Jaguar Health's Study Shows Mytesi (Crofelemer) May Support Treatment of Diarrhea in Cancer Patients Receiving Targeted Therapy While Also Enabling Maintenance and Tolerability of a Higher Dose of the Selected TKI

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SAN FRANCISCO, CA / ACCESSWIRE / October 22, 2019 / Jaguar Health, Inc. (NASDAQ:JAGX) ("Jaguar" or the "Company") announced additional findings today from the recently completed preclinical study evaluating the effects of Mytesi® (crofelemer) on diarrhea induced by a specific tyrosine kinase inhibitor (TKI). The study in healthy dogs was designed to reinforce a scientific rationale for the use of crofelemer when human patients undergo treatment with targeted cancer therapies including, but not limited to, TKIs with or without cycle chemotherapy.

Specifically, the preclinical study showed that crofelemer treatment resulted in lesser incidence and severity of diarrhea with the maintenance and tolerability of a higher dose of the selected TKI. Funded by a third-party manufacturer of an FDA-approved TKI for human use, the study points to potential benefits that the Company hopes to see in future human studies of crofelemer's ability to provide symptomatic relief of noninfectious diarrhea in patients receiving a targeted cancer therapy in an adjuvant or metastatic setting.

The results showed that the animals in the crofelemer groups received approximately 20% higher doses of the TKI than the animals in the placebo group through the four weeks of the treatment period. The TKI dose reductions over the four-week period were statistically higher for the control group compared to the crofelemer QID group and trending toward statistical significance in the BID group. In general, the treatment effect of crofelemer was 1.5 to 2.5 times better than placebo for multiple endpoints in this study.

"Crofelemer is in development for the possible indication of symptomatic relief of cancer therapy-related diarrhea (CTD). We are very excited about these preclinical results and are planning a pivotal trial in CTD patients to evaluate the effects of crofelemer in prevention and/or relief of CTD. Many patients on TKIs require drug holidays or dose reductions in their therapy due to diarrhea. Reduced frequency and severity of diarrhea will allow better maintenance to the therapeutic dose and dosing of any targeted therapies, potentially leading to better clinical outcomes," Lisa Conte, Jaguar's president and CEO, stated. "As we've learned from recent business development discussions with cancer agent manufacturers, adoption and continued use of TKIs and other targeted cancer therapies is directly related to the ability of patients to tolerate use of the therapies, including specifically management of diarrhea."

As previously announced, 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 (125 mg delayed-release tablets) twice or four times a day. 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.

The top line results of the study show that combined crofelemer groups demonstrated superior benefit for "responders" ($p= 0.01$). A key endpoint, a "responder," was defined as any dog having <7 watery stools (diarrhea) 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.

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

Study results also showed improvement in stool consistency as indicated by the reduction in fecal scores for the crofelemer groups compared to the placebo group. Fecal scores are based on a stool scale, a visual tool designed to classify the form of stool into categories that relate to constipation, formed and/or watery stools.

The improvement in tolerability also was reflected in a number of hematological and clinical chemistry parameters. Hematocrit mean changes from baseline on BID and QID were consistently above those of control across the weeks. Mean decreases in albumin for BID and QID were consistently smaller than those of control. Similarly, mean decreases in total protein for BID and QID were consistently smaller than those of control. Mean decreases in creatinine were consistently smaller for BID and QID than for control, as were mean decreases in calcium. These changes are reflective of an improved hydration status in the animals receiving crofelemer.

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.

About Mytesi®

Mytesi (crofelemer) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy (ART). Mytesi is not indicated for the treatment of infectious diarrhea. Rule out infectious etiologies of diarrhea before starting Mytesi. If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen. In clinical studies, the most common adverse reactions occurring at a rate greater than placebo were upper respiratory tract infection (5.7%), bronchitis (3.9%), cough (3.5%), flatulence (3.1%), and increased bilirubin (3.1%).

See full Prescribing Information at Mytesi.com. Crofelemer, the active ingredient in Mytesi, is a botanical (plant-based) drug extracted and purified from the red bark sap of the medicinal *Croton lechleri* tree in the Amazon rainforest. Napo has established a sustainable harvesting program for crofelemer to ensure a high degree of quality and ecological integrity.

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. Our Mytesi® (crofelemer) product is approved by the U.S. FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy.

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 belief that the study in healthy dogs points to potential benefits that the Company hopes to see in future human studies of crofelemer's ability to provide symptomatic relief of noninfectious diarrhea in patients receiving a targeted cancer therapy in an adjuvant or metastatic setting, and Jaguar's efforts to develop crofelemer for the possible indication of symptomatic relief of CTD, including the Company's plan to conduct a pivotal trial in CTD patients to evaluate the effects of crofelemer in prevention and/or relief of CTD. 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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