

PROSPECTUS SUPPLEMENT (TO PROSPECTUS DATED SEPTEMBER 23, 2020)



JAGUAR HEALTH, INC.

Up to \$15,300,000 Shares of Common Stock

On October 5, 2020, we entered into a sales agreement (the “Sales Agreement”) with Ladenburg Thalmann & Co. Inc. (“Ladenburg”) relating to shares of our voting common stock, par value \$0.0001 per share (“Common Stock”). In accordance with the terms of the Sales Agreement, we may offer and sell shares of our Common Stock from time to time through Ladenburg. As of April 2, 2021, we have sold under such registration statement and the prospectus an aggregate of 5,824,479 shares of our Common Stock, pursuant to the Sales Agreement, for gross proceeds of \$7,000,000.

Our Common Stock is listed on the Nasdaq Capital Market under the symbol “JAGX.” On April 8, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.94 per share.

Sales of our Common Stock, if any, under this prospectus supplement may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the “Securities Act”). If authorized by us in writing, Ladenburg may also sell shares of our common stock in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices. Ladenburg is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Ladenburg and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

We will pay Ladenburg a commission equal to 3% of the gross sales price per share of common stock issued by us and sold through it as our sales agent under the Sales Agreement. In connection with the sale of the common stock on our behalf, Ladenburg will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Ladenburg will be deemed to be underwriting commissions or discounts.

As of the date of this prospectus supplement, we are no longer subject to the limitations under General Instruction I.B.6 of Form S-3 and, therefore, we may (if we wish) offer and sell under the registration statement of which this prospectus supplement forms a part shares of our Common Stock without any such “aggregate offering price in excess of one-third of our public float” limitation, from time to time through Ladenburg pursuant to the terms of the Sales Agreement.

Investing in our Common Stock involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page S-10 of this prospectus supplement under the caption “Risk Factors” and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

LADENBURG THALMANN

The date of this prospectus supplement is April 9, 2021

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated September 23, 2020 are part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock through Ladenburg. These sales, if any, will be made pursuant to the terms of the Sales Agreement, a copy of which is incorporated by reference into this prospectus supplement.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates. You should not assume that the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free-writing prospectus is accurate as of any date other than as of the date of this prospectus supplement, the accompanying prospectus or any related free-writing prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. You should read this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions “Where You Can Find More Information” and “Incorporation of Information by Reference” in this prospectus supplement. We have not authorized anyone to provide you with information that is in addition to, or different from, that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have prepared. If anyone provides you with different or inconsistent information, you should not rely on it. We are not offering to sell securities in any jurisdiction where the offer or sale is not permitted.

Unless the context otherwise requires, references in this prospectus supplement to “Jaguar,” the “Company,” “we,” “us,” and “our” refer to Jaguar Health, Inc.

Jaguar Health, our logo, Napo Pharmaceuticals, Mytesi, Canalevia, Equilevia and Neonorm are our trademarks that are used in this prospectus supplement. This prospectus supplement also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ©, ® or ™ symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

PROSPECTUS SUPPLEMENT SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus supplement and in the accompanying prospectus. We urge you to read this entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the section entitled “Risk Factors” and the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the SEC.

Overview

Jaguar is a commercial stage pharmaceuticals company focused on developing novel, plant-based, non-opioid, and sustainably derived prescription medicines for people and animals with GI distress, specifically chronic, debilitating diarrhea. Our wholly owned subsidiary, Napo Pharmaceuticals, Inc. (“Napo”), focuses on developing and commercializing proprietary plant-based human gastrointestinal pharmaceuticals for the global marketplace from plants used traditionally in rainforest areas. Our marketed drug Mytesi (crofelemer 125 mg delayed-release tablets) is a product approved by the U.S. Food and Drug Administration (“FDA”) for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy and the only oral plant-based botanical prescription medicine approved under FDA Botanical Guidance.

Jaguar was founded in San Francisco, California as a Delaware corporation on June 6, 2013. Napo formed Jaguar to develop and commercialize animal health products. Effective as of December 31, 2013, Jaguar was a wholly owned subsidiary of Napo, and Jaguar was a majority owned subsidiary of Napo until the close of our initial public offering on May 18, 2015. On July 31, 2017, the merger of Jaguar Animal Health, Inc. and Napo became effective, at which point Jaguar Animal Health’s name changed to Jaguar Health, Inc. and Napo began operating as a wholly owned subsidiary of Jaguar focused on human health and the ongoing commercialization of Mytesi, and development of follow on indications for, crofelemer. Most of the activities of the Company are now focused on the commercialization of Mytesi and development of follow on indications for crofelemer and a second generation anti secretory product, lechlemer, that has yet to be approved by the FDA. In the field of animal health, we have limited activities which are focused on developing and commercializing first in class gastrointestinal products for dogs, dairy calves, foals, and high value horses.

We believe Jaguar is poised to realize a number of synergistic, value adding benefits—an expanded pipeline of potential blockbuster human follow on indications of crofelemer, and a second generation anti secretory agent, as well as a pipeline of potential animal health indications for crofelemer—upon which to build global partnerships. As previously announced, Jaguar, through Napo, now holds extensive global rights for Mytesi, and crofelemer manufacturing is being conducted at a multimillion-dollar commercial manufacturing facility. Additionally, several of the drug product candidates in Jaguar’s crofelemer pipeline are backed by what we believe are strong Phase 2 clinical proof of concept evidence from completed human clinical trials.

