Jaguar Health Research in Ethnobotanical Medicine Helps Advance Crofelemer Development for Genetically Defined Rare Congenital Gastrointestinal Disorders

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Crofelemer delayed-release tablets are Jaguar's FDA-approved prescription drug under botanical guidance ("botanical drug") derived from the Croton lechleri tree. Crofelemer, in a novel liquid formulation, is being developed as the potential first oral adjunctive therapy for Intestinal Failure (IF) from microvillus inclusion disease (MVID) and short bowel syndrome (SBS)

Crofelemer development with novel formulations for different gastrointestinal disorders reflects a differentiated botanical drug platform integrating ethnobotanical medicine, sustainable harvesting, complex CMC, and novel bioassays to support approval under FDA botanical guidance

Traditional knowledge of Croton lechleri use supported ethnobotanical research that led to development and approval of crofelemer, whose first in class anti-secretory mechanism was characterized through modern pharmacology and mechanism-based bioassays. Recent milestones include continued evaluation in an extension phase for Jaguar family company Napo's pivotal clinical trial of crofelemer as adjunctive therapy to Parenteral Support (PS) for MVID and upcoming ESPGHAN presentations in pediatric MVID and SBS-IF patients

FDA approval of crofelemer as an oral botanical drug highlights the totality-of-evidence and creates a significant practical barrier to generic replication

SAN FRANCISCO, CA / ACCESS Newswire / May 28, 2026 / Jaguar Health, Inc. (NASDAQ:JAGX) (Jaguar) and family company Napo Pharmaceuticals (Napo) today highlighted how the Company's long-standing research in ethnobotanical medicine, sustainable harvesting, and regulatory drug development under botanical guidance ("botanical drug") continues to inform the development of crofelemer as a novel oral adjunctive therapy to PS for rare congenital gastrointestinal intestinal failure (IF) disorders, including microvillus inclusion disease (MVID) and short bowel syndrome (SBS).

It has been through direct research collaboration with indigenous experts on plant and ethnobotanical medicine that Napo team members learned about the use of extracts of *Croton lechleri* to treat a number of gastrointestinal conditions. We have had cross-cultural medical discussions with traditional healers - a methodology that provides an opportunity to elucidate new ways of treating unmet medical needs such as IF. Napo has been collaborating on the long term sustainable harvest of *Croton lechleri* in the Central and Northern Peruvian Amazon for several decades, and this is being done with 19 distinct indigenous cultural groups in more than 30 locations.

Crofelemer is a refined and highly characterized botanical drug substance consisting of a complex oligomeric proanthocyanidin mixture derived from the latex of the *Croton lechleri* tree. Crofelemer is distinct from the raw traditional preparation and is the first and only oral botanical drug *approved by the FDA*. It was developed and approved as a delayed-release tablet through botanical identification, controlled sustainable harvesting, chemical characterization, biological testing, and clinical development.

"We are proud to be collaborating and interdependent with the people and tropical forest ecosystems of Peru. The world continues to learn that the conservation of tropical forests is often most effectively assured by the indigenous peoples who have been sustainably managing these ecosystems for centuries. They are dependent upon the water, air, animals, and plants of the forests for their physical and spiritual well-being, as is the rest of the world. They honor their relationship with the nurturing elements of their tropical forest homes. It is clear that the cultural and ecological health of people and forests are intertwined at multiple levels, and we wish to express our gratitude to these people and communities who have been working with and teaching members of our team for several decades how to sustainably manage this valuable medicinal plant within their ecosystems. They continue to integrate the Dragon's Blood tree, as Croton lechleri is referred to locally, into numerous creative reforestation strategies, as part of their sophisticated agroforestry and medicinal plant production systems," Dr. King added.

