Jaguar Health Reports Phase 3 OnTarget Trial Results for its Cancer Supportive Care Drug Crofelemer

July 23, 2024

Initial results of unprecedented trial including 10 different tumor types indicate that OnTarget did not meet its primary endpoint across all tumor types. Trial did reveal clinically relevant signals for crofelemer in prespecified subgroups of patients with breast and respiratory cancer, including lung cancer.

Jaguar to host investor webcast Tuesday, July 23rd at 8:30 AM Eastern to provide updates on company's cancer supportive care portfolio, including participation from Jaguar scientific team, patient advocates, and leading oncology experts on cancer therapy-related diarrhea (CTD) and oral mucositis; Click here to register for webcast.

SAN FRANCISCO, CA / ACCESSWIRE / July 23, 2024 / Jaguar Health, Inc. (NASDAQ:JAGX) ("Jaguar") today announced the results from its initial analysis of the pivotal Phase 3 OnTarget trial of crofelemer for prophylaxis of diarrhea in adult cancer patients with solid tumors receiving targeted therapy with or without standard chemotherapy. Crofelemer is an FDA-approved prescription drug for the symptomatic relief of diarrhea in adult HIV/AIDS patients receiving antiretroviral therapy. The initial results from the OnTarget study show that the multicenter, double-blind, placebo-controlled pivotal clinical trial did not meet its primary endpoint for the prespecified analysis of all tumor types in the trial.

"While the results of the OnTarget study did not achieve significance for all tumor types receiving various targeted therapies, I am pleased that the subgroup analyses show that crofelemer provides clinically meaningful improvement in the prespecified subgroups of breast and respiratory tumor patients. Clinical meaningfulness of these results is based on the information provided by solid tumor patients from a survey that informed us about the appropriate clinical study design and clinical endpoints, that are important to the patients in this prophylactic trial. We will continue to evaluate important OnTarget findings, with further analyses," said Pablo Okhuysen, MD, Professor of Medicine, University of Texas MD Anderson Cancer Center, Houston, Texas, who is the Principal Investigator of the OnTarget clinical trial. "It is important to note that the prespecified secondary outcomes for this study were based on outcomes that were considered to be meaningful by patients experiencing diarrhea due to targeted therapy."

KEY TAKE-A-WAYS FROM ONTARGET TRIAL

- Unprecedented OnTarget trial included patients with 10 different tumor types and 24 different targeted agents, with and without multiple standard cytotoxic chemotherapies.
- Study did not meet prespecified analysis of primary endpoint for all tumor types.
- Analysis did reveal clinically relevant signals for patients in the prespecified subgroups of breast and respiratory cancers, including lung cancer, who received targeted therapies. These subgroups of patients comprised over 75% of the patients in the trial.
- Breast and lung cancers are two of the three most common cancers, with patients often remaining on targeted therapy over prolonged periods.
- A growing and urgent unmet medical need exists for novel non-opioid chronic agents to treat CTD.
- Results indicate positive signals improved over the initial 12-week phase of study; data for additional 12-week extension phase yet to be analyzed.
- Company expects to engage with FDA after full review of data.

The unprecedented OnTarget trial included patients with 10 different tumor types and 24 different targeted agents, with and without multiple standard cytotoxic chemotherapies. It consisted of two 12-week stages: a 12-week double-blind treatment phase followed by a 12-week double-blind extension phase. The prespecified primary endpoint for the trial was defined as reducing the average number of weekly loose and/or watery stools for all tumor types receiving various targeted therapies over the initial 12-week period of this prophylactic study. Analysis of data for the initial 12-week stage revealed clinically relevant signals for crofelemer over placebo in the prespecified subgroups of breast and respiratory cancer patients, who comprised over 75% of the patients in OnTarget, and it appears that this benefit improved over the initial 12-week stage. The data for the study's 12-week extension phase has not yet been analyzed. The company will complete the analysis of full data for the first and second 12-week periods and will disclose the results in future presentations and publications.

"We believe the OnTarget trial, designed boldly to address a broad array of cancer patients undergoing therapy known to be associated with diarrhea, did not meet the primary endpoint given the heterogenous nature of the patients enrolled in the trial. Nevertheless, we are pleased that our preliminary

analysis of the study data shows a clinically meaningful benefit in response to crofelemer in patients with breast and respiratory cancers, including lung cancer," said Lisa Conte, Founder, President, and Chief Executive Officer of Jaguar. "Breast and lung cancer are two of the top three most common cancer types, and treatment options for breast and lung cancer include the long-term use of targeted therapies that cause high incidences of diarrhea. We will continue to review data from prespecified and non-prespecified OnTarget subgroups and then engage in discussions with the U.S. Food and Drug Administration (FDA) to seek the most efficient pathway to bring crofelemer to these patients and address the important and debilitating side effect of cancer therapy-related diarrhea with the paradigm shifting mechanism of crofelemer. Patient dignity and the ability of patients to adhere with comfort to their cancer therapy is first and foremost in our ongoing development efforts."

Crofelemer was well tolerated in OnTarget, and the adverse event profile was similar to placebo. Most adverse events were related to the cancer therapy and/or the disease itself. The OnTarget findings are based on 287 patients representing all solid tumor types and 24 targeted agents, with or without cytotoxic chemotherapy. Included within the 287 enrolled patients were 37 respiratory cancer patients and 180 breast cancer patients or greater than 75%. The patients were enrolled from 49 sites and included investigators from oncology clinics in the United States, Argentina, Georgia, Serbia, and Taiwan.

"Our deepest gratitude goes to the patients and investigators who participated in this study around the world. We are proud to have completed the first prophylactic, randomized, double-blind study including patient reported outcomes for prevention of cancer therapy-related diarrhea. The study prioritized standard of cancer care for study participants, with Jaguar's endorsement," Conte said. "As Jaguar continues the journey to bring crofelemer to people living with a cancer diagnosis, we remain fully committed to expanding our commercial footprint beyond HIV-related supportive care. In Q4 2024, we will launch the FDA-approved oral mucositis prescription product Gelclair® for the U.S. market. Oral mucositis is a dose-limiting side effect of cancer treatment, with more than one-third of patients discontinuing treatment because of the condition.[1] Additionally, crofelemer is in multiple clinical investigations globally for the orphan indications of short bowel syndrome and microvillus inclusion disease - an ultrarare congenital diarrheal disorder - with proof-of-concept data targeted for end of 2024 and throughout 2025."

Participation Instructions for Webcast

When: Tuesday, July 23, 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 July 23, 2024, Jaguar's expectation that it will complete the analysis of full data for the first and second 12-week

periods and disclose the results in future presentations and publications, Jaguar's expectation that it will engage in discussions with the FDA to seek the most efficient pathway to bring crofelemer to cancer patients and address the side effect of CTD, Jaguar's expectation that it will launch Gelclair in the U.S. in Q4 2024, and Jaguar's expectation that proof-of-concept data from multiple clinical investigations of crofelemer for short bowel syndrome and microvillus inclusion disease will be available by the end of 2024 and throughout 2025. 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] Oncology Nursing Society (ONS): https://www.ons.org/pep/mucositis

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