Heron Therapeutics Announces U.S. FDA Approval of CINVANTI™ (aprepitant) Injectable Emulsion for the Prevention of Acute and Delayed Chemotherapy-Induced Nausea and Vomiting (CINV)

November 9, 2017

- CINVANTI Is the First and Only Polysorbate 80-Free, Intravenous Formulation of an NK_1 Receptor Antagonist Indicated for the Prevention of Acute and Delayed CINV -

- Heron's CINV Franchise Is the Only Franchise to Include Approved Injectable Therapies That Address Both Mechanisms of CINV -

- U.S. Commercial Launch of CINVANTI Is Planned for January 2018 -

- Conference Call and Webcast Today at 4:30 PM EST -

SAN DIEGO--(BUSINESS WIRE)--Nov. 9, 2017-- Heron Therapeutics, Inc. (Nasdaq: HRTX) (the Company or Heron), a commercial-stage biotechnology company focused on developing novel, best-in-class treatments to address some of the most important unmet patient needs, today announced that the U.S. Food and Drug Administration (FDA) has approved CINVANTI™ (aprepitant) injectable emulsion, for intravenous infusion. CINVANTI is a substance P/neurokinin-1 (NK_1) receptor antagonist, indicated in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). With this approval, Heron now is the only company with approved injectable therapies that address the two primary mechanisms of CINV: SUSTOL®, a serotonin-3 ($5\text{-}HT_3$) receptor antagonist, and CINVANTI, an NK_1 receptor antagonist.

CINVANTI is the first and only polysorbate 80-free, intravenous formulation of an NK_1 receptor antagonist indicated for the prevention of acute and delayed CINV. CINVANTI is the first intravenous formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 receptor antagonist to significantly reduce CINV in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy).[i, ii] CINVANTI does not contain polysorbate 80 or any other synthetic surfactant. Pharmaceutical formulations containing polysorbate 80 have been linked to hypersensitivity reactions, including anaphylaxis and irritation of blood vessels resulting in infusion-site pain.[ii, iii,iv]

CINVANTI was approved based on data demonstrating the bioequivalence of CINVANTI to EMEND IV® (fosaprepitant), supporting its efficacy for the prevention of acute and delayed CINV following HEC and MEC.

Results from 2 pivotal randomized, cross-over bioequivalence studies of CINVANTI and EMEND IV showed subjects receiving CINVANTI reported fewer adverse events than those receiving EMEND IV, including substantially fewer infusion-site reactions.[v]

"CINV remains a high unmet medical need in the oncology community, and 5 full days of CINV coverage continues to be our goal. NK_1 receptor antagonists are recommended for routine use with HEC and are a recommended option with MEC. Despite this, NK_1 receptor antagonists are underutilized in CINV. This provides a large opportunity for CINVANTI to help more patients avoid CINV and adhere to their chemotherapy regimens," said Jeffrey F. Patton, M.D., Chief Executive Officer of Tennessee Oncology.

"Aprepitant has long been the standard in the NK_1 class and it remains the only single-agent NK_1 with proven efficacy in preventing CINV in both the acute and delayed phases in HEC and MEC. Because CINVANTI is a novel, polysorbate 80-free IV formulation of aprepitant, it enables physicians to provide patients with standard-of-care efficacy without the potential risk of polysorbate 80-related adverse events, such as infusion-site reactions," said Rudolph M. Navari, M.D., Ph.D., University of Alabama, Birmingham School of Medicine, Director, Cancer Care Program, Division of Hematology Oncology.

"Since both CINVANTI and SUSTOL have been shown to significantly reduce CINV in both the acute and delayed phase, by complementary mechanisms, they are an excellent strategic and operational fit for the Heron commercial team. The commercial team is ready to launch CINVANTI in January of next year," said Barry D. Quart, Pharm.D., Chief Executive Officer of Heron. "To obtain FDA approval for a second product in just over a year is a significant achievement for Heron, and we remain on-track with our third important product, HTX-011, which we expect to file for FDA review in 2018."

Conference Call and Webcast

Heron will host a conference call and webcast on November 9, 2017 at 4:30 PM EST. 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 3496939 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. Please connect to Heron's website several minutes prior to the start of the broadcast to ensure adequate time for any software download that may be

necessary. An archive of today's teleconference and webcast will be available on Heron's website for 60 days following the call.

About CINVANTI (aprepitant) injectable emulsion

CINVANTI is an intravenous formulation of aprepitant, an NK_1 receptor antagonist for the prevention of CINV. CINVANTI is used in combination with a 5-HT_3 receptor antagonist and dexamethasone. Heron developed CINVANTI, a proprietary novel lipid emulsion formulation of aprepitant, to overcome the low water solubility of aprepitant without polysorbate 80 or other synthetic surfactants, with the goal to reduce the risk for infusion-site reactions and hypersensitivity reactions that are reported with EMEND IV.

Please see Full Prescribing Information at www.CINVANTI.com.

Important Safety Information for CINVANTI

CINVANTI is contraindicated in patients with hypersensitivity to any of the components of CINVANTI. Serious hypersensitivity reactions, including anaphylaxis and anaphylactic shock, have been reported with fosaprepitant, a prodrug of aprepitant, and with oral aprepitant. Symptoms including flushing, erythema, dyspnea, hypotension and syncope have been reported. If symptoms occur, discontinue CINVANTI. Do not reinstate if symptoms occur with first-time use.