Mytesi is a novel, first in class anti secretory agent which has a basic normalizing effect, acting locally in the gut, and this mechanism of action has the potential to benefit multiple disorders that cause diarrhea. Mytesi is in development for multiple possible follow on indications, including cancer therapy related diarrhea (“CTD”); orphan drug indications for symptomatic relief of diarrhea in infants and children with congenital diarrheal disorders (“CDD”) and for adult and pediatric patients with short bowel syndrome (“SBS”); and for supportive care for diarrhea relief in inflammatory bowel diseases (“IBD”); diarrhea-predominant irritable bowel syndrome (“IBS-D”); and for idiopathic/functional diarrhea. Additionally, the Company is exploring the conditional marketing authorization regulatory pathway in Europe to support development and commercialization of crofelemer for a proposed indication of diarrhea in acutely infected COVID-19 patients. Subsequent clinical studies may also be conducted in post COVID recovery patients suffering from “long-hauler” syndrome. A second generation proprietary anti secretory agent, lechlemer, is undergoing development for symptomatic relief of diarrhea resulting from cholera. Crofelemer has previously also received an orphan drug designation for treatment of diarrhea associated with SBS.

In October 2020, Napo initiated its pivotal Phase 3 clinical trial of Mytesi for prophylaxis of diarrhea in adult cancer patients receiving targeted therapy. 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 Mytesi in providing prophylaxis of diarrhea in adult cancer patients with solid tumors receiving targeted cancer therapy-containing treatment regimens. Mytesi 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 re-consent to enter into the Stage II 12-week extension phase. The safety and efficacy of orally administered Mytesi 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.

In September 2020, Jaguar launched the Entheogen Therapeutics (“ETI”) initiative to support the discovery and development of novel, natural medicines derived from psychoactive plant compounds for treatment of mood disorders, neuro-degenerative diseases, addiction, and other mental health disorders. The initiative is initially focused on plants with the potential to treat depression and leverages Napo’s proprietary library of approximately 2,300 plants with medicinal properties. According to statistics available from the National Institute of Mental Health Disorders, part of the National Institutes of Health, approximately 9.5% of American adults ages 18 and over will suffer from a depressive illness (major depression, bipolar disorder, or dysthymia) each year.

Field research collaborations conducted in the past by members of the scientific strategy team (“SST”) of Jaguar’s predecessor company Shaman Pharmaceuticals, who are also members of the ETI SST, yielded possible applications for a compound called alstonine. Alstonine is derived from a plant used by traditional healers in Nigeria, and has demonstrated a potential novel mechanism of action for the treatment of difficult to manage conditions such as schizophrenia.

While Jaguar and Napo remain steadfastly focused on the commercial success of Mytesi and on the development of potential crofelemer follow-on indications in the area of gastrointestinal health, the Company believes the same competencies and multi-disciplinary scientific strategy that led to the development of crofelemer will support collaborative efforts with potential partners to develop novel first-in-class prescription medicines derived from psychoactive plants.

Our management team has significant experience in gastrointestinal product development for both humans and animals. Napo was founded 30 years ago to perform drug discovery and development by leveraging the knowledge of traditional healers working in rainforest areas. Ten members of the Jaguar and Napo team have been together for more than 15 years. Dr. Steven King, our chief sustainable supply, ethnobotanical research and intellectual property officer, and Lisa Conte, our founder, president and CEO, have worked together for more than 30 years. Together, these dedicated personnel successfully transformed crofelemer, which is extracted from trees growing in the rainforest, to Mytesi, which is a natural, sustainably harvested, FDA-approved drug available from essentially any pharmacy in the United States.

Recent Developments

ELOC Amendment

On April 7, 2021, the Company entered into an amendment to its equity purchase agreement, dated March 24, 2020 (the “ELOC Agreement”), with Oasis Capital, LLC (“Oasis Capital”), pursuant to which the parties agreed to increase (i) the purchase price per share of Common Stock issuable under the ELOC Agreement from \$0.436 to \$3.00 and (ii) the threshold trading price of the Common Stock for conducting sales under the ELOC Agreement from \$0.5014 to \$3.45 per share. In consideration for Oasis Capital’s entry into the amendment, the Company issued Oasis Capital a common stock purchase warrant exercisable for 100,000 shares of Common Stock (the “ELOC Warrant”) with an exercise price per share equal to \$1.87, the Minimum Price (as defined under Nasdaq Listing Rules) on the date of the amendment. The Company also entered into a registration rights agreement with Oasis Capital, pursuant to which the Company agreed to file one or more registration statements, as permissible and necessary to register under the Securities Act, to register the shares of Common Stock issuable upon exercise of the ELOC Warrant.

Royalty Financing

On March 8, 2021, we have entered into a royalty interest purchase agreement with Streeterville Capital, LLC (“Lender”), an affiliate of Chicago Venture Partners, L.P. (“CVP”), pursuant to which we sold to the Lender a royalty interest (the “Royalty Interest”) entitling Lender to receive \$10 million of future royalties on sales of Mytesi® (crofelemer) for the COVID-related indication (as defined below) and certain up-front license fees and milestone payments from licensees and/or distributors (subject to adjustment as provided below, the “Royalty Repayment Amount”) for an aggregate purchase price of \$5,000,000 (the “Royalty Financing”). We intend to use the proceeds to support regulatory activities associated with our development pipeline, including supporting the development program for crofelemer for the prophylaxis and/or symptomatic relief of inflammatory diarrhea, initially to be studied in a long-hauler COVID-19 recovery patient population (the “COVID-related indication”).

