Napo Pharmaceuticals, a Jaguar Health Family Company, Reports Completion of Last Patient Last Visit for its Pivotal Phase 3 OnTarget Trial of Crofelemer for Preventive Treatment of Cancer Therapy-Related Diarrhea

August 17, 2023

Company on track to report top line data in late October 2023

SAN FRANCISCO, CA / ACCESSWIRE / August 17, 2023 / Napo Pharmaceuticals (Napo), a Jaguar Health, Inc. (NASDAQ:JAGX) family company, today announced that the last patient has completed their final visit for the stage 1 primary endpoint treatment period of Napo's pivotal Phase 3 **OnTarget** trial of crofelemer for preventive treatment of diarrhea in adult cancer patients with solid tumors receiving targeted therapy with or without standard chemotherapy. This trial is studying an indication Napo also refers to as preventive treatment of chemotherapy-induced overactive bowel (CIOB) - which includes symptoms such as chronic debilitating diarrhea (loose and/or watery stools), urgency, and bowel incontinence. Top-line results for the primary endpoint in this trial are expected the last week of October 2023.

"The pivotal Phase 3 OnTarget trial of crofelemer for the preventive treatment of CIOB is our paramount near-term clinical milestone," said Lisa Conte, Jaguar's president and CEO, "and we're very happy to be able to announce that the last enrolled participant in this global trial has completed their stage 1 final visit. The OnTarget trial is evaluating the same formulation of crofelemer that comprises Mytesi®, our FDA-approved, commercially available drug for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy. This is a major milestone for the company and a key step on our journey to making crofelemer available to treat the critical and neglected medical need of CIOB. We are grateful to all the cancer patients who participated in the study and to all the clinical investigators in the U.S., Serbia, Georgia, Argentina, and Taiwan who helped us achieve this important milestone. Our mission is to address not only health issues associated with CIOB, but also to support the quality of life, comfort and dignity of patients living with targeted therapy treatment for months and years, and the ability of patients to be able to comply with their respective chronically administered regimens of targeted therapies."

About the Phase 3 OnTarget Clinical Trial

The OnTarget study is a first-of-its-kind prophylactic clinical trial with a primary endpoint based on patient reported outcomes that address the highly neglected and unmet burden of CIOB, including specifically diarrhea/loose watery stools. This study is evaluating the benefit of crofelemer to prevent or substantially reduce the number of weekly loose and/or watery stools as a continuous measurement over the 12-week treatment period compared to placebo. By completing the targeted enrollment in stage 1, the OnTarget study has approximately 90% power to detect the difference in the incidence and severity of diarrhea between crofelemer and placebo.

The company's expectation is that the double-blind placebo-controlled OnTarget trial will provide evidence that CIOB associated with targeted cancer therapies is chronic, not acute, and impacts the patient's quality of life as well as their ability to remain on their cancer therapy regimens at proven doses for better outcomes. The OnTarget trial is evaluating the effectiveness of crofelemer's novel mechanism of action, intestinal chloride ion channel modulation, to mitigate or substantially reduce chronic cancer therapy-related diarrhea and other symptoms of CIOB.

About Chemotherapy-Induced Overactive Bowel (CIOB)

A significant proportion of patients undergoing cancer therapy experience chemotherapy-induced overactive bowel (CIOB) - which includes symptoms such as chronic debilitating diarrhea (loose and/or watery stools), urgency, and bowel incontinence. Diarrhea has the potential to cause dehydration, and worsen fatigue and non-adherence to treatment in this population. Novel "targeted cancer therapy" agents, such as epidermal growth factor receptor (EGFR) antibodies and tyrosine kinase inhibitors (TKIs), with or without cycle chemotherapy agents, may cause increased electrolyte and fluid content in the gut lumen, which results in passage of loose and/or watery stools (i.e., diarrhea). Diarrhea has been reported as one of the most common side effects of TKIs and may result in cancer therapy drug holidays or reductions from therapeutic dose, potentially impacting patient outcome. Diarrhea is also a common side effect of some approved CDK 4/6 inhibitors. Patients with CTD are 40% more likely to discontinue their chemotherapy or targeted therapy than patients without CTD,[1] and the cost of care of CTD patients is estimated to be 2.9 times higher than for patients who are not experiencing CTD.[2]

About Crofelemer

Crofelemer is the only oral FDA approved prescription drug under botanical guidance. It is plant-based, extracted and purified from the red bark sap of the *Croton lechleri* tree in the Amazon Rainforest. Jaguar family company Napo Pharmaceuticals has established a sustainable harvesting program, under fair trade practices, for crofelemer to ensure a high degree of quality, ecological integrity, and support for Indigenous communities.

About the Jaguar Health Family of Companies

Jaguar Health, Inc. (Jaguar) is a commercial stage pharmaceuticals company focused on developing novel proprietary prescription medicines sustainably derived from plants from rainforest areas for people and animals with gastrointestinal distress, specifically associated with overactive bowel, which includes symptoms such as chronic debilitating diarrhea, urgency, and bowel incontinence. Jaguar family company Napo Pharmaceuticals focuses on developing and commercializing human prescription pharmaceuticals for essential supportive care and management of neglected gastrointestinal symptoms across multiple complicated disease states. Napo Pharmaceuticals' crofelemer drug product candidate is the subject of the OnTarget study, an ongoing pivotal Phase 3 clinical trial for preventive treatment of chemotherapy-induced overactive bowel (CIOB) in adults with cancer on targeted therapy. Jaguar family company Napo Therapeutics is an Italian corporation Jaguar established in Milan, Italy in 2021 focused on expanding crofelemer access in Europe and specifically for orphan and/or rare diseases. Jaguar Animal Health is a Jaguar tradename. Magdalena Biosciences, a joint venture formed by Jaguar and Filament Health Corp., is focused on developing novel prescription medicines derived from plants for mental health indications.

For more information about Jaguar Health, please visit https://jaguar.health. For more information about Napo Pharmaceuticals, visit www.napopharma.com. For more information about Napo Therapeutics, visit napotherapeutics.com. For more information about Magdalena Biosciences, visit magdalenabiosciences.com.

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.

Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that top line results from the OnTarget study will be available in late October 2023, and the expectation that the OnTarget trial will provide evidence that diarrhea associated with targeted cancer therapies is chronic, not acute, and impacts the patient's quality of life as well as their ability to remain on their cancer therapy regimens at proven doses for better outcomes. 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 several 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.

[1] Pablo C. Okhuysen, M.D., The impact of cancer-related diarrhea on changes in cancer therapy patterns: Real world evidence

[2] Eric Roeland, M.D., FAAHPM, Healthcare utilization and costs associated with cancer-related diarrhea

Contact:

hello@jaguar.health
Jaguar-JAGX

SOURCE: Jaguar Health, Inc.