UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934 (Amendment No.)

Filed by the Registrant x

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Check the appropriate box:
- o Preliminary Proxy Statement
- o **Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))**
- o Definitive Proxy Statement
- x Definitive Additional Materials
- o Soliciting Material under §240.14a-12

JAGUAR HEALTH, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):
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- o Fee paid previously with preliminary materials.
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DEAR FELLOW STOCKHOLDERS,

The consistent and encouraging quarter-on-quarter growth in net sales of Mytesi®—Jaguar's first-in-class, FDA-approved anti-secretory, anti-diarrheal agent for our specialty market in people living with HIV/AIDS—in fiscal year 2018 indicates the likelihood of meaningfully greater sales in 2019, and, importantly, increasing medically appropriate utilization in the target patient population.

Total Mytesi prescription volume, which is the combination of new prescriptions and refills, as reported by IQVIA, grew 20% in the fourth quarter of 2018 versus the prior quarter, and increased 94% over the fourth quarter of 2017.

We believe this continuing growth in both sales and prescription volume can be attributed to the consistency of our direct representative efforts to encourage healthcare professionals and prescribers to better identify appropriate patients and to have more meaningful conversations with their patients based on those efforts and our scientific and educational platforms.

A ROBUST PIPELINE

As I've stated before, our near-term focus is to become a stable, cash flow-positive business supported primarily by growth in sales of crofelemer, under the trade name Mytesi, for its current approved indication. Looking ahead, our secondary goal is to drive further growth by initiating business development deals to secure non-dilutive funding to progress our pipeline of potential follow-on indications for Mytesi.

We have a remarkable risk-mitigated product pipeline which contains multiple novel and important potential follow-on indications for Mytesi—a drug product that is already approved for a chronic indication and therefore supported by a chronic safety package. Additionally, GMP commercial manufacturing is in place for Mytesi, and we have proof-of-concept clinical data for most of the planned follow-on indications. The depth of our pipeline provides supportive care solutions for large patient populations across multiple disease indications, and we believe this pipeline will fuel long-term value creation for investors and provide non-dilutive funding opportunities for partner collaborations around the globe.

Diarrhea related to cancer therapy continues to be our lead target for a future indication. A significant proportion of patients undergoing cancer treatment experience diarrhea. Novel targeted cancer therapy agents, such as epidermal growth factor receptor antibodies and tyrosine kinase inhibitors (TKIs), with or without standard chemotherapy agents, may activate natural chloride secretion pathways in the gastrointestinal mucosa, potentially leading to secretory diarrhea.

As we recently announced, our wholly-owned subsidiary, Napo Pharmaceuticals, met with the U.S. Food & Drug Administration (FDA) on March 28, 2019 to discuss the protocol for Napo's planned Phase 3 clinical trial in cancer subjects to evaluate the effects of Mytesi (crofelemer) in prevention and/or relief of cancer therapy-related diarrhea (CTD). We are pleased to report that we had a very collaborative discussion about the clinical trial design that would allow the determination of safety and efficacy of crofelemer in CTD. Napo's planned next step is to continue its interactions with the FDA and incorporate the input from this dialog into the Phase 3 protocol following this very informative discussion.

Our crofelemer pipeline includes other targets for future indications, such as orphan drug designation for congenital diarrheal disease and short bowel syndrome, supportive care for inflammatory bowel disease, diarrhea-predominant irritable bowel syndrome, and idiopathic functional diarrhea. In addition, a second-generation, proprietary anti-secretory agent, lechlemer, is in development for cholera.

Prioritizing our activities and use of resources remains paramount, and we have therefore prioritized in the pipeline those indications which we believe are closest to approval and of greatest interest to potential partners. In support of our focus on the potential CTD indication, two ongoing investigator initiated trials utilizing Mytesi are underway. Enrollment is ongoing for the HALT D study at Georgetown University in breast cancer patients receiving regimens containing Herceptin and Perjeta, which is being funded by Genentech Roche, and interim results are expected to be read out in the first half of 2019. A second investigator-initiated study, being funded by Puma Biotechnology, is evaluating the use of crofelemer in breast cancer patients receiving neratinib-containing regimens, which are reported to have extremely high rates of diarrhea. Additionally, a third-party cancer agent manufacturer is funding Napo's implementation of a nonclinical study, which is underway to evaluate the effects of crofelemer treatment on TKI-induced diarrhea in healthy female dogs. The evaluation of crofelemer effects in dogs receiving TKIs is intended to provide additional scientific rationale and support for the use of crofelemer in providing symptomatic relief of noninfectious diarrhea in human patients receiving TKI-containing regimens in future human clinical investigations.

