively, in pain intensity measured with activity through 48 hours when compared to placebo ($p<0.0001$ and $p=0.0017$, respectively). These pain reductions from HTX-011 were significantly better than that of bupivacaine, which resulted in a reduction of 4% ($p=0.0012$ and $p=0.0366$, respectively). Both the HTX-011 combination and HTX-011 alone maintained control of pain with activity through 72 hours with a 15% ($p=0.0002$) and 11% ($p=0.0058$) reduction compared to placebo, respectively.
- The HTX-011 combination significantly reduced opioid use through 48 and 72 hours compared to placebo ($p=0.0091$ and $p=0.0253$, respectively).

Breast Augmentation (Study 211) Results

Study 211 was a randomized, placebo- and active-controlled, double-blind, Phase 2b dose-finding study in patients undergoing augmentation mammoplasty to evaluate the analgesic efficacy, safety and pharmacokinetics of HTX-011 when administered by instillation into the surgical site or via ultrasound-guided lateral and medial pectoral nerve block before surgery. The study consisted of three cohorts comparing HTX-011 nerve block (60 mg, 120 mg, 240 mg) to the standard dose of bupivacaine 50 mg, administered as a nerve block, and placebo, and a final cohort comparing both HTX-011 400 mg administered by instillation and HTX-011 400 mg administered as a nerve block to the same two control groups. A total of 243 patients were enrolled. The primary endpoint was pain intensity as measured by the AUC from 0 to 24 hours post-surgery (AUC 0-24) compared to placebo. The primary endpoint of the study was achieved:

- HTX-011 400 mg administered by instillation into the surgical site and HTX-011 400 mg administered as a nerve block both resulted in reductions of 22% in pain intensity measured at rest through 24 hours when compared to placebo (p=0.0023 and p=0.0055, respectively). These pain reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 8%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine (p=0.0383).
- With the more conservative assessment of pain with activity, HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions of 24% and 23%, respectively, in pain intensity measured with activity through 24 hours when compared to placebo (p=0.0004 and p=0.0015, respectively). These pain reductions from HTX-011 were approximately double that of bupivacaine administered as a nerve block, which resulted in a reduction of 12%.
- HTX-011 400 mg instillation and HTX-011 400 mg nerve block resulted in reductions in total opioid use of 33% and 26%, respectively, when compared to placebo (p=0.0093 and p=0.0435, respectively). These reductions from HTX-011 were approximately triple that of bupivacaine administered as a nerve block, which resulted in a reduction of 10%. The HTX-011 400 mg instillation reduction was significantly better than that of bupivacaine (p=0.0455).

There was a strong correlation between pain reduction and the pharmacokinetics of HTX-011 in both studies.

HTX-011 was well tolerated in both studies, with a safety profile comparable to placebo and bupivacaine solution. There were no deaths and no clinically meaningful differences in overall adverse events, serious adverse events, premature discontinuations due to adverse events, potential local anesthetic systemic toxicity related adverse events or wound healing.

“Without appropriate pre-emptive pain management, certain total joint replacement procedures such as a total knee arthroplasty can be very painful for patients,” said Paul F. Lachiewicz, M.D., Consulting Professor, Department of Orthopedic Surgery, Duke University; Chapel Hill Orthopedic Surgery and Sports Medicine. “The superior pain relief provided by HTX-011 compared to the current standard of care may provide a significant clinical benefit for patients and, as part of a multimodal pain management regimen, has the potential to significantly reduce the amount of opioid medication required for patients in the early postoperative recovery period.”

“With postoperative opioids serving as a gateway to addiction, there is a large unmet need for non-opioid pain alternatives,” said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. “With the results reported today, we have seen positive results across 7 controlled clinical studies and 5 diverse surgical models, including hernia repair, abdominoplasty, bunionectomy, total knee arthroplasty and breast augmentation. We look forward to submitting an NDA to the FDA for HTX-011 in the second half of 2018.”

Conference Call and Webcast

Heron Therapeutics will host a conference call and webcast today, June 21, 2018, at 8:30 a.m. ET (5:30 a.m. PT). 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 9387615 to join the conference call. A slide presentation accompanying today’s press release and conference call may also be found on Heron’s website at www.herontx.com under the Investor Relations section. The conference call will also be available via webcast under the Investor Relations section of Heron's website. An archive of today’s teleconference and webcast will be available on Heron’s website for 60 days following the call.

About HTX-011 for Postoperative Pain

HTX-011, which utilizes Heron’s proprietary Biochronomer ® drug delivery technology, is an investigational, long-acting, extended-release formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the management of postoperative pain. By delivering sustained levels of both a potent anesthetic and a local anti-inflammatory agent directly to the site of tissue injury, HTX-011 was designed to deliver superior pain relief while reducing the need for systemically administered pain medications such as opioids, which carry the risk of harmful side effects, abuse and addiction. HTX-011 has been shown to reduce pain significantly better than placebo or bupivacaine alone in five diverse surgical models: hernia repair, abdominoplasty, bunionectomy, total knee arthroplasty and breast augmentation. 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. In the second half of 2018, Heron expects to submit a New Drug Application (NDA) to the FDA for HTX-011.

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 that 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 cancer or pain. 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 the timing of the HTX-011 NDA filing and review process and other risks and uncertainties identified in the Company's filings with the 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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