# Jaguar Health Issues Shareholder Letter: Company to Explore Approval Pathway for Crofelemer in Breast and Lung Cancer Based on Phase 3 Results - Investor Webcast August 13th Will Review Q2 Earnings and Further Review OnTarget Trial's Clinically Meaningful Results

August 5, 2024

***In 2022 breast cancer was the most common cancer in women in 157 countries out of 185, and lung cancer is the most common cancer worldwide.[1] Click here to register for webcast.***

***Import permit for crofelemer granted for independent, investigator-initiated proof-of-concept trial in Abu Dhabi of crofelemer in pediatric patients for the rare and orphan disease indications of microvillus inclusion disease (MVID) and short bowel syndrome (SBS) with intestinal failure***

**SAN FRANCISCO, CA / ACCESSWIRE / August 5, 2024 /** Jaguar Health, Inc. (NASDAQ:JAGX) ("Jaguar") today issued a letter to shareholders from the company's founder, president, and chief executive officer, Lisa Conte.

Dear Fellow Shareholders,

Jaguar will be hosting a webcast, providing a review of earnings for the second quarter of 2024, at 8:30 a.m. Eastern on Tuesday, August 13, 2024. We will also further review the data and regulatory strategy for the clinically meaningful results we reported July 23, 2024 - identified in patients with breast and respiratory cancer, including lung cancer - in the initial data from our recently completed phase 3 OnTarget trial of crofelemer. OnTarget broadly and boldly studied the prophylaxis of diarrhea in adult cancer patients with 10 distinct types of solid tumors receiving targeted therapy, with or without standard chemotherapy; yet the meaningful clinical signals are in breast and lung cancer patients, two of the three most common cancer diagnoses. We are collaborating with our clinical and scientific advisers to evaluate the significance of these clinical outcome signals in order to prepare for scientific publication submission and FDA meetings, as we plan to explore the pathway of approval to make crofelemer, our novel, oral plant-based prescription medicine, available to breast and lung cancer patients for cancer therapy-related diarrhea (CTD).

The breast and lung results in OnTarget are a responder analysis, as was the primary endpoint in the phase 3 ADVENT trial that led to FDA approval of crofelemer for its currently commercialized indication, under the brand name Mytesi®, for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. As we were pleased to announce last week, the results of two independent investigator-initiated responder analysis studies of crofelemer in diarrhea-predominant inflammatory bowel syndrome (IBS-D) populations - one in functional diarrhea and one in chronic idiopathic diarrhea - showed a benefit in patients and have been accepted for poster presentations at the American College of Gastroenterology Annual Scientific Meeting, which takes place October 25-30, 2024 in Philadelphia. We are driven and motivated by the paradigm-shifting mechanism of action of crofelemer, which continues to demonstrate clinical robustness in responder analysis trials for multiple gastroenterological conditions. "The functional diarrhea study showed that crofelemer may be a particularly useful option in those patients without a significant pain component to their symptoms, and it may be safe and effective in functional diarrhea, particularly given that its mechanism of action is not constipating," commented Judy Nee, MD, the principal investigator for the study. Dr. Nee is a gastroenterologist at Beth Israel Deaconess Medical Center and an assistant professor at Harvard Medical School. She serves as co-director of the GI Motility Lab at Beth Israel, and specializes in GI motility disorders and functional GI diseases such as IBS, chronic diarrhea, and constipation, as well as movement disorders of the esophagus.

As a global "basket" trial designed to attempt to identify any solid tumor patient that could benefit from crofelemer prophylaxis, OnTarget was an incredibly ambitious study - but rightly so. If we had not swung for the fences with this study, and, for example, had only evaluated breast cancer patients in OnTarget - a tumor type for which evidence of crofelemer's effectiveness already exists for CTD - we would not have discovered the important clinical result in patients with respiratory and lung cancer. In the end, Jaguar is a mission-driven company. Our mission is to change patients' lives for the better. Our mission is unwavering, and we are inspired by the clinical evidence we have seen related to supportive care, patient comfort, and patient dignity, and by the potential that crofelemer's novel and paradigm-shifting mechanism of action may have to impact outcomes for certain complex disease states.