Interest will accrue on the Royalty Repayment Amount at a rate of 5% per annum from the closing of the Royalty Financing until the one-year anniversary of such closing and then 10% per annum thereafter, compounding quarterly. The Company will be obligated to make minimum royalty payments on a monthly basis beginning on the earlier of (i) March 8, 2024 (i.e., 36 months following the closing of the Royalty Financing) and (ii) 30 days following the full satisfaction of the Prior Royalty Interests (as defined below), but in no event less than 18 months from March 8, 2021 in an amount equal to the greater of (A) \$250,000 (which increases to \$400,000 beginning 6 months following the closing of the royalty financing, \$600,000 beginning 12 months following the closing of the Royalty Financing, and \$750,000 beginning 18 months following the closing of the Royalty Financing) and (B) the royalty payments to which Lender is entitled, consisting of (1) 10% of the Company's net sales of crofelemer for the COVID-related indication (including any improvements, modifications and follow-on products, collectively, the "Included Products"), (2) 10% of worldwide revenues related to upfront licensing fees and milestone payments from licensees and/or distributors, but specifically excluding licensing fees and/or milestone payments that are (A) reimbursements of clinical trial expenses or (B) associated with the license of Included Products from the Company to Napo EU S.p.A. and (3) 50% of royalties collected from licenses of the Included Products to third parties. For more information regarding the Royalty Financing, see our [Current Report on Form 8-K filed with the SEC on March 11, 2021](#) and incorporated herein by reference.

The Royalty Financing follows an earlier (i) royalty financing consummated in October 2020 whereby Iliad Research and Trading, L.P. acquired a royalty interest from the Company at a purchase price of \$6 million (the "Iliad Royalty Interest") as disclosed in the Company's Current Report on Form 8-K filed on October 9, 2020 and (ii) royalty financing consummated in December 2020 whereby Uptown Capital, LLC (formerly Irving Park Capital, LLC) acquired a royalty interest from the Company at a purchase price of \$6 million (the "UC Royalty Interest" and, together with the Iliad Royalty Interest, the "Prior Royalty Interests") as disclosed in the Company's Current Report on Form 8-K filed on December 29, 2020.

Memorandum of Understanding

On February 18, 2021, we signed a memorandum of understanding (the "MOU") with the lead sponsor of a to-be-formed special purpose acquisition company (the "Dragon SPAC"), which is pursuing listing on AIM Italia. Per the MOU, Napo EU S.p.A., our wholly-owned subsidiary in Italy ("Napo EU"), will be the named target of the Dragon SPAC and has granted the Dragon SPAC exclusivity to negotiate and finalize the documentation for a contemplated merger transaction. Based on the MOU, we anticipate providing an exclusive license to Napo EU for the development, manufacture and commercialization of all planned crofelemer indications in Europe (excluding Russia), which rights and obligations shall be assumed by the combined company following a merger of Napo EU with the Dragon SPAC. The cornerstone of the license agreement will be the proposed COVID-related indication; however, the expected license will include all crofelemer pipeline indications of Napo with certain obligations to be met by Napo EU to maintain the license, indication by indication.

The Dragon SPAC is in the process of being formed with lead sponsorship by Josh Mailman, a well-known, New York City-based impact investor. Mailman co-founded Social Venture Network (now Social Venture Circle) in 1987, founded the Threshold Foundation in 1981, and founded Business for Social Responsibility in 1992. He is also the managing director of Serious Change L.P., a \$100 million privately held impact fund he started in 2006, serves on the boards of Benefithub, Giving Assistant, Baltix Design, and Red Rabbit, and is an advisor to Social Venture Circle and the Threshold Foundation.

Secured Debt Issuance

On January 19, 2021, we and Napo entered into a note purchase agreement with Lender pursuant to which we issued to Lender a secured promissory note (the "Note") in the aggregate principal amount of \$6,220,813 (the "Note Offering"). The initial principal balance of the Note includes \$195,813 representing prepaid interest for the first twelve months and \$25,000 to cover Lender's transaction expenses. We will use the proceeds to fund development of our NP-300 (lechlemer) drug product candidate for the indication of the symptomatic relief of diarrhea from cholera and general corporate purposes, including our product pipeline activities. The Note bears interest at 3.25% per annum and matures on January 20, 2025. Interest will be prepaid each 12 months at the beginning of the period. For more information regarding the Note Offering, see our [Current Report on Form 8-K filed with the SEC on January 22, 2021](#) and incorporated herein by reference.

Registered Direct Offering

On January 13, 2021, we entered into a securities purchase agreement with the purchasers named therein (collectively, the "Investors"), pursuant to which we agreed to issue and sell, in a registered public offering by us directly to the Investors (the "Registered Direct Offering"), an aggregate of 4,437,870 shares of Common Stock at an offering price of \$3.38 per share for gross proceeds of approximately \$15 million before deducting the placement agent fee and related offering expenses. For more information regarding the Registered Direct Offering, see our [Current Report on Form 8-K filed with the SEC on January 14, 2021](#) and incorporated herein by reference.

