Heron Therapeutics Highlights Progress in Pain Management and CINV Franchises and Announces New Development Program

January 11, 2021

- Preliminary Full-Year 2020 Net Product Sales for CINV Franchise of Approximately $88.3 Million, versus Guidance of $85 Million -

- Full-Year 2021 Net Product Sales Guidance for CINV Franchise of $130 Million to $145 Million -

- New Drug Application for HTX-011 for Postoperative Pain Management is Under Review in the US with a May 12, 2021 PDUFA Date -

- Preliminary Results From Phase 1b Bunionectomy Study with HTX-034 Shows Pain Reduction Through 96 Hours with 45.5% of Patients Opioid-Free Through Day 15 -

- Preliminary Results from Phase 1 Study of Low Dose HTX-019 IV Injection Demonstrated Bioequivalence to Approved Oral Aprepitant 40 mg Dose for Prevention of Postoperative Nausea and Vomiting -

SAN DIEGO, Jan. 11, 2021 /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 highlights progress in its pain management and chemotherapy-induced nausea and vomiting (CINV) franchises and announces a new development program for postoperative nausea and vomiting (PONV).

Recent Corporate Progress

Pain Management Franchise

- **New Drug Application Resubmission for HTX-011 Under Review:** The New Drug Application (NDA) resubmission for HTX-011, an investigational agent for the management of postoperative pain, submitted November 12, 2020 to the U.S. Food and Drug Administration (FDA), continues under review. The FDA set a Prescription Drug User Fee Act (PDUFA) goal date of May 12, 2021.

- **Low Dose HTX-034 Produced Greater Pain Reduction to Bupivacaine, the Current Standard-of-Care, Through 96 hours in Bunionectomy Study:** In the Phase 1b portion of this Phase 1b/2 double-blind, randomized, active-controlled dose-escalation study in 33 patients undergoing bunionectomy, the reduction in pain intensity observed with the lowest dose of HTX-034 evaluated (containing 21.7 mg of bupivacaine plus meloxicam and aprepitant) was greater than the bupivacaine 50 mg solution group through 96 hours.
    - In addition, 45.5% of HTX-034 patients remained opioid-free through Day 15 with median opioid consumption of 2.5 milligram morphine equivalents (same as one 5 mg oxycodone pill) through 72-hours, a 71% reduction compared to bupivacaine solution.
    - The expanded Phase 2 portion of the study for HTX-034 will begin this quarter.

CINV Franchise

- **Fourth-Quarter 2020 Net Product Sales:** Preliminary fourth-quarter 2020 net product sales for the CINV franchise were approximately $20.3 million. This included net product sales of approximately $20.0 million for CINVANTI® (aprepitant) injectable emulsion and approximately $0.3 million for SUSTOL® (granisetron) extended-release injection, compared to $34.6 million and $0.5 million, respectively, for the same periods in 2019. Heron believes the most significant impact of the generic arbitrage is over and expects to grow CINVANTI market share in 2021 and beyond.

- **Full-Year 2020 Net Product Sales:** Preliminary full-year 2020 net product sales for the CINV franchise were approximately $88.3 million versus guidance of $85 million. This included net product sales of approximately $87.6 million for CINVANTI and approximately $0.7 million for SUSTOL, compared to $132.2 million and $13.8 million, respectively, for the same periods in 2019. On October 1, 2019, the Company discontinued all discounting of SUSTOL, which resulted in significantly lower SUSTOL net product sales. Heron expects SUSTOL to return to growth in 2021 and beyond.

- **Full-Year 2021 Net Product Sales Guidance:** Heron expects full-year 2021 net product sales for the CINV franchise of

$130 million to $145 million.

PONV Franchise

- **HTX-019 Achieved Bioequivalence to Approved Oral Aprepitant 40 mg Dose for Prevention of PONV:** A new IND for HTX-019 (aprepitant injectable emulsion) for PONV was approved by the FDA in late September of 2020. In the Phase 1 bioequivalence study, HTX-019 32 mg as a 30-second intravenous (IV) injection was bioequivalent to oral aprepitant 40 mg, which is approved for the prevention of PONV. An NDA for HTX-019 is planned in late 2021 for prevention of PONV in adults.

Corporate Update

- **Year-End 2020 Cash Balance:** Heron ended 2020 with approximately $208.5 million in cash, cash equivalents and short-term investments.

