Jaguar Health Subsidiary Napo Pharmaceuticals Initiates Pivotal Phase 3 Clinical Trial of Crofelemer (Mytesi) for Prophylaxis of Diarrhea in Adult Cancer Patients Receiving Targeted Cancer Therapy

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A Significant Proportion of Patients Receiving Targeted Cancer Therapy Experience Diarrhea

Initial Tranche of Non-dilutive Financing Transaction Increased from $5 Million to $6 Million by Mutual Consent with Lender, Providing Additional Q4 2020 Funding for Pivotal Phase 3 Clinical Trial and a Total Potential of $17 Million

SAN FRANCISCO, CA / ACCESSWIRE / October 7, 2020 / Jaguar Health, Inc. (NASDAQ:JAGX) announced today that the company's wholly owned subsidiary, Napo Pharmaceuticals, Inc. (Napo), has initiated its pivotal Phase 3 clinical trial of crofelemer (Mytesi®) for prophylaxis of diarrhea in adult cancer patients receiving targeted therapy ("cancer therapy-related diarrhea" (CTD)).

The Phase 3 pivotal clinical trial is a 24-week (two 12-week stages), randomized, placebo-controlled, double-blind study to evaluate the safety and efficacy of crofelemer (Mytesi) in providing prophylaxis of diarrhea in adult cancer patients with solid tumors receiving targeted cancer therapy-containing treatment regimens. Crofelemer or placebo treatment will start concurrently with the targeted cancer therapy regimen. The primary endpoint will be assessed at the end of the initial (Stage I) 12-week double-blind placebo-controlled primary treatment phase. After completing the Stage I treatment phase, the subjects will have the option to remain on their assigned treatment arm and reconsent to enter into the Stage II 12-week extension phase. The safety and efficacy of orally administered crofelemer will be evaluated for the prophylaxis of diarrhea in adult cancer patients receiving targeted cancer therapies with or without standard chemotherapy regimens. The assessment of the frequency of diarrhea will be measured by the number of loose and/or watery stools for the Stage I treatment period. Additional details about the trial can be viewed on the clinicaltrials.gov website. The National Clinical Trial number for the trial is NCT04538625.

"The initiation of this pivotal Phase 3 clinical trial for prophylaxis of diarrhea in cancer patients receiving targeted therapy regimens is a key milestone for Mytesi as we evaluate its potential to prevent and/or mitigate the intensity and severity of diarrhea experienced by cancer patients receiving targeted cancer therapy regimens, which may include various combinations with standard chemotherapy regimens," said Pravin Chaturvedi, PhD, Napo Pharmaceuticals/Jaguar Health Chair, Scientific Advisory Board and acting Chief Scientific Officer.

Pablo Okhuysen, MD, the National Principal Investigator for the trial, stated, "Patients undergoing targeted cancer therapies frequently experience diarrhea as a side effect affecting their quality of life. Severe diarrhea can lead to dehydration, electrolyte imbalances and hospitalization and can compromise the efficacy of cancer treatments. Traditionally, symptomatic management of diarrhea has relied on the use of opioid anti-motility agents which are sub-optimal in terms of efficacy and can cause unwanted constipation and central nervous system side effects. There have been no substantial changes to this approach in recent years and cancer therapy related diarrhea remains an important unmet medical need for patients with cancer. New agents are needed. Crofelemer has previously been found to be effective in providing diarrhea relief in patients with HIV/AIDS receiving antiretroviral therapy and is well tolerated in that setting. We are excited to study crofelemer, a minimally absorbed, anti-secretory agent that has no significant drug-drug interactions for its potential to prevent diarrhea in cancer patients receiving tyrosine kinase inhibitors and other targeted therapies."

Dr. Okhuysen is Professor of Medicine, Department of Infectious Diseases, Infection Control, and Employee Health, Division of Internal Medicine, at the University of Texas, MD Anderson Cancer Center in Houston, TX.

According to the Centers for Disease Control and Prevention (CDC), approximately 650,000 cancer patients in the U.S. receive chemotherapy in an outpatient oncology clinic each year. A significant proportion of patients undergoing cancer therapy experience diarrhea, and diarrhea has the potential to cause dehydration, potential infections, and non-adherence to treatment in this population.

