Jaguar Health Achieves Statistically Significant Top Line Results in Study Evaluating Crofelemer for Treatment of Diarrhea Related to Targeted Cancer Therapy

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Preclinical Study Results Expected to Provide Key Supportive Data for Future Clinical Investigations Evaluating Crofelemer for Treatment of Noninfectious Diarrhea in Human Cancer Patients Receiving Targeted Cancer Therapy

SAN FRANCISCO, CA / ACCESSWIRE / August 19, 2019 /Jaguar Health, Inc. (NASDAQ:JAGX) ("Jaguar" or the "Company") announced today that statistically significant top line results have been achieved in a key preclinical pharmacological study to evaluate the effects of crofelemer on diarrhea induced in healthy dogs by a maximally tolerated dose of a specific tyrosine kinase inhibitor (TKI) ("the Study"). The results of the Study, which was funded by a third-party cancer agent manufacturer of an FDA-approved TKI, are expected to provide additional scientific rationale and support for the use of crofelemer in providing symptomatic relief of noninfectious diarrhea in human patients receiving TKI-and/or-other targeted cancer therapy-containing regimens in future human clinical investigations.

The top line results of the Study show that combined crofelemer groups demonstrated superior benefit for "responders" (p= 0.01).

"We are very excited by these results, and hope to see a similar outcome in the interim data, expected to be available in the third quarter of this year, and final data, of a Phase 2 investigator initiated clinical study at Georgetown in human breast cancer patients receiving the targeted cancer therapy regimens Herceptin and Perjeta," Lisa Conte, Jaguar's president and CEO, stated. "Certain targeted cancer therapy agents have been reported to have 90% or higher incidence of diarrhea, which can impair the therapeutic use due to dose-reductions and/or result in discontinuation of such agents."

The Study randomized 24 healthy Beagle dogs into three parallel groups over a treatment period of 28-days dosed with the TKI and placebo or crofelemer (crofelemer 125 mg delayed-release tablets) up to four times a day. Specifically, one group of dogs received crofelemer twice daily (BID group) with the TKI; another group received crofelemer four times daily (QID group) with the TKI; and the third group received placebo capsules four times a day (placebo group) with the TKI.

A key endpoint, a "responder," was defined as any dog having <7 watery stools per week for at least two out of the four weeks of the Study. This clinical endpoint is similar to the "responder" analysis conducted for crofelemer 125 mg delayed-release tablets in the pivotal ADVENT trial that led to the approval of crofelemer 125 mg delayed-release tablets for the symptomatic relief of diarrhea in adult HIV/AIDS patients on antiretroviral therapy.

Top line results show that dogs enrolled in the QID group were 26.8 times more likely to be a "responder" than dogs in the placebo group (p=0.02). Specifically, 7/8 of the dogs in the QID group were "responders" compared to 3/8 of the dogs in the placebo group. Furthermore, dogs randomized to the BID group were 17.8 times more likely to be a "responder" when compared to dogs randomized to the control group (p=0.03). Specifically, 6/8 dogs in the BID group were "responders" compared to 3/8 dogs in the placebo group. There was no significant difference between dosing crofelemer twice daily compared to four times daily in providing symptomatic relief from diarrhea in the dogs. As stated above, the combined BID and QID groups demonstrated superior benefit for "responders" (p= 0.01).

An additional endpoint evaluated the total number of watery stools during the study between the placebo and the two crofelemer treatment groups in the study. This analysis showed that dogs receiving placebo had approximately 33% higher incidence of watery stools when compared to the dogs randomized to the crofelemer BID or QID groups (p=0.04).

"The results from this key preclinical Study shows concordance and remarkable similarity to the substantial benefits that were observed in the pivotal human trial of crofelemer (ADVENT trial) that resulted in the approval of the drug for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy. We are applying our lessons from the ADVENT trial and this preclinical Study in our next clinical study design that we are discussing with the FDA to allow the conduct of a single pivotal study for cancer therapy-related diarrhea in all solid tumor human patients," stated Dr. Pravin Chaturvedi, Jaguar's Chair of the Scientific Advisory Board and Chief Scientific Officer of Napo Pharmaceuticals, Inc., the Company's wholly-owned, human-health focused subsidiary.

Dr. Michael Guy, DVM, MS, PhD, Jaguar's vice president and clinical veterinarian, commented, "No opioids or loperamide were utilized in the Study, as is often the case when targeted therapy is administered to mitigate severe diarrhea, causing alternative issues with absorption of the lifesaving medication, constipation, and lethargy. We are quite impressed with the powerful statistical significance we've seen with only 24 dogs. Furthermore, dogs are an important model predictive of the benefit of the first-in-class mechanism of action of crofelemer in human patients."

Crofelemer is an orally administered botanical (plant-based) drug extracted and purified from the red bark sap of the medicinal *Croton lechleri* tree in the Amazon rainforest. As previously announced, crofelemer is in development for the possible indication of symptomatic relief of cancer therapy-

related diarrhea (CTD). A significant proportion of patients undergoing cancer therapy experience diarrhea, which can cause some patients to discontinue their treatment or reduce their treatment dosage. Novel targeted cancer therapy agents, such as epidermal growth factor receptor antibodies and TKIs, with or without cycle chemotherapy agents, may activate intestinal chloride secretory pathways, leading to increased chloride secretion into the gut lumen, coupled with significant loss of water, that would result in secretory diarrhea.

The Company will report additional data from the Study as further analysis is completed.

About Jaguar Health, Inc.

Jaguar Health, Inc. is a commercial stage pharmaceuticals company focused on developing novel, sustainably derived gastrointestinal products on a global basis. Our wholly-owned subsidiary, Napo Pharmaceuticals, Inc., focuses on developing and commercializing proprietary human gastrointestinal pharmaceuticals for the global marketplace from plants used traditionally in rainforest areas.

For more information about Jaguar, please visit jaguar.health. For more information about Napo, visit napopharma.com.

Forward-Looking Statements

Certain statements in this press release constitute “forward-looking statements.” These include statements regarding the expectation that the results of the Study, which was funded by a third-party cancer agent manufacturer of an FDA-approved TKI, will provide additional scientific rationale and support for the use of crofelemer in providing symptomatic relief of noninfectious diarrhea in human patients receiving TKI-and/or-other targeted cancer therapy-containing regimens in future human clinical investigations, and the expectation that the interim results of a Phase 2 study will be available in the third quarter of this year. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “aim,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this release are only predictions. Jaguar has based these forward-looking statements largely on its current expectations and projections about future events. These forward-looking statements speak only as of the date of this release and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond Jaguar’s control. Except as required by applicable law, Jaguar does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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