Risks Related to Our Business

Our business, and our ability to execute our business strategy, is subject to a number of risks as more fully described in the section titled “Risk Factors.” These risks include, among others, the following:

- We have a limited operating history, expect to incur further losses as we grow and may be unable to achieve or sustain profitability.
- We expect to incur significant additional costs as we continue commercialization efforts for current prescription drug candidates or other product candidates, and undertake the clinical trials necessary to obtain any necessary regulatory approvals, which will increase our losses.
- Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our Common Stock.
- We are substantially dependent on the success of our current lead human prescription drug product, Mytesi and Canalevia, our prescription drug product candidate for dogs with chemotherapy induced diarrhea (CID) and exercise-induced diarrhea (EID), and cannot be certain that necessary approvals will be received for planned Mytesi follow-on indications or Canalevia or that these product candidates will be successfully commercialized, either by us or any of our partners.
- The results of earlier studies may not be predictive of the results of our pivotal trials or other future studies, and we may be unable to obtain any necessary regulatory approvals for our existing or future prescription drug product candidates under applicable regulatory requirements.
- Development of prescription drug products, and, to a lesser extent, non-prescription products, for the human health and animal health market is inherently expensive, time-consuming and uncertain, and any delay or discontinuance of our current or future pivotal trials, or dosage or formulation studies, would harm our business and prospects.
- Even if we obtain any required regulatory approvals for our current or future prescription drug product candidates, they may never achieve market acceptance or commercial success.
- We are dependent upon imported active pharmaceutical ingredients and contract manufacturers for supplies of our current prescription drug product candidates and non-prescription products and intend to rely on contract manufacturers for commercial quantities of any of our commercialized products.
- If we are not successful in identifying, developing and commercializing additional prescription drug product candidates and non-prescription products, our ability to expand our business and achieve our strategic objectives may be impaired.
- We have material weaknesses in our internal control over financial reporting related to staff turnover in our accounting department. We did not maintain a sufficient complement of internal personnel with appropriate knowledge, experience and/or training commensurate with our financial reporting requirements. We did not have adequate policies and procedures in place to ensure the timely, effective review of assumptions used in measuring the fair value of certain financial instruments. We did not have adequate policies and procedures in place to ensure the timely, effective review of compliance with contractual covenants in certain financial instruments. If we fail to remediate the material weakness, or experience any additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our Common Stock.

Corporate Information

We were incorporated in the State of Delaware on June 6, 2013. Our principal executive offices are located at 200 Pine Street, Suite 400, San Francisco, CA 94014 and our telephone number is (415) 371-8300. Our website address is <https://jaguar.health>. The information contained on, or that can be accessed through, our website is not part of this prospectus supplement. Our Common Stock is listed on the Nasdaq Capital Market and trades under the symbol "JAGX."

On June 3, 2019, we filed an amendment to our Third Amended and Restated Certificate of Incorporation to effect on June 7, 2019, a 1-for-70 reverse split of our Common Stock. Accordingly, all of the stock figures and related market, conversion and exercise prices in this prospectus supplement have been adjusted to reflect the reverse split.

THE OFFERING

Common stock offered by us	Shares of our Common Stock having an aggregate offering price of up to \$15,300,000.
Manner of offering	“At the market offering” that may be made from time to time through or to Ladenburg, as sales agent or principal. See “Plan of Distribution” on page S-21 of this prospectus supplement.
Common stock outstanding prior to this offering	127,908,578 shares
Common stock to be outstanding after this offering	135,635,850 shares, assuming sale of 7,727,272 shares at a price of \$1.98 per share, which was the closing price of our Common Stock on The Nasdaq Capital Market on April 1, 2021. The actual number of shares issued will vary depending on the sales prices under this offering.
Use of proceeds	We intend to use the net proceeds from this offering for working capital and general corporate purposes. We reserve the right, at the sole discretion of our management, to reallocate the proceeds of this offering in response to developments in our business and other factors. See “Use of Proceeds” on page S-19.
Risk factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our Common Stock.
Nasdaq Capital Market symbol	“JAGX”.

We have two classes of common stock: (i) voting common stock, par value \$0.0001 per share, and (ii) non-voting common stock, par value \$0.0001 per share. The shares offered by us in this offering are voting common stock.

The number of shares of our common stock to be outstanding after this offering is based on 127,906,558 shares of our voting common stock and 2,020 shares of our non-voting common stock outstanding as of March 31, 2021, which excludes the following:

- 1,590,354 shares of common stock issuable upon exercise of warrants outstanding as of March 31, 2021, with a weighted-average exercise price of \$2.51
- 4,449,472 shares of common stock issuable upon exercise of outstanding options as of March 31, 2021, with a weighted-average exercise price of \$4.29;
- 6,025,412 shares of common stock remain available for grant under the 2014 Stock Incentive Plan, and 329,182 shares of common stock have been issued under the 2020 Employee Inducement Plan;
- 170,818 shares of common stock issuable upon exercise of outstanding inducement options as of March 31, 2021, with a weighted-average exercise price of \$0.89; and
- 5,613 shares of common stock issuable upon vesting of outstanding restricted stock unit awards (“RSUs”), as of March 31, 2021.

RISK FACTORS

Investing in our Common Stock involves a high degree of risk. You should carefully consider the risks factor described below. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our most recent Annual Report on Form 10-K, as revised or supplemented by our most recent Quarterly Report on Form 10-Q, each of which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. If any of these risks actually occurs, our business, business prospects, financial condition or results of operations could be seriously harmed. In such an event, the market price of our Common Stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may harm our business, financial condition, results of operations and prospects.

Risks Related to this Offering

Our management team and board of directors will have immediate and broad discretion over the use of the net proceeds from this offering and we may use the net proceeds in ways with which you disagree.