Of the 287 patients enrolled in the OnTarget study, 37 had respiratory cancers, and 180 had breast cancer. Combined, the 217 patients in these two groups represented more than 75% of the patients randomized in the OnTarget study. The clinical meaningfulness of these results is based on information provided by solid tumor patients from a survey we conducted before drafting the clinical protocol for OnTarget. Patients drive the mission of Jaguar. We do not believe that any cancer therapy-related side effect, whether it be extreme fatigue, debilitating diarrhea, neuropathy, oral mucositis, chronic pain, or any other should ever be viewed as acceptable or tolerable. This belief is a core message of our ongoing *Make Cancer Less Shitty* campaign, which seeks to broadly acknowledge the rigors of both short-term and perpetual treatment by sharing the voices and stories of individuals with that lived experience.

A growing and urgent unmet medical need exists for novel non-opioid chronic agents to treat chronically affected patients. We thankfully now live in the age of targeted therapies for cancer treatment, and thanks to these amazing drugs, cancer patients and metastatic cancer patients are living longer - 5, 10, 20 years longer - frequently rendering cancer a chronic ailment with which to live. However, the chronic use of targeted therapies means side effects often continue in perpetuity. As a breast cancer survivor, I know firsthand that no cancer therapy-related side effect should ever be viewed as acceptable or tolerable. The key is to live, not just survive. This is why patient dignity and quality of life, and the ability of patients to comfortably adhere to their cancer therapy, are first and foremost in our ongoing development efforts.

**Jaguar's Focus on Rare and Orphan Diseases**

Crofelemer, as a novel, first-in-class anti-secretory antidiarrheal drug that has a normalizing effect on electrolyte and fluid balance in the gut, has the potential to benefit multiple disorders that cause GI distress, including diarrhea and abdominal discomfort. The robustness of crofelemer's "normalizing" effect on gut activity is further embodied in development efforts for the drug for targeted rare and orphan disease indications - Jaguar's other clinical core focus area. As previously announced, with strong leadership and participation from Jaguar family companies Napo Pharmaceuticals and Napo Therapeutics, we are supporting independent, investigator-initiated proof-of-concept studies of crofelemer for microvillus inclusion disease (MVID) and short bowel syndrome (SBS) with intestinal failure in the U.S., EU and Middle East/North Africa (MENA) regions, with results expected before the end of 2024 and throughout 2025. Crofelemer has received Orphan Drug designation in the US and EU for both MVID and SBS.

I am pleased to announce that the required import permit for crofelemer has been granted for the planned investigator-initiated proof-of-concept trial in Abu Dhabi in pediatric patients for MVID and SBS with intestinal failure. We have worked for years to bring this clinical investigation in the MENA region to reality. Cultures associated with consanguineous marriages are associated with an increased risk of congenital disorders.

MVID, an ultrarare congenital diarrheal disorder, is a severe infantile disease characterized by diarrhea, malabsorption, and acid/base instability, requiring intensive parenteral support for nutritional and fluid management, and there are currently no approved drug treatments.

Some SBS patients are subject to intestinal failure, often requiring parenteral nutrition (PN) up to 7 days a week. Intestinal failure is associated with significant morbidity and mortality, and high medical expenses associated with PN. SBS patients with intestinal failure also have severe chronic diarrhea, and the associated sequelae from diarrhea, including significant dehydration, metabolic acidosis or alkalosis and malnutrition, and other secondary symptoms. Many times, these symptoms become life-threatening.

In accordance with the guidelines of specific EU countries, published proof-of-concept data from clinical investigations in SBS and MVID could support reimbursed early patient access to crofelemer for these debilitating conditions in those countries while crofelemer is completing the clinical investigation required for full regulatory approval. We are aiming for proof-of-concept data in the end of 2024 and throughout 2025.

**Jaguar's Focus on Medicines Derived from Plants for Mental Health Disorders**

Jaguar's Entheogen Therapeutics Initiative (ETI) aims to discover and develop groundbreaking, novel, natural medicines derived from psychoactive plants for treatment of mood disorders, neuro-degenerative diseases, addiction, and other mental health disorders. The initiative leverages our proprietary library of 2,300 medicinal plants and 3,500 plant extracts. Magdalena Biosciences, a joint venture we formed with Filament Health, holds an exclusive license to the portion of our plant library focused on developing novel, FDA-approved botanical drugs derived from psychoactive plants to treat and possibly cure mental health indications and mood disorders. Jaguar currently owns approximately 40-percent of Magdalena.

