Proof-of-Concept Results Show Jaguar Health's Crofelemer Reduced Total Parenteral Nutrition in Third Intestinal Failure Orphan Disease Patient

June 30, 2025

As recently announced, initial proof-of-concept results from this ongoing investigator-initiated trial (IIT) show crofelemer reduced the required total parenteral nutrition in the first participating microvillus inclusion disease (MVID) patient by up to 27% and in the first participating short bowel syndrome patient by up to 12.5%

The first two patients in this IIT were taken off crofelemer after 12 weeks of treatment for a period intended to last 30 days, per the study protocol, but were promptly placed back on daily crofelemer treatment because their symptoms worsened

Company strategy: Seek business development partnerships for license to develop and commercialize Jaguar's intestinal failure products, resulting in non-dilutive funding for Jaguar

SAN FRANCISCO, CA / ACCESS Newswire / June 30, 2025 / Jaguar Health, Inc. (NASDAQ:JAGX) (Jaguar) family companies Napo Pharmaceuticals (Napo) and Napo Therapeutics today announced that initial proof-of-concept results show that a novel liquid formulation of crofelemer reduced the required total parenteral nutrition (TPN) and supplementary intravenous fluids in a third intestinal failure patient. This is the second pediatric patient with intestinal failure due to the orphan disease short bowel syndrome (SBS-IF) who was treated with crofelemer. To date, three patients with intestinal failure due to SBS-IF or microvillus inclusion disease (MVID) have been treated with crofelemer in this exploratory, single-arm open label non-randomized IIT in Abu Dhabi.

As announced, and as presented April 26, 2025 at the Annual ELITE PED-GI Congress, initial proof-of-concept results from this study show that crofelemer, Jaguar's novel plant-based anti-secretory prescription drug, reduced the required TPN and supplementary intravenous fluids in the first participating MVID patient by up to 27% and in the first participating SBS-IF patient by up to 12.5%. 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.

"We're very pleased to report that the second pediatric SBS-IF patient participating in this IIT exhibited a similar response for TPN reduction, further exemplifying that crofelemer's paradigm-shifting antisecretory mechanism of action may 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," said Lisa Conte, Jaguar's Founder and CEO. "This SBS-IF patient was administered the highest dose of crofelemer provided for in the approved protocol for the IIT, with no resulting safety issues."

Per the IIT protocol, as announced, the initial pediatric MVID patient participating in the study was taken off crofelemer after 12 weeks of treatment for an intended period of 30 days. However, after just 8 days, the patient's parents requested reinitiation of crofelemer dosing, as the patient's symptoms worsened - evidenced by increased stool output and decreased urine output - and the patient was restarted on daily treatment with crofelemer. The initial pediatric SBS-IF patient participating in the study also had crofelemer withdrawn per the protocol after 12 weeks. This patient then exhibited a relapse of symptoms and was put back on daily treatment with crofelemer, and has since been maintaining a significant TPN reduction. Jaguar plans to continue supplying crofelemer to Dr. Mohamad Miqdady, the principal investigator for this IIT, for the patients participating in this study for as long as Dr. Miqdady feels is medically necessary.

Dr. Miqdady has submitted initial proof-of-concept data from the ongoing IIT in Abu Dhabi for all three above-referenced patients to a major international pediatric gastroenterological conference for consideration for presentation.

Jaguar, through Jaguar family companies Napo and Napo Therapeutics, is currently supporting two independent proof-of-concept IITs, and conducting two placebo-controlled Phase 2 studies, of crofelemer in patients with intestinal failure due to MVID and SBS-IF in the United States, European Union, and/or Middle East/North Africa regions.

Completion of Napo's randomized double-blind, placebo-controlled Phase 2 study of crofelemer in pediatric MVID patients is expected in mid-2026 as planned.

"Our strategy is to seek business development partnerships for license rights for development and commercialization of Jaguar's intestinal failure products - with the goal of generating non-dilutive funding for Jaguar," said Conte. "Given the ultrarare nature of MVID, and the groundbreaking initial proof-of-concept results from the ongoing IIT in Abu Dhabi, even a small number of MVID patients showing benefit with crofelemer may allow Napo to explore pathways for expedited regulatory approval."

Based on the initial findings of the ongoing IIT in Abu Dhabi, crofelemer's paradigm-shifting antisecretory mechanism of action appears to have the potential to provide a novel therapeutic option to reduce TPN and associated complications, including liver, renal, and cognitive deficits, as well as

infections from IV infusion, in patients with intestinal failure due to MVID and short bowel syndrome. The observed groundbreaking TPN reduction is particularly compelling for MVID, an ultrarare pediatric disease characterized by severe diarrhea and malabsorption that requires intensive parenteral support for nutritional and fluid management and for which no approved drug treatments exist, or any potential approach to reduce TPN.

The initial proof-of-concept data in MVID supports crofelemer's potential inclusion in the European Medicines Agency's (EMA) PRIME program that may accelerate regulatory approval pathways in the EU for this indication. This data may also support qualification of crofelemer for the FDA's Breakthrough Therapy program for expedited regulatory approval in the US. Additional proof-of-concept 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 IIT in Abu Dhabi is being conducted by Dr. Miqdady at Sheikh Khalifa Medical City (SKMC), a flagship tertiary hospital in the United Arab Emirates and the largest teaching medical center in Abu Dhabi. Dr. Miqdady, a recognized leader in pediatric gastroenterology, serves as the Chief of Pediatric Gastroenterology, Hepatology and Nutrition at SKMC. He is an American board-certified pediatric GI, hepatology and nutrition professor at Khalifa University in Abu Dhabi, and also serves as a member of Napo's Scientific Advisory Board. Dr. Miqdady completed his Fellowship in Pediatric Gastroenterology at Baylor College of Medicine and Texas Children's Hospital in Houston.

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 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. 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 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 completion of Napo's Phase 2 study of crofelemer in pediatric MVID patients will occur mid-2026, Jaguar's expectation that its strategy of seeking business development partnerships for license rights for development and commercialization of Jaguar's intestinal failure products may support generation of non-dilutive funding for Jaguar, Jaguar's expectation that even a small number of MVID patients showing benefit with crofelemer may allow Napo to explore pathways for expedited regulatory approval of crofelemer for MVID, Jaguar's expectation that crofelemer's mechanism of action may have the potential to provide a novel therapeutic option to reduce TPN and associated complications, including liver, renal, and cognitive deficits, as well as infections from IV infusion, in pediatric MVID and SBS-IF patients, Jaguar's expectation that proof-of-concept data in MVID may support crofelemer's potential inclusion in the EMA's PRIME program for expediated and assisted regulatory approval and in the FDA's Breakthrough Therapy program for expedited regulatory approval in the US, Jaguar's expectation that additional proof-of-concept results from IITs will be available throughout 2025, and Jaguar's expectation that published data from clinical investigations in MVID and SBS-IF could support reimbursed early patient access to crofelemer for MVID and SBS-IF. 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.

Contact:

hello@jaguar.health

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