"Crofelemer represents a differentiated pharmaceutical development story: traditional medicinal knowledge helped identify a promising botanical source, and modern drug development transformed that knowledge into a highly characterized FDA-approved prescription drug under botanical guidance," said Lisa Conte, Jaguar's Founder, President, and CEO. *"We believe Jaguar's experience with crofelemer - including sustainable harvesting, botanical CMC, mechanism-based bioassays, clinical development, and regulatory engagement, is directly relevant as we advance crofelemer for rare intestinal failure disorders such as microvillus inclusion disease and short bowel syndrome with intestinal failure. We also believe the specialized know-how required to develop and manufacture crofelemer represents a distinct competency for Jaguar."*

Jaguar's family company, Napo Pharmaceuticals, is developing a novel crofelemer powder for oral solution for rare and orphan gastrointestinal disorders involving intestinal failure, including MVID and SBS-IF. This investigational formulation is distinct from Mytesi®, the FDA-approved delayed-release tablet formulation of crofelemer indicated for symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral

therapy.

MVID is an ultrarare congenital enteropathy with life-threatening dehydration beginning in infancy. Patients with MVID require life-sustaining and lifelong PS, including total parenteral nutrition (TPN) and supplemental intravenous fluids, to maintain hydration, electrolyte balance, nutrition, and support growth. In addition to MVID pathology, TPN is associated with significant co-morbidities. SBS-IF is a serious condition in which patients are unable to absorb sufficient fluids and nutrients through the intestine and also require life-sustaining PS for daily nutritional, electrolyte, and fluid requirements.

Recent clinical, scientific, and regulatory milestones in crofelemer intestinal failure development

Jaguar has recently announced multiple milestones supporting the Company's crofelemer development strategy for intestinal failure:

- **Clinical trial extension phase in MVID:** Jaguar continues its pivotal trial in MVID with an extension phase for oral liquid crofelemer. The company has also announced active-treatment-only continuation of its pivotal multicenter clinical trial in pediatric patients with MVID to support a potential New Drug Application (NDA) for crofelemer powder for oral solution targeted for mid-2027.

- **ESPGHAN late-breaking abstracts:** Jaguar announced acceptance of two late-breaking abstracts for liquid oral crofelemer treatment of intestinal failure in pediatric patients at the 58th Annual Meeting of the European Society for Pediatric Gastroenterology, Hepatology & Nutrition (ESPGHAN). These include presentations related to pediatric intestinal failure patients receiving liquid oral crofelemer as an investigational drug under separate investigator-initiated and expanded access studies.

- **Prior proof-of-concept results presented at NASPGHAN 2025:** Jaguar previously announced initial proof-of-concept results showing that a liquid formulation of crofelemer reduced required TPN and/or supplementary intravenous fluids, collectively referred to as parenteral support (PS), in patients with intestinal failure due to MVID and SBS-IF of up to 37% in the first participating MVID patient and up to 15% in participating SBS-IF patients

- **Botanical drug CMC publication:** A recent review article by Luo and Wu, *"CMC Challenges and Solutions in Botanical IND & NDA Development - Lessons Learned from Four Approved Botanical Drugs,"* published in *Botanical Drugs*, discusses Mytesi/crofelemer as a key FDA-approved botanical drug case study. The article highlights the CMC and quality-control challenges associated with botanical drugs and describes how crofelemer required eco-geographic raw material controls, mechanism-relevant chloride-channel bioassays, and multi-batch clinical consistency evidence to support FDA approval. **Crofelemer CMC complexity represents a potent barrier to generic or competitive replication.**

"Crofelemer's complexity is not simply a scientific challenge - it is also a strategic differentiator. The modern development of crofelemer illustrates why botanical drug development requires specialized expertise," said Steven King, PhD, Jaguar's Chief Sustainable Supply, Ethnobotanical Research, and Intellectual Property Officer. *"Traditional medicinal use of Croton lechleri provided an important ethnobotanical starting point, yet crofelemer is a refined and highly characterized extract derived from Croton lechleri latex. Its development required research on sustainable harvesting, collaboration with multiple indigenous communities, conservation, pharmacology, quality control, manufacturing, and clinical research. This is the kind of long-term translational work that can connect traditional medicinal knowledge to modern drug development in a responsible and scientifically rigorous way."*

Crofelemer's first-in-class anti-secretory mechanism of action involves inhibitory modulation of intestinal chloride ion secretion through effects on two chloride ion channels in the intestinal membrane, including the cystic fibrosis transmembrane conductance regulator (CFTR) and calcium-activated chloride channels. This novel anti-secretory mechanism may be relevant to reducing the need for PS in rare intestinal failure disorders through reductions of excessive intestinal fluid loss and reduced needs for parenteral support.