"We are excited to initiate Napo's pivotal trial of Mytesi for CTD, and happy that the initial tranche has increased from $5 million to $6 million, by mutual consent with Jaguar's lender, for the previously announced non-dilutive royalty financing transaction - which now has the potential to total $17 million. This additional Q4 2020 funding may enable Napo to bring on more study sites sooner for the pivotal Phase 3 clinical CTD trial, potentially providing for more rapid enrollment for this important indication," said Lisa Conte, Jaguar's president and CEO.

"Managing cancer therapy related diarrhea provides a measure of control and return of dignity, as we've heard from patients. Moreover, reducing frequency of watery stools in cancer patients may allow better adherence to the therapeutic dosing of targeted therapies as well as chemotherapy, potentially leading to better clinical outcomes. Our pivotal trial for CTD will use the same formulation and dosing that is used for the currently commercialized Mytesi for the symptomatic relief of HIV/AIDS-associated diarrhea in adult patients receiving antiretroviral therapy," Conte continued.

Novel "targeted cancer therapy" agents, such as epidermal growth factor receptor (EGFR) antibodies and tyrosine kinase inhibitors (TKIs), with or

without cycle chemotherapy agents, may activate intestinal chloride ion channel-mediated secretory pathways, leading to increased electrolyte and fluid content in the gut lumen, which results in passage of loose/watery stools (i.e. secretory diarrhea). Diarrhea has been reported as one of the most common side effects of TKIs, including the recently approved irreversible pan-HER TKI neratinib (Nerlynx®), with occurrence ranging from 86% to >95% in published studies. Diarrhea is also a common side effect of some CDK 4/6 inhibitors.

Mytesi is a non-opiate, plant-based, chloride ion channel modulating antidiarrheal medicine that is FDA approved for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS receiving antiretroviral therapy. The only oral plant-based prescription medicine approved under FDA Botanical Guidance, Mytesi has a novel mechanism of action that works locally in the gut by gently and effectively modulating and normalizing the flow of water and electrolytes with minimal systemic absorption. Crofelemer was purified by Napo scientists and is sustainably harvested from the Amazon Rainforest.

About Jaguar Health, Inc.

Jaguar Health, Inc. is a commercial stage pharmaceuticals company focused on developing novel, plant-based, sustainably derived gastrointestinal products on a global basis. Our wholly owned subsidiary, Napo Pharmaceuticals, Inc., focuses on developing and commercializing proprietary plant-based human gastrointestinal pharmaceuticals for the global marketplace from plants used traditionally in rainforest areas. Our Mytesi® (crofelemer) product is approved by the U.S. FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy and the only oral plant-based prescription medicine approved under FDA Botanical Guidance.

For more information about Jaguar, please visit https://jaguar.health. For more information about Napo, visit www.napopharma.com.

About Mytesi®

Mytesi (crofelemer) 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. Crofelemer, the active ingredient in Mytesi, is a botanical (plant-based) drug extracted and purified from the red bark sap of the medicinal *Croton lechleri* tree in the Amazon Rainforest. Napo has established a sustainable harvesting program for crofelemer to ensure a high degree of quality and ecological integrity.

Forward-Looking Statements

Certain statements in this press release constitute "forward-looking statements." These include statements regarding the development of crofelemer for the potential additional indication of prophylaxis and symptomatic relief of CTD, the expectation that reducing frequency of watery stools in cancer patients may allow better adherence to the therapeutic dosing of targeted therapies as well as chemotherapy, potentially leading to better clinical outcomes, the expectation that the previously announced non-dilutive royalty financing transaction has the potential to total $17 million, and the expectation that the additional Q4 2020 funding may enable Napo to bring on more study sites sooner for the pivotal Phase 3 clinical CTD trial, potentially providing for more rapid enrollment. 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 a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond Jaguar's control. Some of the factors that could affect our actual results are included in the periodic reports on Form 10-K and Form 10-Q that we file with the Securities and Exchange Commission. 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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