In addition, Napo has accepted a request for support for an investigator-initiated trial of crofelemer at Sheikh Khalifa Medical City in Abu Dhabi for congenital diarrheal disorders (CDDs) in children. The incidence of CDDs is much more prevalent in this part of the world, where consanguineous marriages, such as marriages between cousins, are part of the culture, and therefore we have access to a meaningful number of patients in this region to study for these rare disorders.

Our final prioritized pipeline goal involves filing an investigational new drug application for lechlemer for the planned cholera indication, along with efforts to pursue a tropical disease priority review voucher (PRV) from the FDA for this possible indication. We believe lechlemer, which has the same mechanism of action as crofelemer and is significantly less costly to produce, may support efforts to receive a PRV for symptomatic relief of severe diarrhea in cholera patients. PRVs are granted by the FDA to drug developers as an incentive to develop treatments for neglected diseases and rare pediatric diseases. Additionally, we believe lechlemer represents a long-term pipeline opportunity as a second-generation anti-secretory agent, on a global basis, for multiple gastrointestinal diseases—especially in resource-constrained countries where cost of goods is a factor, because, in part, requirements often exist in such regions for drug prices to decrease annually.

As a reminder, Mytesi is the first oral drug approved under FDA botanical guidance, which does not provide for a generic product pathway. Lechlemer is also a drug candidate under botanical guidance, potentially enjoying the same exclusivity opportunity.

Cholera is an acute diarrheal illness that kills thousands of people worldwide each year due to rapid dehydration in the first few to 48 hours after infection, a period sometimes called the death zone. We have presented Phase 2 data on crofelemer from the highly regarded International Center for Diarrheal Disease Research (ICDDR) in Bangladesh—often referred to as the cholera hospital—for symptomatic relief of severe watery diarrhea in cholera patients, and we plan to follow the same study design for a trial conducted in association with ICDDR to support development of lechlemer for the potential cholera indication.

Across our pipeline, our continuing goal is to progress to clinical work with non-dilutive support from potential corporate partners, which we are actively pursuing globally. As we announced this past September, Jaguar and Canadian specialty pharmaceutical company Knight Therapeutics have entered into a distribution license and supply agreement granting Knight the exclusive right to commercialize Mytesi and related Napo products in Canada and Israel.

In summary, we believe we're in a highly favorable position, possessing this pipeline within a first-in-class anti-secretory product for which pipeline risk is mitigated—because crofelemer, Mytesi, is already approved for chronic administration, we hold extensive global rights, we have proof of concept clinical

data for most of our planned follow-on indications, commercial manufacturing is in place in an FDA-approved facility, and outside corporate interest exists, as demonstrated by our recently enacted partnership with Knight. We believe we're moving in the right direction. We're increasing awareness among HIV physicians, we're increasing awareness among gastroenterologists, and we're increasing utilization in the patient population.

SUPPORTING ANIMALS

To support our effort to become a stable, cash-flow-positive operational business supported primarily by growth in Mytesi sales for its current approved indication, we have, as previously announced, dramatically reduced our expenditures on the animal health side of the business. We are, however, continuing initiatives related to Canalevia (crofelemer delayed-release tablets), our drug product candidate for chemotherapy-induced diarrhea (CID) in dogs, as well as Equilevia and Neonorm, our non-prescription products for total gut health in dairy calves, foals, and equine athletes.

As previously announced, Jaguar has received Minor Use in a Minor Species (MUMS) designation, per the requirements of The Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act), for Canalevia for CID in dogs. To obtain conditional approval of a MUMS drug, a company must submit CMC, Environmental Impact, and Target Animal Safety data identical to that required for a new animal drug application (NADA) as well as data suggesting a reasonable expectation of effectiveness. After the submission and the review of the application, the FDA through the FDA's Center for Veterinary Medicine (CVM) can then grant a conditional approval (CA-1). This approval allows for commercialization of the product, while the sponsor continues to collect the substantial evidence of effectiveness required for a full NADA approval. A sponsor that gains approval or conditional approval for a MUMS-designated drug then receives seven years of marketing exclusivity.