"We have made important advances in 2020 in both our pain management and CINV franchises, highlighted by receiving an EU marketing authorization for ZYNRELEF™ (also known as HTX-011), the rapid resubmission to the FDA of the NDA for HTX-011, very promising clinical data with HTX-034, and maintaining stronger than expected net product sales for CINVANTI. We are also excited to announce the development of HTX-019 for PONV, a market that is approximately 20-times larger than CINV, with an expected NDA submission late this year," said Barry Quart, Pharm.D., Chairman and Chief Executive Officer of Heron. "2021 should be a transformational year for Heron with significant growth in our CINV products with net product sales guidance of $130 million - $145 million and the anticipated launch of HTX-011, if approved by the FDA."

About HTX-011 for Postoperative Pain (ZYNRELEF in the European Union and European Economic Area)

HTX-011, an investigational non-opioid analgesic, 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. The U.S. FDA granted Breakthrough Therapy designation to HTX-011 and the NDA received Priority Review designation. A complete response letter (CRL) was received from the FDA regarding the NDA for HTX-011 in June 2020 relating to non–clinical information. No clinical safety or efficacy issues and no chemistry, manufacturing and controls (CMC) issues were identified. Heron resubmitted an NDA to the FDA for HTX-011 in November 2020 and the FDA set a PDUFA goal date of May 12, 2021. Heron is working to respond to a list of questions received from Health Canada in July 2020. In September 2020, the European Commission (EC) granted a marketing authorization for ZYNRELEF (also known as HTX-011) for the treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. The EC's centralized marketing authorization is valid for the 27 countries that are members of the European Union, and the other countries in the European Economic Area, including the United Kingdom.

About HTX-034 for Postoperative Pain

HTX-034, an investigational non-opioid analgesic, is a triple-acting, fixed-dose combination of the local anesthetic bupivacaine with a low dose of the nonsteroidal anti-inflammatory drug meloxicam and aprepitant, an additional agent that further potentiates the activity of bupivacaine. HTX-034 is formulated in the same proprietary polymer as HTX-011. By combining two different mechanisms that each enhance the activity of the local anesthetic bupivacaine, HTX-034 is designed to provide superior and prolonged analgesia. Local administration of HTX-034 in a validated preclinical postoperative pain model resulted in sustained analgesia for 7 days.

About CINVANTI (Aprepitant) Injectable Emulsion

CINVANTI, in combination with other antiemetic agents, is indicated in adults 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 as a single-dose regimen, delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen, and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen. CINVANTI is an IV formulation of aprepitant, a substance P/neurokinin-1 (NK_1) receptor antagonist (RA). CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK_1 RA to significantly reduce nausea and vomiting in both the acute phase (0–24 hours after chemotherapy) and the delayed phase (24–120 hours after chemotherapy). The FDA-approved dosing administration included in the United States prescribing information for CINVANTI is a 30-minute IV infusion or a 2-minute IV injection.

CINVANTI is under investigation for the treatment of COVID-19 as a daily 2-minute IV injection when added to the current standard of care.

Please see full prescribing information at www.CINVANTI.com.

About HTX-019 for Postoperative Nausea and Vomiting

HTX-019 is an IV injectable emulsion formulation designed to directly deliver aprepitant, the active ingredient in EMEND® capsules, which is the only NK_1 RA to be approved in the United States for the prevention of PONV in adults. The FDA-approved dosing for oral EMEND is 40 mg capsules within 3 hours prior to induction of anesthesia for surgery. In a Phase 1 clinical trial, HTX-019 32 mg as a 30-second IV injection was demonstrated to be bioequivalent to oral aprepitant 40 mg.

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 RA that utilizes Heron's Biochronomer® 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 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: adjustments to the preliminary fourth-quarter 2020 and full-year 2020 net product sales for the CINV franchise in connection with completion of financial closing procedures and an audit for the 2020 fiscal year; risks associated with the full-year 2021 net product sales guidance for the CINV franchise; whether the FDA approves the NDA for HTX-011; the timing of the commercial launch of HTX-011 in the U.S., if approved; the timing of the commercial launch of ZYNRELEF in Europe; the timing of Health Canada's NDS review process for HTX-011; whether Health Canada issues a Notice of Compliance for the NDS for HTX-011; the timing and results of studies for the HTX-034 and PONV development programs; the expected future balances of Heron's cash, cash equivalents and short-term investments; the expected duration over which Heron's cash, cash equivalents and short-term investments balances will fund its operations; the extent of the impact of the ongoing Coronavirus Disease 2019 (COVID-19) pandemic on our business; 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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