Heron Announces Positive Topline Results From Pivotal Phase 3 Clinical Trials of HTX-011 in Bunionectomy and Hernia Repair

March 19, 2018

- HTX-011 Achieved All Primary and Key Secondary Endpoints -

- HTX-011 Produced Statistically Significant Reductions in Both Pain Intensity and Need for Opioids through 72 hours Post-Surgery Compared to Placebo and Bupivacaine Solution, the Standard-of-Care -

- Significantly More Patients Receiving HTX-011 Were Opioid-Free through 72 hours after Surgery and Significantly Fewer HTX-011 Patients Experienced Severe Pain at Any Time -

- NDA Filing Targeted for 2H 2018 -

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

SAN DIEGO--(BUSINESS WIRE)--Mar. 19, 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 its completed Phase 3 studies of the investigational agent HTX-011 in subjects undergoing bunionectomy (Study 301/EPOCH1) and hernia repair (Study 302/EPOCH2). HTX-011 achieved all primary and key secondary endpoints in both Phase 3 trials, demonstrating statistically significant reductions in both pain intensity and the use of opioid rescue medications through 72 hours following surgery.

HTX-011 is the first and only long-acting local anesthetic to demonstrate in Phase 3 studies significantly reduced pain and opioid use compared to bupivacaine solution, the current standard-of-care local anesthetic for postoperative pain control, through 72 hours.

The primary and key secondary endpoints for both Phase 3 studies were identical.

- The primary endpoint was pain intensity as measured by the Area Under the Curve (AUC) score from 0 to 72 hours post-surgery (AUC 0-72) compared to placebo.

Key secondary endpoints in order of evaluation were:

- comparison of AUC 0-72 of pain intensity to bupivacaine solution;
- the total amount of opioid rescue medication consumption compared to placebo through 72 hours after surgery;
- the proportion of patients who received no opioid rescue medication after surgery compared to bupivacaine solution; and
- the total opioid consumption through 72 hours after surgery compared to bupivacaine.

Bunionectomy (Study 301/EPOCH1) Results

EPOCH1 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 60 mg compared to the standard dose of bupivacaine solution (50 mg) and placebo for post-operative pain control following bunionectomy surgery in 412 subjects. All primary and key secondary endpoints were achieved:

- There was a 27% reduction in pain intensity as measured by AUC 0-72 when comparing HTX-011 to placebo ($p<0.0001$).
- There was an 18% reduction in pain as measured by AUC 0-72 when comparing HTX-011 to bupivacaine solution ($p=0.0002$).
- Over 72 hours post-surgery, patients receiving HTX-011 consumed 37% less opioids than placebo patients ($p<0.0001$) and 25% less opioids than patients receiving bupivacaine solution ($p=0.0022$).
- 29% of patients receiving HTX-011 required no opioid medication for 72 hours post-surgery compared to only 2% receiving placebo ($p<0.0001$) and 11% receiving the standard-of-care, bupivacaine solution ($p=0.0001$). These results parallel the significantly reduced incidence of severe pain in patients receiving HTX-011 compared to both placebo (36% reduction; $p<0.0001$) and bupivacaine (29% reduction; $p<0.0001$).

Hernia Repair (Study 302/EPOCH2) Results

EPOCH2 was a randomized, placebo- and active-controlled, double-blind, Phase 3 clinical study evaluating the efficacy and safety of locally administered HTX-011 at 300 mg compared to the standard dose of bupivacaine solution (75 mg) and placebo for post-operative pain control following hernia repair surgery in 418 subjects. All primary and key secondary endpoints were achieved:

- There was a 23% reduction in pain intensity as measured by AUC 0-72 when comparing HTX-011 to placebo (p=0.0004).
- There was a 21% reduction in pain as measured by AUC 0-72 when comparing HTX-011 to bupivacaine solution (p<0.0001).
- Over 72 hours post-surgery, patients receiving HTX-011 consumed 38% less opioids than placebo patients (p=0.0001) and 25% less opioids than patients receiving bupivacaine solution (p=0.0240).
- 51% of patients receiving HTX-011 required no opioid medication for 72 hours post-surgery compared to only 22% receiving placebo (p<0.0001) and 40% receiving the standard-of-care, bupivacaine solution (p=0.0486). These results parallel the significantly reduced incidence of severe pain in patients receiving HTX-011 compared to both placebo (40% reduction; p<0.0001) and bupivacaine (19% reduction; p=0.0372).

HTX-011 was well tolerated in both studies, with a safety profile comparable to placebo and bupivacaine solution. There were no drug-related serious adverse events or discontinuations due to drug-related adverse events in HTX-011-treated patients, and there were fewer opioid-related adverse events in HTX-011-treated patients.

HTX-011 is the first and only long-acting anesthetic designed to address both postoperative pain and inflammation in a single administration at the surgical site. The unique synergy of bupivacaine and meloxicam in HTX-011 has consistently been shown to reduce pain over 72 hours significantly better than bupivacaine alone in multiple diverse surgical models. HTX-011 is administered as a single-dose application via needle-free syringe to directly coat the affected tissue within the surgical site prior to suturing, which makes HTX-011's route of administration faster, easier and potentially safer compared to numerous injections required with current local anesthetics.

"Acute use of opioid pain medications for postoperative pain control is directly linked to over 2 million new persistent opioid users every year and up to 440,000 new cases of Opioid Use Disorder annually, making postoperative opioid use an important contributor to the opioid epidemic in the United States. In addition, with more than a billion opioid pills taken home after surgery every year for postoperative pain control, there is an enormous concern about diversion of these pills and a desperate need for effective non-opioid alternatives," said Eugene R. Viscusi, MD, 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, PA. "The Phase 3 results with HTX-011 suggest it may be a promising foundation in non-opioid multimodal pain management in a wide range of surgical procedures."

"My family has endured unspeakable tragedy, losing our son, Tyler, to a heroin overdose that could have been prevented if he was not first exposed to opioids following a routine elbow surgery. Physicians, patients and families need new, more effective pain management options to address postsurgical pain so that we can lessen the number of people that are exposed to harmful opioids, stopping addiction before it starts," said Travis Bornstein, Founder Hope United.

"With today's results, HTX-011 is the only locally administered anesthetic to demonstrate superior pain relief and a reduction in opioid use as compared to not only placebo, but also the current standard-of-care, bupivacaine solution, in Phase 3 studies," said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron Therapeutics. "We look forward to submitting a New Drug Application for HTX-011 to the U.S. Food and Drug Administration in the second half of 2018. If approved, we believe that HTX-011 could have a significant impact on the opioid crisis by reducing the use of opioids after surgery, while at the same time allowing patients to experience less pain."

Conference Call and Webcast

Heron Therapeutics will host a conference call and webcast today, March 19, 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 1369799 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 prevention 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 three diverse surgical models: bunionectomy, hernia repair and abdominoplasty. HTX-011 is being investigated in ongoing Phase 2 studies in nerve block (breast augmentation) and total knee arthroplasty. The Phase 3 program for HTX-011 is now complete and Heron today reported positive topline data from its pivotal bunionectomy and hernia repair studies. HTX-011 was granted Fast Track Designation from the FDA in the fourth quarter of 2017. In the second half of 2018, Heron expects to file an 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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