Proof-of-Concept Results Show Crofelemer Reduced Total Parenteral Nutrition in Patients with Rare Diseases Microvillus Inclusion Disease (MVID) and Short Bowel Syndrome with Intestinal Failure (SBS-IF) by up to 27% and 12.5% - Potential to Modify Disease Progression in Intestinal Failure Patients

April 30, 2025

Jaguar to host investor webcast today at 8:30 AM Eastern to review the initial results from the proof-of-concept study of crofelemer for MVID and SBS-IF presented April 26 at the Annual ELITE PED-GI Congress; Click here to register

There are no approved drug treatments for MVID, an ultrarare pediatric disease characterized by severe diarrhea and malabsorption that requires intensive parenteral support for nutritional and fluid management including total parenteral nutrition (TPN) - which carries the risk of morbidity, infections, metabolic complications, liver and kidney problems, and neurodevelopmental delay

This proof-of-concept data in MVID supports crofelemer's potential inclusion in the European Medicines Agency's (EMA) PRIME program for expediated and assisted regulatory approval in the EU as well as FDA's Breakthrough Therapies program for expedited regulatory approval in the US

SAN FRANCISCO, CA / ACCESS Newswire / April 30, 2025 / Jaguar Health, Inc. (NASDAQ:JAGX) (Jaguar) family companies Napo Pharmaceuticals (Napo) and Napo Therapeutics today announced initial proof-of-concept results showing that a novel liquid formulation of crofelemer reduced the required TPN and/or supplementary intravenous fluids, collectively referred to as parenteral support (PS) in patients with intestinal failure due to microvillus inclusion disease (MVID) and short bowel syndrome (SBS-IF) by up to 27% and 12.5% respectively. In addition, this data showed that crofelemer reduced stool volume output and/or frequency of watery stools, and increased urine output - an indicator of improved nutrient oral absorption.

These initial results were recently presented at the Annual ELITE PED-GI Congress by Dr. Mohamad Miqdady, a recognized leader in pediatric gastroenterology who serves as the Chief of Pediatric Gastroenterology, Hepatology and Nutrition at Sheikh Khalifa Medical City (SKMC) in Abu Dhabi in the United Arab Emirates. He is the Principal Investigator for this ongoing exploratory, single-arm open label non-randomized investigator-initiated trial of a novel liquid formulation of crofelemer, Jaguar's novel plant-based anti-secretory prescription drug, for various congenital diarrheal disorders (CDD), including MVID and SBS-IF.

"We are not aware of any other intervention that has shown the ability to reduce the required administration of lifelong parenteral support including TPN, thus potentially improving nutrient absorption in patients with MVID," said Lisa Conte, Jaguar's Founder and CEO.

"As I was pleased to announce at the Annual ELITE PED-GI Congress, the initial proof-of-concept results of this study indicate that the novel liquid formulation of crofelemer being evaluated in this investigational study reduced the required weekly amount of TPN and/or supplementary intravenous fluids in participating MVID and SBS-IF patients," said Dr. Miqdady, the principal investigator for the study. "Patients with MVID and SBS-IF suffer from devastating diarrhea and dehydration caused by these debilitating, lifelong conditions and often require lifelong TPN up to 7 days a week for greater than 50% of the time. While crucial for these patients, TPN carries a significant risk of morbidity, including infections, metabolic complications, liver and kidney function problems - as well as a risk of neurodevelopmental delay. There are currently no approved drugs that reduce TPN needs in these patients and, given how rare MVID is, an open label study was warranted. Based on the initial findings from this study, crofelemer's novel antisecretory mechanism of action appears to have the potential to provide a novel therapeutic option to modify disease progression due to the reductions in TPN and associated comorbidities in MVID and SBS-IF patients and improve their quality of life."

Per the study protocol, the pediatric MVID patient was taken off crofelemer after 12 weeks of treatment for a period of 30 days. "However, after just 8 days, the patient's parents requested reinitiation of crofelemer dosing, as the patient's symptoms were worsening - evidenced by increased stool output and decreased urine output. Hence we restarted the patient on daily treatment with crofelemer," continued Dr. Miqdady.

