Phase 2 Study Initiated to Evaluate Jaguar Health's Crofelemer for Microvillus Inclusion Disease (MVID), an Ultrarare Congenital Diarrheal Disorder

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The study is one of five clinical efforts - three proof-of-concept investigator-initiated trials (IIT) and two Phase 2 studies - of crofelemer for the rare disease indications of MVID and/or short bowel syndrome with intestinal failure (SBS-IF) in the US, EU, and/or Middle East/North Africa regions; availability of first IIT proof-of-concept results potentially in Q1 2025

Crofelemer, Jaguar's novel plant-based prescription drug, has been granted Orphan-Drug Designation by the FDA and the European Medicines Agency (EMA) for both MVID and SBS-IF

SAN FRANCISCO, CA / ACCESSWIRE / December 18, 2024 / Jaguar Health, Inc. (NASDAQ:JAGX) (Jaguar) family companies Napo Pharmaceuticals (Napo) and Napo Therapeutics today announced that Napo's Phase 2 study to evaluate the efficacy of crofelemer, Jaguar's novel plant-based anti-secretory prescription drug, for the indication of MVID in pediatric patients, has been initiated.

"The initiation of this double blind, placebo-controlled study in pediatric MVID patients is a key milestone for Jaguar," said Lisa Conte, Jaguar's founder, president, and CEO. "This study is one of five clinical efforts in rare diseases - three IIT proof-of-concept (POC) studies and two Phase 2 studies - for crofelemer for the orphan disease indications of MVID and/or SBS-IF in the United States, European Union, and/or Middle East/North Africa (MENA) regions. These studies are evaluating a novel oral powder for solution formulation of crofelemer - which is different from the FDA-approved oral formulation of crofelemer delayed-release tablets, Mytesi ® , available for people living with HIV/AIDS. Dosing of the first patient in each of these five studies is expected to occur during December 2024 and January 2025, with the availability of the first IIT POC result potentially in Q1 2025, with additional IIT POC results expected throughout 2025. In accordance with the guidelines of specific EU countries, published data from clinical investigations in MVID and SBS-IF could support reimbursed early patient access to crofelemer for these debilitating conditions in those countries."

The clinical protocol for the Phase 2 study in pediatric MVID patients has received regulatory clearances from the U.S. Food and Drug Administration (FDA) and the EMA, and the trial will be conducted at clinical sites in the US, Europe, and the MENA region.

"MVID and SBS-IF, rare and severe diseases requiring intensive parenteral nutrition (PN) and support, have severe morbidity and mortality implications as well as impacting the quality of life of both patients and their caregivers," Conte said. "In addition to the clinical endpoints, we plan to assess the quality-of-life impact on patients and caregivers as part of both the above-referenced Phase 2 studies."

MVID is an ultrarare pediatric disease, with an estimated prevalence of a couple of hundred patients globally. It is characterized by severe diarrhea and malabsorption, requiring intensive parenteral support for nutritional and fluid management. Each MVID patient is a unique patient; their journey requires very careful management of their nutritional needs, and there are currently no approved drug treatments for MVID.

"We expect that, if even just a very small number of patients show benefit with the extremely safe profile of crofelemer, this may potentially allow approval in the U.S. for crofelemer for MVID; support reimbursed early patient access to crofelemer for MVID in specific EU countries; and qualify crofelemer for participation in PRIME for MVID. PRIME is an EMA program providing enhanced interaction and early dialogue with developers of promising medicines that target an unmet medical need, with the goal of optimizing development plans and speeding up evaluation so the medicine can reach patients earlier," Conte said.

Crofelemer has been granted Orphan-Drug Designation by the FDA and the EMA for SBS-IF and MVID.

About Crofelemer
Crofelemer is a novel, oral plant-based prescription medicine purified from the red bark sap, also referred to as "dragon's blood," of the *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 dosing of the first patient in each of the five rare disease studies will occur during December 2024 and January 2025, Jaguar's expectation that the availability of the first IIT POC result may potentially occur in Q1 2025, Jaguar's expectation that additional IIT POC results may be available throughout 2025, Jaguar's expectation that, in accordance with the guidelines of specific EU countries, published data from clinical investigations could support early patient access to crofelemer for SBS-IF or MVID in these countries, Jaguar's expectation that it will assess the quality-of-life impact of SBS-IF and/or MVID on patients and caregivers as part of both Phase 2 studies of crofelemer, and Jaguar's expectation that, if even just a very small number of patients show benefit with crofelemer, this may allow approval in the U.S. for crofelemer for MVID, support reimbursed early patient access to crofelemer for MVID in specific EU countries, and qualify crofelemer for participation in PRIME for MVID. 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.

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