Jaguar Health Provides Update on Meeting with FDA Discussing Statistically Significant Results of Responder Analysis of Breast Cancer Patients in Phase 3 OnTarget Trial and Potential Approval Pathway for Crofelemer

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Productive and collaborative discussion on proposed pathway by the company to bring crofelemer to approval for cancer therapy-related diarrhea (CTD) in patients with metastatic breast cancer receiving selected targeted therapies

The currently estimated US metastatic breast cancer population would qualify as an orphan population, which aligns with company's core focus on orphan diseases

Company plans to promptly pursue authorization to initiate expanded access program for patients with breast cancer who may not be eligible for a potential pivotal treatment trial with crofelemer in patients with metastatic breast cancer

SAN FRANCISCO, CA / ACCESS Newswire / June 9, 2025 / Jaguar Health, Inc.(NASDAQ:JAGX) (Jaguar) family company Napo Pharmaceuticals (Napo) today provided a recap on the company's assessment of the in-person Type C Meeting on May 28, 2025 with the Division of Gastroenterology of the U.S. Food and Drug Administration (FDA) to discuss the statistically significant responder analysis results for adult patients with breast cancer in Napo's recently conducted Phase 3 OnTarget trial.

"We were very happy to take part in the face-to-face Type C Meeting, the catalyst for which was the positive data in the subpopulation of breast cancer patients from our OnTarget trial," said Lisa Conte, Jaguar's founder, president, and CEO. "Napo proposed two simultaneous potential pathways during the meeting for making crofelemer available to metastatic breast cancer patients with the significant unmet medical need of CTD: conducting a pivotal treatment trial to facilitate approval of crofelemer for CTD in this focused patient population; and the prompt pursuit of authorization to initiate an expanded access program for breast cancer patients with CTD who may not be eligible for this study, including breast cancer patients in the adjuvant and neoadjuvant settings. We are pleased with the constructive and productive discussion that took place with the FDA during the meeting. Last week the FDA formally acknowledged both of these key discussion points in correspondence to Napo. We plan to submit a protocol to the FDA for a pivotal treatment trial for a smaller number of metastatic breast cancer patients using crofelemer."

Patient advocates participated in the Type C Meeting to share their raw and personal experience with CTD, including a metastatic breast cancer patient with uncontrollable diarrhea who received a prescription for crofelemer.

"The design of the protocol for OnTarget was based on a survey of cancer patients. Today there are close to 100 approved targeted cancer agents. Thanks to these amazing drugs, metastatic cancer patients are living longer, frequently rendering cancer, and CTD, chronic ailments with which to live. To deepen our understanding of the current population of metastatic cancer breast with CTD, and ensure the clinical meaningfulness of the design of the anticipated pivotal treatment trial, we plan to conduct a new survey of this cancer patient population," Conte said.

The currently estimated US metastatic breast cancer population potentially qualifies as an orphan population, in alignment with the company's core focus on orphan diseases. The company therefore intends to request orphan drug designation from the FDA for the CTD indication in this population. Given crofelemer's novel and paradigm-shifting mechanism of action, the company also plans to seek Breakthrough Therapy designation and/or Fast Track designation from the FDA to support potentially expedited regulatory approval in the US for crofelemer for CTD in metastatic breast cancer patients.

"Embracing a sharp strategic focus on orphan indications seems to fit with the new administration's efforts and philosophy," said Conte. "Dr. Marty Makary, the new Commissioner of the FDA, commented in April 2025 that the agency will open a new regulatory pathway based on what he called a 'plausible mechanism,' focusing mainly on rare or incurable diseases."

As expressed during the Type C Meeting, the data from the first-of-its-kind prophylactic OnTarget study is invaluable, providing new insights into the natural history of the important and debilitating side effect of CTD. Diarrhea is a common side effect of targeted cancer therapies and can lead to dose changes, treatment delays, and often cessation of lifesaving cancer therapy. The benefit to risk ratio of crofelemer is well-documented, as the active agent has been commercialized for the approved indication of HIV-related diarrhea since 2012, with no crofelemer-related reported serious adverse events.

In both the US and European Union, crofelemer has been granted orphan drug designation for the orphan diseases of short bowel syndrome with intestinal failure and microvillus inclusion disease. Crofelemer has been granted orphan drug designation for treatment of diarrhea in cholera in the US, where cholera is an orphan disease. Orphan drug designation in the US qualifies the sponsor of a drug for various development incentives, including tax credits for qualified clinical testing and relief of filing fees. Additionally, orphan drug designation in the US provides a seven-year period of

marketing exclusivity to the first sponsor who obtains marketing approval for the designated orphan drug.

While the multicenter, double-blind, placebo-controlled OnTarget pivotal trial did not meet its primary endpoint, the subgroup of adult breast cancer patients achieved statistically significant results in the responder analysis. In the responder analysis of patients with breast cancer on targeted therapies, crofelemer CTD prophylaxis resulted in a greater proportion of monthly responders of diarrhea improvement compared to placebo. Patients with breast cancer accounted for 183 of the 287 participants in this unprecedented prophylactic clinical trial of crofelemer for diarrhea in adults with 10 solid tumor types receiving targeted therapy with or without standard chemotherapy.

The OnTarget results in breast cancer patients were the subject of a poster presentation on December 11, 2024, at the San Antonio Breast Cancer Symposium, and additional significant results in adult breast cancer patients from the OnTarget study have been accepted for presentation as an oral rapid e-poster at the Multinational Association of Supportive Care in Cancer (MASCC) Annual Meeting in June 2025 in Seattle, Washington.

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 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 currently estimated US metastatic breast cancer population qualifies as an orphan population, Jaguar's expectation that the company will submit a protocol to the FDA for a pivotal treatment trial for a smaller number of metastatic breast cancer patients using crofelemer, Jaguar's expectation that it will promptly pursue authorization to initiate an expanded access program for patients with breast cancer who may not be eligible for a potential pivotal treatment trial with crofelemer in patients with metastatic breast cancer patients, and that the expanded access program would potentially include breast cancer patients in the adjuvant and neoadjuvant settings, Jaguar's expectation that Napo will conduct a clinical trial of crofelemer for treatment of CTD in patients with metastatic breast cancer, Jaguar's plans to seek Breakthrough Therapy designation and/or Fast Track designation from the FDA to support potentially expedited regulatory approval in the US for crofelemer for CTD in metastatic breast cancer patients, and Jaguar's expectation that additional significant results in adult breast cancer patients from the OnTarget study will be presented at the 2025 MASCC Annual Meeting. 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