"I'm very excited by these preliminary results. There is no treatment for MVID, and these patients have to be on lifelong TPN. Every reduction in TPN counts. The more you manage to taper the time and amount of TPN in MVID patients, the better for these patients, and it has a significant impact on their quality of life as well as on the hepatic and renal complications these patient face," said Dr. Christos Tzivinikos, Founder of the Pediatric GI Department at Al Jalila Children's Specialty Hospital in Dubai, and a Clinical Assistant Professor at Mohammed Bin Rashid University of Medicine and Health Sciences in Dubai. Dr. Tzivinikos is a clinical investigator in Napo's recently initiated placebo-controlled double-blind Phase 2 study of crofelemer for MVID in pediatric patients.

The investigator-initiated trial in Abu Dhabi is evaluating the safety and effectiveness of crofelemer in pediatric patients with intestinal failure and

includes an assessment of crofelemer's potential to be safely administered to patients with intestinal failure from MVID, SBS, and other congenital diarrheal disorders (CDD) in optimum dose levels for the patients.

"Based on preliminary communications with European Medicines Agency (EMA) regulatory members that focus on PRIME (Priority Medicines), a program that provides enhanced interactions and early dialogue for development of novel medicines targeting unmet medical needs, we are excited by these findings from Dr. Miqdady's study," said Pravin Chaturvedi, PhD, Chair of Napo's and Jaguar's Scientific Advisory Board (SAB) and Jaguar's Chief Scientific Officer. "With these initial results, given the ultrarare nature of MVID, even a small number of MVID patients showing benefit with crofelemer may allow Napo to explore pathways for expedited regulatory approval in Europe. Crofelemer may qualify for participation in PRIME in the European Union and potentially in the U.S. Food and Drug Administration's (FDA) Breakthrough Therapies program."

This study is being conducted at SKMC, a flagship tertiary hospital in the UAE and the largest teaching medical center in Abu Dhabi, by Dr. Miqdady. He is an American board-certified pediatric GI, hepatology and nutrition professor at Khalifa University in Abu Dhabi, and serves as a member of Napo's SAB. Dr. Miqdady completed his Fellowship in Pediatric Gastroenterology at Baylor College of Medicine and Texas Children's Hospital in Houston.

Jaguar, through Napo Pharmaceuticals and Napo Therapeutics, is currently supporting three POC investigator-initiated trials (IITs), and conducting two placebo-controlled Phase 2 studies, for crofelemer for SBS-IF and/or MVID patients in the United States, European Union, and/or Middle East/North Africa regions. The company's Phase 2 study to evaluate the efficacy of crofelemer for MVID in pediatric patients has been initiated, as has the company's Phase 2 study to evaluate the efficacy of crofelemer for SBS-IF in adults. In addition to the initiation of the POC IIT of crofelemer in Abu Dhabi in pediatric patients for various CDDs, including SBS-IF or MVID, the dosing for the IIT in the U.S. to evaluate crofelemer for SBS-IF in adults has also begun. Initiation of the third IIT is planned for the second half of 2025.

Additional POC results from IITs are expected throughout 2025 and will provide additional preliminary data on the safety and potential effectiveness of crofelemer for these highly unmet clinical needs. 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.

The Annual Elite Ped-GI Congress is designed to provide information about high level, clinically significant updates and comprehensive trends relevant to the practice of pediatric gastroenterological, nutrition and liver disorders. Napo was a Bronze-level sponsor of the 2025 Annual ELITE PED-GI Congress.

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 focuses on developing and commercializing human prescription pharmaceuticals for essential supportive care and management of neglected gastrointestinal symptoms across multiple complicated disease states. 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 host an investor webcast on April 30, 2025, Jaguar's expectation that crofelemer's novel antisecretory mechanism of action may have the potential to provide a novel therapeutic option to modify disease progression through reduction in TPN needs and associated comorbidities in patients with intestinal failure due to MVID, SBS and other dehydrating conditions and improve their quality of life, Jaguar's expectation that a third IIT of crofelemer will initiate in the second half of 2025, Jaguar's expectation that additional POC results from IITs will be available throughout 2025 and will provide additional preliminary data on the safety and potential effectiveness of crofelemer for these highly unmet clinical needs, Jaguar's expectation that, if even just a very small number of MVID patients show benefit with crofelemer, this may potentially allow pathways for regulatory approval in the U.S. and other regions for crofelemer for MVID and qualify crofelemer for participation in PRIME and in the FDA's Breakthrough Therapies program for MVID, and Jaguar's expectation that, in accordance with the guidelines of specific European Union countries, published data from clinical investigations in MVID and SBS-IF could support reimbursed early patient access to crofelemer for these debilitating conditions in specific European Union countries. 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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press release