The net proceeds from this offering will be immediately available to our management to use at their discretion. We currently intend to use the net proceeds as discussed under “Use of Proceeds” in this prospectus supplement. The precise amount and timing of the application of these proceeds will depend upon a number of factors, such as the timing and progress of our product development and commercialization efforts, our funding requirements and the availability and costs of other funds. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Depending on the outcome of our efforts and other unforeseen events, our plans and priorities may change and we may apply the net proceeds of this offering in different manners than we currently anticipate. Accordingly, our management and board of directors will have significant discretion and flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management and board of directors with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not result in a favorable, or any, return for us or our stockholders. The failure of our management to use such funds effectively could have a material adverse effect on our business, prospects, financial condition, and results of operations.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the as adjusted net tangible book value per share of our Common Stock outstanding prior to this offering. Assuming that an aggregate of 7,727,272 shares of our Common Stock are sold during the term of the Sales Agreement at a price of \$1.98 per share, the last reported sale price of our Common Stock on the Nasdaq Capital Market on April 1, 2021, for aggregate gross proceeds of \$15,300,000, after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$1.77 per share, representing the difference between our pro forma as adjusted net tangible book value per share as of December 31, 2020 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options and warrants may result in further dilution of your investment. See the section entitled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

The actual number of shares we will issue under the sales agreement with Ladenburg, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement with Ladenburg and compliance with applicable law, we have the discretion to deliver placement notices to Ladenburg at any time throughout the term of the sales agreement. The number of shares that are sold by Ladenburg after delivering a placement notice will fluctuate based on the market price of the Common Stock during the sales period and limits we set with Ladenburg.

There is a limited trading market for our Common Stock, which could make it difficult to liquidate an investment in our Common Stock, in a timely manner.

Our Common Stock is currently traded on The Nasdaq Capital Market. Because there is a limited public market for our Common Stock, investors may not be able to liquidate their investment whenever desired. We cannot assure that there will be an active trading market for our Common Stock and the lack of an active public trading market could mean that investors may be exposed to increased risk. In addition, if we failed to meet the criteria set forth in SEC regulations, various requirements would be imposed by law on broker-dealers who sell our securities to persons other than established customers and accredited investors. Consequently, such regulations may deter broker-dealers from recommending or selling our Common Stock, which may further affect its liquidity.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our Common Stock or other securities convertible into or exchangeable for our Common Stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our Common Stock, or securities convertible or exchangeable into Common Stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our current or future human products and product candidates, if approved, and generate product or other revenue.

We currently have limited sales, marketing or distribution capabilities, and prior to Napo's launch of Mytesi for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy, and our launch of Neonorm for preweaned dairy calves, we had no experience in the sale, marketing and distribution of human or animal health products. There are significant risks involved in building and managing a sales organization, including our potential inability to attract, hire, retain and motivate qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively oversee a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities and entry into adequate arrangements with distributors or other partners would adversely impact the commercialization of Mytesi, and, if approved, Canalevia. If we are not successful in commercializing Mytesi, for its currently approved indication or for any potential Mytesi follow-on indication, either on our own or through one or more distributors, or in generating upfront licensing or other fees, including through the contemplated merger transaction between the Dragon SPAC and Napo EU and associated licensing arrangement that is currently under discussions, we may never generate significant revenue and may continue to incur significant losses, which would harm our financial condition and results of operations.

Risks Related to Our Common Stock

Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of The Nasdaq Capital Market, such as the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock.

The delisting of our common stock from Nasdaq may make it more difficult for us to raise capital on favorable terms in the future. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. Further, if we were to be delisted from The Nasdaq Capital Market, our common stock would cease to be recognized as covered securities and we would be subject to regulation in each state in which we offer our securities.

We have material weaknesses in our internal control over financial reporting related to staff turnover in our accounting department. We did not maintain a sufficient complement of internal personnel with appropriate knowledge, experience and/or training commensurate with our financial reporting requirements. We did not have adequate policies and procedures in place to ensure the timely, effective review of assumptions used in measuring the fair value of certain financial instruments. We did not have adequate policies and procedures in place to ensure the timely, effective review of compliance with contractual covenants in certain financial instruments. If we fail to remediate the material weakness, or experience any additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our Common Stock.

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

In connection with preparation of our financial statements for the year ended December 31, 2020, we identified material weaknesses in our internal control over financial reporting related to our financial statement preparation and review process. The primary factors contributing to the material weaknesses were as follows:

- We did not have adequate policies and procedures in place to ensure the timely and effective preparation and review of the financial statements.

- We did not have sufficient resources with appropriate knowledge, experience and/or training commensurate with our financial reporting requirements to assist us in our timely and efficient preparation and review over our financial reporting

To remediate the material weaknesses described above, management will add controls to further enhance and revise the design of the existing controls including:

- Establishing policies and procedures to ensure timely review, by qualified personnel, of assumptions used in measuring fair value of certain financial instruments.
- Reassessing the design and operation of internal controls over financial reporting and review procedures over the preparation of our financial statements.
- Hiring permanent accounting personnel and used consultants to provide support during our quarterly and annual preparation, review, and reporting of our financial statements.
- Maintaining adequate internal qualified personnel to properly supervise and review the information provided by the outside consulting technical experts to ensure certain significant complex transactions and technical matters were properly accounted for.

We cannot assure you that the planned measures in response to these material weaknesses will be sufficient to remediate such material weaknesses or to avoid potential future material weaknesses.

If we are unable to remediate these material weaknesses, or if we identify one or more other material weaknesses in our internal control over financial reporting, we will continue to be unable to conclude that our internal controls are effective. If we are unable to confirm that our internal control over financial reporting is effective we could lose investor confidence in the accuracy and completeness of our financial reports, which could cause the price of our Common Stock to decline.