As announced, Jaguar recently executed an out-license deal with Magdalena for a botanical drug candidate for possible schizophrenia and psychoses indications and for development with potential corporate partners. Sourced from a medicinal plant that has a long history of use by traditional healers, the drug candidate demonstrates antipsychotic activity and has a mechanism of action distinct from currently FDA-approved therapies for schizophrenia and other mental conditions that present psychotic symptoms. The drug candidate may have the potential to be the first in a new class of plant-based antipsychotic compounds.

Magdalena's near-term goal is to be in the clinic initiating next year for target indications such as schizophrenia, anxiety, depression, and ADHD. Many botanical drugs have a long history of safe use in traditional medicines, which may be documented and reviewed in scientific literature. Existing scientific literature on safety may accelerate the safety review process for a botanical drug, reducing the scope and financial burden for extensive safety studies. Additionally, botanical drugs, by virtue of their complexity, have the added benefit of being difficult to genericize. Hence there are often multiple opportunities for creating 'trade-secrets,' as well as novel patents around a botanical drug substance, its processing, its formulation, and so forth, as is the exclusivity position of crofelemer, the only oral drug approved under botanical guidance.

We thank you, our shareholders, for your support and your dedication to our mission to bring innovate drugs with truly novel mechanisms of action to patients in need around the world, and we hope you can join our investor webcast on August 13th.

Sincerely,

Lisa Conte
Founder, President, and Chief Executive Officer

**Participation Instructions for Webcast**
When: Tuesday, August 13, 2024 at 8:30 AM Eastern Time
Participant Registration & Access Link: **Click Here**

**Replay Instructions for Webcast**
Replay of the webcast on the investor relations section of Jaguar's website: (click here)

**About the Phase 3 OnTarget Clinical Trial**

The multicenter double-blind, placebo-controlled OnTarget study is a first-of-its-kind prophylactic clinical trial with a primary endpoint based on patient-reported outcomes that address the highly neglected and unmet burden of cancer therapy-related diarrhea. The study evaluated the efficacy of crofelemer, a botanical drug that modulates intestinal chloride ion channels, for its ability to prevent or substantially reduce cancer therapy-related diarrhea over the 12-week treatment period, compared to placebo. The trial involved 10 different tumor types and 24 different targeted agents, with and without multiple standard cytotoxic chemotherapies. Patients then had the opportunity to continue in a blinded 12-week extension of their phase 1

therapy. A majority of the patients chose to continue.

**About Crofelemer**

Crofelemer is the only oral prescription drug approved under FDA botanical guidance. It is plant-based, extracted and purified from the red bark sap of the *Croton lechleri* tree in the Amazon rainforest. Jaguar family company 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 (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 at makecancerlessshitty.com and on X, Facebook & Instagram

**Forward-Looking Statements**

Certain statements in this press release constitute "forward-looking statements." These include statements regarding Jaguar's expectation that it will conduct an investor webcast on August 13, 2024, Jaguar's expectation that the company may conduct scientific publication submissions and meet with the FDA after evaluating the significance of the clinical outcome signals from the OnTarget trial, Jaguar's expectation that an approval pathway may exist to make crofelemer available to breast and lung cancer patients for CTD, the expectation that crofelemer may be a particularly useful option in functional diarrhea patients without a significant pain component to their symptoms and that crofelemer may be safe and effective in functional diarrhea, Jaguar's expectation that crofelemer's mechanism of action may have the potential to impact outcomes for certain complex disease states, Jaguar's expectation that crofelemer has the potential to benefit multiple disorders that cause GI distress, including diarrhea and abdominal discomfort, Jaguar's expectation that the results of investigator-initiated proof-of-concept studies of crofelemer for MVID and SBS with intestinal failure in the U.S., EU and MENA regions will be available before the end of 2024 and throughout 2025, Jaguar's expectation that, in accordance with the guidelines of specific EU countries, published proof-of-concept data from clinical investigations in SBS and MVID could support reimbursed early patient access to crofelemer for these debilitating conditions in those countries while crofelemer is completing the clinical investigation required for full regulatory approval, the expectation that the botanical drug candidate that is the subject of the recent out-license deal from Jagaur to Magdalena may have the potential to be the first in a new class of plant-based antipsychotic compounds, the expectation that Magdalena may be in the clinic initiating next year for target indications such as schizophrenia, anxiety, depression, and ADHD, and the expectation that existing scientific literature on safety may accelerate the safety review process for a botanical drug, reducing the scope and financial burden for extensive safety studies. 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.

[1] Source: https://www.who.int/news-room/fact-sheets/detail/breast-cancer

**Contact:**

hello@jaguar.health

**SOURCE:** Jaguar Health