Use of pimozide with CINVANTI is contraindicated due to the risk of significantly increased plasma concentrations of pimozide, potentially resulting in prolongation of the QT interval, a known adverse reaction of pimozide.

Use of CINVANTI may result in clinically significant CYP3A4 Drug Interactions. Aprepitant is a substrate, weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4. Use with other drugs that are CYP3A4 substrates may result in increased plasma concentration of the concomitant drug. Use of CINVANTI with strong or moderate CYP3A4 inhibitors (*e.g.*, ketoconazole, diltiazem) may increase plasma concentrations of aprepitant and result in an increased risk of adverse reactions related to CINVANTI. Use of CINVANTI with strong CYP3A4 inducers (*e.g.*, rifampin) may result in a reduction in aprepitant plasma concentrations and decreased efficacy of aprepitant.

Co-administration of CINVANTI with warfarin, a CYP2C9 substrate, may result in a clinically significant decrease in the International Normalized Ratio (INR) of prothrombin time. Monitor the INR in patients on chronic warfarin therapy in the 2-week period, particularly at 7 to 10 days, following initiation of CINVANTI with each chemotherapy cycle.

The efficacy of hormonal contraceptives may be reduced during administration of and for 28 days following the last dose of CINVANTI. Advise patients to use effective alternative or back-up methods of non-hormonal contraception during treatment with CINVANTI and for 1 month following administration of CINVANTI or oral aprepitant, whichever is administered last.

Avoid use of CINVANTI in pregnant women as alcohol is an inactive ingredient for CINVANTI. There is no safe level of alcohol exposure in pregnancy.

No dosage adjustment is necessary for patients with mild to moderate hepatic impairment (Child-Pugh score 5 to 9). There are no clinical or pharmacokinetic data in patients with severe hepatic impairment (Child-Pugh score greater than 9). Additional monitoring for adverse reactions in these patients may be warranted when CINVANTI is administered.

In general, use caution when dosing elderly patients as they have a greater frequency of decreased hepatic, renal or cardiac function and concomitant disease or other drug therapy.

The most common adverse reactions with the 3-day oral aprepitant regimen in conjunction with MEC (≥1% and greater than standard therapy) were fatigue and eructation.

The most common adverse reactions with the single-dose intravenous fosaprepitant regimen in conjunction with HEC were generally similar to that seen in prior HEC studies with oral aprepitant. In addition, infusion site reactions (3%) occurred.

The most common adverse reactions with a single-dose of CINVANTI (≥2%) were headache and fatigue.

Please see Full Prescribing Information at www.CINVANTI.com.

About SUSTOL (granisetron) extended-release injection

SUSTOL is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. SUSTOL is an extended-release, injectable 5-HT_3 receptor antagonist that utilizes Heron's Biochronomer® polymer-based drug delivery technology to maintain therapeutic levels of granisetron for ≥5 days. The SUSTOL global Phase 3 development program was comprised of two, large, guideline-based clinical studies that evaluated SUSTOL's efficacy and safety in more than 2,000 patients with cancer. SUSTOL's efficacy in preventing nausea and vomiting was evaluated in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy).

Please see Full Prescribing Information at www.SUSTOL.com.

About Chemotherapy-Induced Nausea and Vomiting (CINV)

While chemotherapy is one of the most effective and commonly used therapies to help patients fight cancer, it is accompanied by debilitating side effects, including varying degrees of nausea and vomiting, often attributed as a leading cause of premature discontinuation of cancer treatment. The goal of antiemetic therapy is to prevent CINV in both the acute phase (0 – 24 hours after chemotherapy) and delayed phase (24 – 120 hours after chemotherapy). The National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) have categorized chemotherapy regimens based on the degree to which they cause nausea and vomiting: low emetogenic chemotherapy (LEC); moderately emetogenic chemotherapy (MEC); and highly emetogenic chemotherapy (HEC).

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. The Phase 2 development program for HTX-011 was designed to target the many patients undergoing a wide range of surgeries who experience significant postoperative pain. Heron has recently initiated the HTX-011 Phase 3 program and expects to file an NDA in 2018.

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 commercial launch of CINVANTI; postmarketing safety information for SUSTOL and CINVANTI; the potential market opportunity for CINVANTI; whether the HTX-011 Phase 2 study results are indicative of the results in future studies; the timing of completion and results of the Phase 3 studies for HTX-011; the timing of the NDA filing for HTX-011; 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.

[i] EMEND [aprepitant] capsules [US package insert] (Rev. May 2017).

[ii] EMEND [fosaprepitant dimeglumine] for injection [US package insert] (Rev. August 2017).

[iii] Joerger, M. (2012). "Prevention and handling of acute allergic and infusion reactions in oncology." Ann Oncol 23 Suppl 10: x313-319.

[iv] Leal, A. D., K. C. Kadakia, S. Looker, C. Hilger, K. Sorgatz, K. Anderson, A. Jacobson, D. Grendahl, D. Seisler, T. Hobday and C. L. Loprinzi (2014). "Fosaprepitant-induced phlebitis: a focus on patients receiving doxorubicin/cyclophosphamide therapy." Support Care Cancer 22(5): 1313-1317.

[v] Ottoboni, T., G. Boccia, M.R. Keller, M. Cravets, N. Clendeninn, B. Quart. "Bioequivalence of HTX-019 (aprepitant IV) and fosaprepitant in healthy subjects." Presented at Hematology/Oncology Pharmacy Association Annual Conference, March 29-April 1, 2017, Anaheim, CA.

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