We currently have a limited amount of Common Stock available for new securities issuances, which may restrict us from accessing additional capital through the sale of new securities.

Our Third Amended and Restated Certificate of Incorporation, as amended, authorizes us to issue up to 150,000,000 shares of Common Stock, 127,906,558 of which are issued and outstanding and 12,580,327 of which are reserved for issuance upon exercise of options and warrants and vesting of RSUs as of March 31, 2021. Accordingly, we have a limited number of shares of Common Stock available for additional issuances. Our failure to increase our authorized shares may restrict our ability to access additional capital through the sale of new securities, which may harm our financial position and business prospects.

If our shares become subject to the penny stock rules, it would become more difficult to trade our shares.

The SEC has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than \$5.00, other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system. If we do not retain a listing on The Nasdaq Capital Market and if the price of our Common Stock is less than \$5.00, our Common Stock will be deemed a penny stock. The penny stock rules require a broker-dealer, before a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that before effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive (i) the purchaser's written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for our Common Stock, and therefore stockholders may have difficulty selling their shares.

The price of our Common Stock could be subject to volatility related or unrelated to our operations, and purchasers of our Common Stock could incur substantial losses.

We have experienced and may continue to experience significant volatility in the price of our Common Stock. From November 1, 2020 through March 31, 2021, the share price of our Common Stock ranged from a high of \$4.47 to a low of \$0.19. The reason for the volatility in our stock is not well understood and may continue. Factors that may have contributed to such volatility include, but are not limited to, those discussed previously in this “Risk Factors” section of this prospectus supplement and incorporated by reference into this prospectus supplement from our Annual Report on Form 10-K, as updated by subsequent reports, and others, such as:

- delays in the commercialization of Mytesi, Neonorm, Canalevia, Equilevia or our other current or future prescription drug product candidates and non-prescription products;
- any delays in, or suspension or failure of, our current and future studies;
- announcements of regulatory approval or disapproval of any of our current or future product candidates or of regulatory actions affecting our company or our industry;
- manufacturing and supply issues that affect product candidate or product supply for our studies or commercialization efforts;
- quarterly variations in our results of operations or those of our competitors;
- changes in our earnings estimates or recommendations by securities analysts;
- the payment of licensing fees or royalties in shares of our Common Stock;
- announcements by us or our competitors of new prescription drug products or product candidates or non-prescription products, significant contracts, commercial relationships, acquisitions or capital commitments;
- announcements relating to future development or license agreements including termination of such agreements;
- adverse developments with respect to our intellectual property rights or those of our principal collaborators;
- commencement of litigation involving us or our competitors;
- any major changes in our board of directors or management;
- new legislation in the United States relating to the prescription, sale, distribution or pricing of gastrointestinal health products;
- product liability claims, other litigation or public concern about the safety of our prescription drug product or product candidates and non-prescription products or any such future products;
- market conditions in the human or animal health industry, in general, or in the gastrointestinal health sector, in particular, including performance of our competitors;
- future issuances of shares of Common Stock or other securities;
- uncertainties related to COVID-19;
- general economic conditions in the United States and abroad; and
- market speculation regarding any of the foregoing

In addition, the stock market, in general, or the market for stocks in our industry, in particular, may experience broad market fluctuations, which may adversely affect the market price or liquidity of our common stock. Any sudden decline in the market price of our common stock could trigger securities class-action lawsuits against us. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the time and attention of our management would be diverted from our business and operations. We also could be subject to damages claims if we were found to be at fault in connection with a decline in our stock price.

The trading price of our shares of Common Stock has recently increased significantly to a level that we do not believe is consistent with any recent change in our financial condition or results of operations. If the trading price of our shares of common stock decreases rapidly, investors could lose a significant portion of their investment.

The trading price of our shares of Common Stock has recently increased significantly. On December 31, 2020, the closing price of our shares of Common Stock on the Nasdaq Capital Market was \$0.82 per share. We believe that the sharp increase in the trading price of our shares of Common Stock is the result of a number of factors outside our control, including social media posts that have drawn attention to our company and increased trading in our shares of Common Stock by retail investors. These social media posts were not sponsored or endorsed by us. There has been no recent change in our financial condition or results of operations that is consistent with the increase in the trading price of our shares of Common Stock. The recent increase in the trading price of our shares of Common Stock may not be sustained. In the event of a rapid decrease in the trading price of our shares of Common Stock, investors could lose a significant portion of their investment.

A possible “short squeeze” due to a sudden increase in demand of our Common Stock that largely exceeds supply may lead to further price volatility in our Common Stock.

Investors may purchase shares of our Common Stock to hedge existing exposure in our Common Stock or to speculate on the price of our Common Stock. Speculation on the price of our Common Stock may involve long and short exposures. To the extent aggregate short exposure exceeds the number of shares of our Common Stock available for purchase in the open market, investors with short exposure may have to pay a premium to repurchase our Common Stock for delivery to lenders of our Common Stock. Those repurchases may in turn, dramatically increase the price of our Common Stock until investors with short exposure are able to purchase additional shares of Common Stock to cover their short position. This is often referred to as a “short squeeze.” A short squeeze could lead to volatile price movements in shares of our Common Stock that are not directly correlated to the performance or prospects of our company and once investors purchase the shares necessary to cover their short position the price of our Common Stock may decline.

You may not be able to resell our Common Stock when you wish to sell them or at a price that you consider attractive or satisfactory.