"Biopharma investors and business development partners often focus on synthetic small molecules, biologics, gene therapies, and other familiar innovation categories," Conte added. "*Crofelemer demonstrates another model of innovation: a botanical drug discovered through ethnobotanical research, developed through rigorous pharmaceutical standards, approved by FDA in one indication, and now being evaluated in genetically defined rare GI disorders with substantial unmet medical need. We believe this combination of scientific differentiation, regulatory precedent, CMC complexity, and rare disease development creates a compelling opportunity for patients in need and all Jaguar stakeholders."*

About Crofelemer

Crofelemer is Jaguar's novel, oral, plant-based prescription drug derived from the latex of the *Croton lechleri* tree. Crofelemer is approved in tablet formulation by the U.S. FDA under the brand name Mytesi® for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy. Crofelemer is a first-in-class anti-secretory agent acting locally in the gastrointestinal tract.

Jaguar family companies, Napo Pharmaceuticals, Inc., and Napo Therapeutics s.P.A. are developing crofelemer for multiple potential follow-on indications, with a novel powder for oral solution for rare intestinal failure (IF) disorders such as microvillus inclusion disease (MVID) and short bowel syndrome with intestinal failure (SBS-IF), as well as other indications involving intestinal fluid loss.

About Mytesi®

Mytesi® (crofelemer delayed-release tablets) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy (ART). Mytesi is not indicated for the treatment of infectious diarrhea. Rule out infectious etiologies of diarrhea before starting Mytesi. If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen. In clinical studies, the most common adverse reactions occurring at a rate greater than placebo were upper respiratory tract infection (5.7%), bronchitis (3.9%), cough (3.5%), flatulence (3.1%), and increased bilirubin (3.1%). See full Prescribing Information at Mytesi.com.

About Jaguar Health, Napo Pharmaceuticals, and Napo Therapeutics s.P.A.

Jaguar Health, Inc. is a commercial-stage pharmaceutical company focused on developing novel, plant-based, sustainably derived prescription medicines for people and animals with gastrointestinal distress, including chronic, debilitating disorders. Jaguar's family companies, Napo Pharmaceuticals and Napo Therapeutics, focus on developing and commercializing proprietary human prescription pharmaceuticals for rare diseases

from plants used traditionally in rainforest areas.

For more information about Jaguar Health, please visit https://jaguar.health.

Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that crofelemer may be developed for microvillus inclusion disease (MVID) and short bowel syndrome with intestinal failure (SBS-IF); Jaguar's belief that crofelemer's mechanism of action may be relevant to serious rare disorders characterized by excessive intestinal fluid loss; Jaguar's expectations regarding the potential therapeutic utility of crofelemer in rare gastrointestinal disorders; Jaguar's plans to pursue development pathways for crofelemer in microvillus inclusion disease (MVID) and short bowel syndrome with intestinal failure (SBS-IF); and Jaguar's belief that its ethnobotanical research, sustainable sourcing expertise, botanical CMC capabilities, and FDA botanical drug development experience represent differentiating capabilities.

In some cases, forward-looking statements can be identified by terms such as "believe," "may," "will," "expects," "plans," "anticipates," "intends," "potential," "continue," "designed," or similar expressions. These statements involve substantial risks and uncertainties, including risks related to Jaguar's ability to successfully develop crofelemer for microvillus inclusion disease (MVID), short bowel syndrome with intestinal failure (SBS-IF), or other potential indications; the risk that clinical studies may not demonstrate safety or efficacy; the risk that regulatory authorities may not agree with Jaguar's proposed development or approval pathways; the risk that Jaguar may not be able to obtain or maintain regulatory approvals; the risk that Jaguar may not be able to secure sufficient financing, partnerships, or other resources to advance its development programs; and other risks described in Jaguar's filings with the Securities and Exchange Commission.

Forward-looking statements speak only as of the date they are made. Jaguar undertakes no obligation to update any forward-looking statements, except as required by applicable law.

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