Heron Therapeutics Announces Initiation of Phase 2 Clinical Study of CINVANTI® for the Treatment of COVID-19

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SAN DIEGO, July 16, 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 the initiation of the GUARDS-1 Study, a Phase 2 clinical study evaluating CINVANTI (aprepitant) injectable emulsion in early hospitalized patients with Coronavirus Disease 2019 (COVID-19). The study initiation follows clearance from the U.S. Food and Drug Administration (FDA) of Heron's Investigational New Drug application for CINVANTI for the treatment of COVID-19.

CINVANTI is an intravenous formulation of aprepitant, a substance P/neurokinin-1 (NK_1) receptor antagonist (RA) approved for use for the prevention of chemotherapy-induced nausea and vomiting in patients with cancer. Substance P, and its receptor NK_1, is distributed throughout the body in the cells of many tissues and organs, including the lungs. COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is associated with lower respiratory tract inflammation that often progresses to Acute Respiratory Distress Syndrome (ARDS). ARDS is associated with high mortality.

Heron's rationale for the investigation of CINVANTI for the treatment of COVID-19 is based on multiple potential mechanisms for activity. Suppressing the cytokine storm could be a crucial step to prevent the clinical deterioration of patients with COVID-19. Administration of aprepitant injectable emulsion to these patients is expected to decrease the production and release of inflammatory cytokines mediated by the binding of substance P to NK_1 receptors, which could prevent the progression of lung injury to ARDS. A hallmark of COVID-19 is a non-productive neurogenic cough, likely due to the increased susceptibility of lung tissue to neurogenic inflammation caused by the disease. Recent studies have demonstrated that administration of oral aprepitant resulted in significantly decreased severity of cough in patients with neurogenic cough associated with advanced lung cancer. Additionally, aprepitant may have direct antiviral activity. Using a computational screening approach, aprepitant was found to have the ability to form hydrogen bonds to key residues within the binding pocket of the main protease of SARS-CoV-2, which is a key enzyme required for replication. CINVANTI is approved for administration as a 2-minute intravenous injection. For these potential benefits, the plasma concentrations of aprepitant produced with the 2-minute intravenous injection of CINVANTI could provide a unique advantage over other methods of administration.

GUARDS-1, also referred to as Study HTX-019-202, is a randomized, placebo-controlled, double-blinded, Phase 2 study designed to investigate the efficacy and safety of adding daily dosing of CINVANTI for 14 days as a 2-minute intravenous injection to standard of care to reduce mortality and the need for assisted ventilation in early hospitalized adult patients with a confirmed SARS–CoV-2 infection. The use of remdesivir through the Emergency Use Authorization and dexamethasone as standard of care are both permitted in the study. The study will include up to approximately 100 adult patients who are hospitalized with a confirmed SARS-CoV-2 infection less than 24 hours prior to randomization. Importantly, the participating clinical study sites have a high concentration of racial and ethnic minority patients affected by COVID-19.

"The COVID-19 pandemic has impacted millions of Americans. With the rate of hospitalization increasing in many states, many intensive care units (ICUs) are reaching capacity. Identifying marketed drugs that may keep more patients out of the ICUs is the most efficient way to impact the current crisis," said Barry Quart, Pharm.D., President and Chief Executive Officer of Heron. "With an existing commercial supply chain for CINVANTI and a positive safety profile in over 1 million single-dose administrations to patients with cancer who also receive dexamethasone, we are hopeful that we can deliver an effective therapeutic option for patients with COVID-19."

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.

IMPORTANT SAFETY INFORMATION

Contraindications

CINVANTI is contraindicated in patients with hypersensitivity to any of the components of CINVANTI.

Concurrent use of pimozide with CINVANTI is contraindicated.

Warnings and Precautions

Clinically Significant CYP3A4 Drug Interactions

Aprepitant is a substrate, weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4.

- Use of CINVANTI with other drugs that are CYP3A4 substrates may result in increased plasma concentration of the concomitant drug.
    - 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 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 CINVANTI.

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, during or soon after administration of CINVANTI have occurred. Symptoms including dyspnea, eye swelling, flushing, pruritus, and wheezing have been reported. If hypersensitivity reactions occur, discontinue CINVANTI. Do not reinitiate CINVANTI in patients who experience these symptoms with previous use.

Decrease in INR with Concomitant Warfarin

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.

Risk of Reduced Efficacy of Hormonal Contraceptives

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.

Use in Specific Populations

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.

Adverse Reactions

The most common adverse reactions are:

- Single-dose fosaprepitant with MEC (≥2%): fatigue, diarrhea, neutropenia, asthenia, anemia, peripheral neuropathy, leukopenia, dyspepsia, urinary tract infection, pain in extremity.
- 3-day oral aprepitant with MEC (≥1% and greater than standard therapy): fatigue and eructation.
- Single-dose fosaprepitant with HEC: generally similar to 3-day oral aprepitant. In addition, infusion site reactions (3%) occurred.
- Single-dose CINVANTI (≥2%): headache and fatigue. The safety profile of CINVANTI in healthy subjects who received a single 2-minute injection was similar to that seen with a 30-minute infusion.

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: the timing and results of the studies for the HTX-019-202 development program; the potential market opportunity for HTX-019-202; 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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