The listing of our Common Stock on The Nasdaq Capital Market does not assure that a meaningful, consistent and liquid trading market exists. Although our Common Stock is listed on The Nasdaq Capital Market, until recently, trading volume in our Common Stock has been limited and an active trading market for our shares may not be sustained. If an active market for our Common Stock is not sustained, you may be unable to sell your shares when you wish to sell them or at a price that you consider attractive or satisfactory. The lack of an active market may also adversely affect our ability to raise capital by selling securities in the future, or impair our ability to license or acquire other product candidates, businesses or technologies using our shares as consideration.

If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our stock, our stock price and trading volume could decline.

The trading market for our Common Stock depends in part on the research and reports that industry or financial analysts publish about us or our business. We do not influence or control the reporting of these analysts. If one or more of the analysts who do cover us downgrade or provide a negative outlook on our company or our industry, or the stock of any of our competitors, the price of our Common Stock could decline. If one or more of these analysts ceases coverage of our company, we could lose visibility in the market, which in turn could cause the price of our Common Stock to decline.

You may be diluted by conversions of outstanding shares of non-voting common stock and exercises of outstanding options and warrants.

As of March 31, 2021, we had (i) outstanding options to purchase an aggregate of 4,449,472 shares of our Common Stock at a weighted average exercise price of \$4.29 per share, (ii) outstanding options to purchase an aggregate of 170,818 shares of our Common Stock issuable upon exercise of outstanding inducement options as of March 31, 2021, with a weighted-average exercise price of \$0.89 per share, (iii) 1,590,354 shares of Common Stock issuable upon exercise of warrants outstanding as of March 31, 2021, with a weighted-average exercise price of \$2.51, and (v) 5,613 shares of Common Stock issuable upon vesting of outstanding RSUs.

The exercise of such options and warrants and conversion of the non-voting common stock will result in further dilution of your investment. In addition, you may experience further dilution if we issue Common Stock in the future. As a result of this dilution, you may receive significantly less in net tangible book value than the full purchase price you paid for the shares in the event of liquidation.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our third amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could adversely affect the rights of our common stockholders or be used to deter a possible acquisition of our company;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least 75% of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our third amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

These provisions could inhibit or prevent possible transactions that some stockholders may consider attractive.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation generally may not engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, (iv) any action asserting a claim that is governed by the internal affairs doctrine or (v) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our amended and restated bylaws. This choice-of-forum provision may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. Alternatively, if a court were to find this provision of our amended and restated bylaws inapplicable or unenforceable with respect to one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could harm our business and financial condition.

We do not intend to pay dividends on our Common Stock, and your ability to achieve a return on your investment will depend on appreciation in the market price of our Common Stock.

We currently intend to invest our future earnings, if any, to fund our growth and not to pay any cash dividends on our Common Stock. Because we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market price of our Common Stock. We cannot be certain that our Common Stock will appreciate in price.

The requirements of being a public company, including compliance with the reporting requirements of the Exchange Act and the requirements of the Sarbanes-Oxley Act, may strain our resources, increase our costs and distract management, and we may be unable to comply with these requirements in a timely or cost-effective manner.

Our initial public offering had a significant, transformative effect on us. Prior to our initial public offering, our business operated as a privately-held company, and we were not required to comply with public reporting, corporate governance and financial accounting practices and policies required of a publicly-traded company. As a publicly-traded company, we incur significant additional legal, accounting and other expenses compared to historical levels. In addition, new and changing laws, regulations and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations thereunder, as well as under the Sarbanes-Oxley Act, the JOBS Act and the rules and regulations of the SEC and The Nasdaq Capital Market, may result in an increase in our costs and the time that our board of directors and management must devote to our compliance with these rules and regulations. These rules and regulations have substantially increased our legal and financial compliance costs and diverted management time and attention from our product development and other business activities.

The Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our internal control over financial reporting annually and the effectiveness of our disclosure controls and procedures quarterly. In particular, Section 404 of the Sarbanes-Oxley Act, or Section 404, requires us to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on, and our independent registered public accounting firm potentially to attest to, the effectiveness of our internal control over financial reporting. We have needed to expend time and resources on documenting our internal control over financial reporting so that we are in a position to perform such evaluation when required. As a smaller reporting company ("SRC"), we expect to avail ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. However, we may no longer avail ourselves of this exemption when we cease to be an SRC. When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Our compliance with applicable provisions of Section 404 requires that we incur substantial accounting expense and expend significant management time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

Issuances of shares of Common Stock or securities convertible into or exercisable for shares of Common Stock following this offering, as well as the exercise of options and warrants outstanding, will dilute your ownership interests and may adversely affect the future market price of our Common Stock.

The issuance of additional shares of our Common Stock or securities convertible into or exchangeable for our Common Stock could be dilutive to stockholders if they do not invest in future offerings. We intend to use the net proceeds from this offering to continue to fund the development of our business and for general corporate purposes, which may include capital expenditures and funding our working capital needs. We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements, which may cause your ownership interest to be diluted.

In addition, we have a significant number of options and warrants to purchase shares of our Common Stock outstanding. If these securities are exercised or converted, you may incur further dilution. Moreover, to the extent that we issue additional options or warrants to purchase, or securities convertible into or exchangeable for, shares of our Common Stock in the future and those options, warrants or other securities are exercised, converted or exchanged, stockholders may experience further dilution.

We effected two reverse stock splits since January 1, 2018, and have received stockholder approval for a third reverse stock split, which if effectuated which may not achieve one or more of our objectives.

