European Medicines Agency Grants Orphan Drug Designation for Crofelemer for Microvillus Inclusion Disease (MVID), a Second Rare Disease Indication

October 17, 2022

MVID, a rare congenital diarrheal disorder (CDD) condition, is a life-threatening autosomal recessive disease that affects newborns and children and leads to significant morbidity and mortality from intestinal failure, including severe secretory diarrhea

Presentation expected in December 2022 of initial results of an investigator-initiated proof-of-concept trial of crofelemer for CDD and short bowel syndrome (SBS) with intestinal failure, supporting the potential for expanded patient access to crofelemer in 2023 in Europe

Pravin Chaturvedi, PhD, Jaguar's Chief Scientific Officer and Chair of the Scientific Advisory Board, Receives First Boston Biotechnology Summit Lifetime Achievement Award

SAN FRANCISCO, CA / ACCESSWIRE / October 17, 2022 / Jaguar Health (NASDAQ:JAGX) and Napo Therapeutics, the Italian corporation established by Jaguar Health in Italy in 2021 that focuses on development and commercialization of crofelemer in orphan and rare diseases, thus expanding access to crofelemer to patients in Europe, today announced that the European Commission has adopted the decision to grant Orphan Drug Designation (ODD) for crofelemer for the indication of microvillus inclusion disease (MVID), a rare congenital diarrheal disorder (CDD) condition, in the European Union following review of the ODD application Napo Therapeutics submitted to the European Medicines Agency (EMA) in May 2022.

"This is a very welcome development for crofelemer, a new molecular entity that has been granted two orphan designations by the EMA in less than one year, as crofelemer received ODD for short bowel syndrome (SBS) from the EMA in December 2021," said Massimo Mineo, CEO of Napo Therapeutics. "The recognition of ODD in Europe for crofelemer for MVID is a key Napo Therapeutics milestone under the company's exclusive crofelemer license agreement with Jaguar, and receipt of this new ODD supports some specific regulatory pathways for this serious form of CDD, which remains a significant unmet medical need, especially in pediatric patients."

"CDDs are a group of inherited chronic enteropathies characterized by heterogeneous etiology, and each type of CDD is thus a different disease with a different pathogenetic mechanism," said Martire Particco, MD, Chief Medical Officer of Napo Therapeutics. "MVID is a life-threatening and rare autosomal recessive disease that affects newborns and children and leads to significant morbidity and even death from severe secretory diarrhea."

CDD and SBS patients are both subject to intestinal failure, often requiring parenteral nutrition up to 7 days a week, and the immense associated morbidity, mortality, and medical expense. CDD and SBS patients also share a primary common symptom: chronic diarrhea, and therefore associated sequelae from diarrhea, including significant dehydration, metabolic acidosis or alkalosis and malnutrition, and other secondary symptoms, and these symptoms emerge either early or late, and many times become life-threatening.

Napo Therapeutics' mission is to provide access to Jaguar Health's proprietary first-in-class plant-based medicine crofelemer in Europe to address such significant rare disease indications. The company's initial focus is on the clinical development and registration in Europe of crofelemer for short bowel syndrome with intestinal failure (SBS-IF) and subsequently for CDD.

Jaguar is currently supporting an investigator-initiated proof-of-concept study of crofelemer in patients with SBS or CDD with intestinal failure, with a planned endpoint of reduction of requirement of weekly volume of parenteral nutrition. The investigator is targeting a presentation in December 2022 of initial results from the study at a global GI conference in Dubai. In accordance with the guidelines of specific EU countries, publications of such data could support early patient access of crofelemer for SBS or CDD with intestinal failure by mid-2023 through programs in Europe for these devastating diseases for which there is a significant unmet medical need.

Sponsors who obtain ODD for their drug can benefit from Scientific Advice from the EMA for clinical trials for the orphan indication and receive market exclusivity for a period of ten years once the medicine is approved for commercialization.

On October 14, 2022, Pravin Chaturvedi, PhD, Jaguar's Chief Scientific Officer and Chair of the Scientific Advisory Board, received a First Boston Biotechnology Summit Lifetime Achievement Award during the Boston Biotechnology Summit. "We congratulate Dr. Chaturvedi on this wonderful and very well-deserved accomplishment! During his impressive 30+ year career in the pharmaceutical industry, Dr. Chaturvedi has developed and brought to market seven pharmaceutical products in the U.S., and his list of accomplishments includes designing the successful Phase 3 ADVENT trial of crofelemer that resulted in approval of the drug in the U.S., now marketed under the name Mytesi®, for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy," said Lisa Conte, Jaguar's president and CEO.

The Boston Biotechnology Summit is an exclusive, Trans-Atlantic bridge designed to foster innovative synergies between biotech and pharma companies, healthcare-focused cities, regional clusters and institutional, philanthropic and strategic investors. The Summit's intent is to spark projects,

their financing, and strategic deals to solve unmet medical needs to improve patient lives globally.

About Crofelemer

Crofelemer is a botanical (plant-based) drug extracted and purified from the red bark sap, also referred to as "dragon's blood," of the medicinal *Croton lechleri* tree in the Amazon Rainforest. Napo Pharmaceuticals, Jaguar Health's wholly owned U.S. subsidiary, 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 Jaguar Health, Napo Pharmaceuticals, Napo Therapeutics & Jaguar Animal Health

Jaguar Health, Inc. is a commercial stage pharmaceuticals company focused on developing novel, plant-based, non-opioid, and sustainably derived prescription medicines for people and animals with GI distress, including chronic, debilitating diarrhea. Jaguar Health's wholly owned subsidiary, Napo Pharmaceuticals, Inc., focuses on developing and commercializing proprietary plant-based human pharmaceuticals from plants harvested responsibly from rainforest areas. Our crofelemer drug product candidate is the subject of the OnTarget study, an ongoing pivotal Phase 3 clinical trial for prophylaxis of diarrhea in adult cancer patients receiving targeted therapy. Jaguar Health is the majority shareholder of Napo Therapeutics S.p.A. (f/k/a Napo EU S.p.A.), an Italian corporation established by Jaguar Health in Milan, Italy in 2021 that focuses on expanding crofelemer access in Europe. Jaguar Animal Health is a tradename of Jaguar Health.

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

About Mytesi®

Mytesi (crofelemer) is an antidiarrheal indicated in the U.S. 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.

Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that the publication of proof-of-concept data of crofelemer for CDD and SBS could support early patient access of crofelemer for CDD and SBS in Europe by mid-2023 in accordance with the guidelines of specific EU countries, and the expectation that the investigator of the proof-of-concept study of crofelemer for CDD and SBS will present initial results from the study in December 2022 at a global GI conference in Dubai. 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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