We believe there is an important unmet medical need for the treatment of CID in dogs. Certain cancer treatment agents provided to dogs are human drugs, or have the same mechanism of action as human cancer drugs, and these agents and mechanisms of action often have meaningful rates of diarrhea in humans as well.

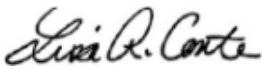
As announced March 20, 2019, Jaguar has now completed three of the four required technical sections—the CMC, Effectiveness, and Environmental Impact technical sections—of the Company's application for conditional approval of Canalevia for CID in dogs. We anticipate filing the Target Animal Safety technical section with CVM in the second quarter of this year. With receipt of conditional approval for this indication, we would expect to conduct the commercial launch of Canalevia for CID in dogs in 2020.

Our non-prescription product line is a stable generator of moderate and recurring revenue from a solid inventory base and essentially no promotional effort.

MYTESI, MYTESI, MYTESI

At Jaguar and Napo, we continue to remain laser-focused on driving Mytesi sales. We believe Mytesi will be a successful, first-in-class entry to gastrointestinal care—in the U.S. and internationally—and has the ability to grow long-term and remain exclusively on the market for that long-term growth. I am extremely pleased with our achievements in 2018 and grateful for the ongoing support and dedication of our employees, stockholders, and all our stakeholders as we continue efforts to grow sales and progress multiple possible follow-on indications for Mytesi.

Sincerely,



Lisa A. Conte
Chief Executive Officer & President
May 1, 2019

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.

Important Additional Information
You are urged to read the proxy statement filed with the SEC on April 29, 2019 related to Jaguar's 2019 Annual Meeting of Stockholders. Free copies of the proxy statement and other documents filed by Jaguar with the SEC are available through the SEC's web site at www.sec.gov. In addition, the proxy statement and related materials may also be obtained free of charge from Jaguar by directing such requests to: Jaguar Health, Inc., Attention: Karen S. Wright, 201 Mission Street, Suite 2375, San Francisco, CA 94105 (415.371.8300 phone). Jaguar and certain of its directors and executive officers may be deemed to be participants in the solicitation of proxies.

Forward-Looking Statements
Certain statements in this Stockholders Letter constitute "forward-looking statements." These include statements regarding the likelihood of meaningfully greater sales and increasing medically appropriate utilization in the target patient population in 2019, the Company's plans to become a stable, cash flow-positive business supported primarily by growth in sales of crofelemer, under the trade name Mytesi, for its current approved indication, the Company's plans to drive further growth by initiating business development deals to secure non-dilutive funding to progress the Company's pipeline of potential follow-on indications for Mytesi, the belief that the Company's pipeline will fuel long-term value creation for investors and provide non-dilutive funding opportunities for partner collaborations around the globe, the expectation that Napo will continue its interactions with the FDA and incorporate the input from the Company's dialog with the FDA into the protocol for the planned Phase 3 clinical trial in cancer subjects to evaluate the effects of Mytesi (crofelemer) in prevention and/or relief of CTD, the expectation that interim results from the HALT D study will be read out in the first half of 2019, the belief that the studies in dogs receiving TKIs will provide additional scientific rationale and support for the use of crofelemer in providing symptomatic relief of noninfectious diarrhea in human patients receiving TKI-containing regimens in future human clinical investigations, the belief that lechlemer may support efforts to receive a PRV from the FDA for the possible cholera indication, the belief that lechlemer represents a long-term pipeline opportunity as a second-generation anti-secretory agent, on a global basis, for multiple gastrointestinal diseases, the belief that lechlemer may enjoy an exclusivity opportunity under botanical guidance, the Company's plans to conduct a study in association with ICDDR to support development of lechlemer for the potential cholera indication, the belief that there is an important unmet medical need for the treatment of CID in dogs, the expectation that the Company will file the Target Animal Safety technical section with CVM for the potential CID indication for Canalevia in dogs in the second quarter of this year, the expectation that, with receipt of conditional approval for the CID indication for Canalevia in dogs, the Company will conduct the commercial launch of Canalevia for CID in dogs in 2020, and the belief that Mytesi will be a successful, first-in-class entry to gastrointestinal care—in the U.S. and internationally—and has the ability to grow long-term and remain exclusively on the market for that long-term growth. 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 letter 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 letter 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. 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.