Jaguar Health Announces Submission of Orphan Drug Designation Application to the FDA for Crofelemer for Cholera-Related Diarrhea

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Cholera is an acute diarrheal illness caused by infection of the intestine with the bacterium Vibrio cholerae

Crofelemer previously granted Orphan Drug Designation by the FDA and the EMA for both short bowel syndrome and microvillus inclusion disease

SAN FRANCISCO, CA / ACCESSWIRE / February 12, 2024 / Jaguar Health (NASDAQ:JAGX) today announced that Jaguar family company Napo Pharmaceuticals (Napo) has submitted an Orphan Drug Designation (ODD) application to the U.S. Food and Drug Administration (FDA) for crofelemer, the company's novel plant-based prescription drug, for the symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral, and parasitic infections including *Vibrio cholerae*, the bacterium that causes cholera.

Due to the very low incidence and prevalence of cholera in the United States, cholera is an orphan indication in this country. Rare diseases, also referred to as orphan indications, are a core Jaguar development focus. In 2024 and 2025, Jaguar expects results from 5 proof-of-concept studies of crofelemer, the company's novel plant-based prescription drug, from at least 8 clinical sites, including Cleveland Clinic, on three continents for the rare disease indications of microvillus inclusion disease (MVID) - an ultrarare congenital diarrheal disorder (CDD) - and short bowel syndrome (SBS). In accordance with the guidelines of specific European Union countries, published data from such clinical investigations could support reimbursed early patient access to crofelemer for these debilitating conditions in 2025 while the company pursues approval of crofelemer for SBS and MVID from the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA). In August 2023 the FDA activated Napo's Investigational New Drug (IND) application for a new crofelemer powder for oral solution formulation for the treatment of MVID.

"We are very pleased that the ODD application for crofelemer for cholera-related diarrhea has been submitted," said Steven King, PhD, Jaguar's Chief Sustainable Supply, Ethnobotanical Research & IP Officer. "The company previously presented Phase 2 data on crofelemer for the treatment of devastating dehydration in cholera patients from the renowned International Centre for Diarrhoeal Disease Research (icddr,b) in Bangladesh. Receipt of orphan drug designation would qualify the company for various development incentives, including tax credits for qualified clinical testing and relief of filing fees, and provide the company with a seven-year period of marketing exclusivity if marketing approval is approved for crofelemer for this indication in the U.S. We expect to pursue ODD designation for crofelemer for this indication from the European Medicines Agency (EMA) as well in the future."

Crofelemer has been granted ODD by the FDA and the EMA for both MVID and SBS. The Orphan Drug Act (ODA) in the U.S. provides for granting special status to a small molecule drug or biological product to treat a rare disease or condition upon request of a sponsor. This status is referred to as orphan drug designation (or sometimes "orphan status"). In the EU, receipt of ODD supports some specific regulatory pathways, and 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.

Although cholera is an orphan indication in the U.S., it is estimated that, worldwide, 1.3 to 4 million cholera cases and 21,000 to 143,000 cholera-related deaths occur each year, according to the Centers for Disease Control and Prevention of the U.S. Department of Health & Human Services. Approximately one in 10 infected persons will have severe disease characterized by profuse watery diarrhea, vomiting, and leg cramps. In these people, rapid loss of body fluids leads to dehydration and shock. Without treatment, death can occur within hours. Cholera is now endemic in many countries outside the U.S. Preliminary data issued January 11, 2024 by the World Health Organization (WHO) indicates that the number of cholera cases reported in 2023 in WHO Member States as of December 15, 2023 surpassed that of 2022. Nearly a year has passed since WHO classified the global resurgence of cholera as a grade 3 emergency, the highest internal level for a health emergency requiring a comprehensive response at the three levels of the organization.

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. Jaguar Health 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, bowel incontinence, and cramping pain. 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, a 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. that emerged from Jaguar's Entheogen Therapeutics Initiative (ETI), is focused on developing novel prescription medicines derived from plants for mental health indications.

For more information about:

Jaguar Health, visit https://jaguar.health

Napo Pharmaceuticals, visit www.napopharma.com

Napo Therapeutics, visit napotherapeutics.com

Magdalena Biosciences, visit magdalenabiosciences.com

Visit Jaguar on LinkedIn: https://www.linkedin.com/company/jaguar-health/

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Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that results from 5 proof-of-concept studies of crofelemer from at least 8 clinical sites, including Cleveland Clinic, on three continents will be available in 2024 and 2025 for the indications of MVID and SBS, Jaguar's expectation that, in accordance with the guidelines of specific European Union countries, published data from such clinical investigations could support reimbursed early patient access to crofelemer for MVID and SBS in 2025 while the company pursues approval of crofelemer for SBS and MVID from the EMA and the FDA, and Jaguar's expectation that it will pursue ODD designation for crofelemer for cholera-related diarrhea from the EMA in the future. 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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