FDA Approves Orphan-Drug Designation for Jaguar Health's Crofelemer for Treatment of Diarrhea in Cholera

December 17, 2024

World Health Organization (WHO) has classified the global resurgence of cholera at the highest internal level for emergencies; 1.3 to 4 million cholera cases and 21,000 to 143,000 cholera-related deaths occur each year worldwide

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 European Medicines Agency (EMA) for both short bowel syndrome and microvillus inclusion disease

SAN FRANCISCO, CA / ACCESSWIRE / December 17, 2024 / Jaguar Health(NASDAQ:JAGX) (Jaguar) family company Napo Pharmaceuticals (Napo) today announced that the U.S. Food and Drug Administration (FDA) has granted orphan-drug designation (ODD) to crofelemer, the company's novel plant-based prescription drug, for treatment of diarrhea in cholera.

"We are very pleased that crofelemer has been granted orphan-drug designation for this important indication," 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 qualifies the company for various development incentives, including tax credits for qualified clinical testing and relief of filing fees, and provides 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 for crofelemer for this indication from the EMA as well in the future."

Due to the very low incidence and prevalence of cholera in the United States, cholera is an orphan indication in this country. Crofelemer is also the subject of five other rare/orphan disease-related clinical efforts - three investigator-initiated trial (IIT) proof-of-concept studies and two Phase 2 studies - for the indications of short bowel syndrome with intestinal failure (SBS-IF) and/or microvillus inclusion disease (MVID) in the US, European Union, and/or Middle East/North Africa regions. Dosing of the first patient in each of these five studies is expected to occur throughout December 2024 and Q1 2025, with availability of IIT proof-of-concept results potentially in Q2 2025. In accordance with the guidelines of specific EU countries, published data from clinical investigations in SBS-IF and MVID could support reimbursed early patient access to crofelemer for these debilitating conditions in those countries.

Crofelemer has also been granted ODD by the FDA and the EMA for both MVID and SBS.

Additionally, Jaguar intends to pursue orphan-drug designation and a Tropical Disease Priority Review Voucher for the indication of treatment of diarrhea in cholera with a proprietary second-generation anti-secretory agent, NP-300, which, like crofelemer, is sustainably derived from the *Croton lechleri* tree. Priority review vouchers are transferable, and in past transactions by other companies have sold for values ranging from $67 million to $350 million, which provides for a potential immediate return on investment upon approval of NP-300 for the indication of treatment of diarrhea in cholera.

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.[1] 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. From January 1, 2024 to July 28, 2024, a cumulative total of 307,433 cholera cases and 2,326 deaths were reported from 26 countries across five World Health Organization (WHO) regions.[2] WHO classified the global resurgence of cholera as a grade 3 emergency in January 2023, the highest internal level for emergencies in WHO.[2] Based on the number of outbreaks and their geographic expansion, alongside the shortage of vaccines and other resources, WHO continues to assess the risk at the global level as very high and the event remains classified as a grade 3 emergency.[2]

About Orphan-Drug Designation in the US and European Union

The Orphan Drug Act 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.

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 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 (Napo) focuses on developing and commercializing human prescription pharmaceuticals for essential supportive care and management of neglected gastrointestinal symptoms across multiple complicated disease states. Napo's crofelemer is FDA-approved under the brand name Mytesi® for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral 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 the *Make Cancer Less Shitty* patient advocacy program on Bluesky, X, Facebook & Instagram

Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that the company will pursue ODD for crofelemer for treatment of diarrhea in cholera from the EMA in the future, Jaguar's expectation that dosing of the first patient in each of three IITs and two Phase 2 studies of crofelemer for SBS-IF and/or MVID will occur throughout December 2024 and Q1 2025, Jaguar's expectation that IIT proof-of-concept results for crofelemer for SBS-IF and/or MVID could potentially be available in Q2 2025, Jaguar's expectation that, in accordance with the guidelines of specific EU countries, published data from clinical investigations in SBS-IF and MVID could support reimbursed early patient access to crofelemer for these debilitating conditions in those countries, Jaguar's expectation that it will also pursue the indication of treatment of diarrhea in cholera with NP-300, Jaguar's expectation that it will pursue orphan-drug designation for NP-300 for treatment of diarrhea in cholera, and Jaguar's expectation that NP-300 may qualify for a Tropical Disease Priority Review Voucher if NP-300 is approved by the FDA for treatment of diarrhea in cholera. 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.

[1]https://www.cdc.gov/cholera/about/index.html#:~:text=Most%20people%20who%20get%20cholera,ill%20patients%20can%20survive%20cholera

[2]https://www.who.int/publications/m/item/multi-country-outbreak-of-cholera--external-situation-report--17---15-august-2024

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