We have effected two reverse stock splits since January 1, 2018, and have received stockholder approval authorizing our board of directors to effectuate a reverse stock split at a ratio not less than 1-for-2 and not greater than 1-for 20, with the exact ratio, if approved and effected at all, to be set within that range at the discretion of our board of directors and publicly announced by us on or before December 9, 2021. While we currently have no intentions to effectuate a reverse stock split, we may do so in the future for various reasons, including to increase the per share market price of our common stock to the extent required to remain in compliance with the Nasdaq minimum bid price requirement or increase the number of authorized shares of our common stock available for issuance.

If we were to effectuate a reverse stock split, there can be no assurance that the market price per share of our common stock after a reverse stock split will remain unchanged or increase in proportion to the reduction in the number of shares of our common stock outstanding before the reverse stock split. The market price of our shares may fluctuate and potentially decline after a reverse stock split. Accordingly, the total market capitalization of our common stock after a reverse stock split may be lower than the total market capitalization before the reverse stock split. Moreover, the market price of our common stock following a reverse stock split may not exceed or remain higher than the market price prior to the reverse stock split.

Additionally, there can be no assurance that a reverse stock split will result in a per-share market price that will attract institutional investors or investment funds or that such share price will satisfy investing guidelines of institutional investors or investment funds. As a result, the trading liquidity of our common stock may not necessarily improve. Further, if a reverse stock split is effected and the market price of our common stock declines, the percentage decline may be greater than would occur in the absence of a reverse stock split.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the documents incorporated by reference into it contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in or incorporated by reference into this prospectus supplement, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing of receipt of clinical trial, field study and other study data, and likelihood of success, commercialization plans and timing, other plans and objectives of management for future operations, and future results of current and anticipated products are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

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 prospectus supplement are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus supplement and are subject to a number of risks, uncertainties and assumptions including those listed in the “Risk Factors” incorporated by reference into this prospectus supplement from our Annual Report on Form 10-K, as updated by subsequent reports. Forward-looking statements are subject to inherent risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do 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.

USE OF PROCEEDS

We currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include capital expenditures, product development and commercialization expenditures.

As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. The precise amount and timing of the application of these proceeds will depend upon a number of factors, such as the timing and progress of our product development and commercialization efforts, our funding requirements and the availability and costs of other funds. As a result, our management will have broad discretion in the allocation and use of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the proceeds of this offering. The actual use and allocation of proceeds realized from this offering will depend upon our operating revenues and cash position and our working capital requirements and may change. We may also invest the net proceeds temporarily in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities, until we use them for their stated purposes.

DILUTION

If you purchase shares in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of Common Stock and the as adjusted net tangible book value per share of our Common Stock after this offering.

Our net tangible book value as of December 31, 2020 was \$(7.1 million), or \$(0.06) per share of Common Stock (based upon 114,024,388 outstanding shares of Common Stock). “Net tangible book value” is total assets minus the sum of liabilities and intangible assets. “Net tangible book value per share” is net tangible book value divided by the total number of shares of Common Stock outstanding.

Our pro forma net tangible book value as of December 31, 2020 would have been approximately \$11.9 million, or \$0.10 per share of Common Stock (based upon 120,471,812 outstanding shares of Common Stock), after giving effect to (i) the issuance of 2,009,554 shares of Common Stock through Ladenburg pursuant to the Sales Agreement and (ii) the issuance of 4,437,870 shares of Common Stock in the Registered Direct Offering.

After giving effect to (i) the pro forma adjustments described above and (ii) the sale by us in this offering of 7,727,272 shares of Common Stock pursuant to the Sales Agreement at an assumed offering price of \$1.98 per share, the last reported sale price of our Common Stock on The Nasdaq Capital Market on April 1, 2021, and after deducting estimated offering expenses of approximately \$554,000 payable by us, our pro forma as adjusted net tangible book value as of December 31, 2020 would have been \$26.6 million, or \$0.21 per share of Common Stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$0.11 per share to our existing shareholders and an immediate dilution in pro forma as adjusted net tangible book value of approximately \$1.77 per share to investors participating in this offering

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution:

Public offering price per share		\$	1.98
Historical net tangible book value per share as of December 31, 2020	\$	(0.06)	
Pro forma increase in net tangible book value per share attributable to the pro forma transactions described above	\$	0.16	
Pro forma net tangible book value per share as of December 31, 2020	\$	0.10	
Increase in net tangible book value per share attributable to this offering	\$	0.11	
Pro forma as adjusted net tangible book value per share after this offering.		\$	0.21
Dilution per share to new investors in this offering		\$	1.77

The table above assumes for illustrative purposes that an aggregate of 7,727,272 shares of our Common Stock are sold during the term of the sales agreement with Ladenburg at a price of \$1.98 per share, the last reported sale price of our Common Stock on The Nasdaq Capital Market on April 1, 2021, for aggregate gross proceeds of \$15,300,000.

The shares pursuant to the Sales Agreement are being sold from time to time at various prices. An increase of \$0.50 per share in the price at which the shares are sold from the assumed offering price of \$1.98 per share shown in the table above, assuming all of our Common Stock in the aggregate amount of \$15,300,000 during the term of the Sales Agreement is sold at that price, would not change our pro forma as adjusted net tangible book value per share after the offering of \$0.21 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$2.27 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$0.50 per share in the price at which the shares are sold from the assumed offering price of \$1.98 per share shown in the table above, assuming all of our Common Stock in the aggregate amount of \$15,300,000 during the term of the Sales Agreement is sold at that price, would decrease our pro forma as adjusted net tangible book value per share after the offering to \$0.20 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$1.28 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The number of shares of our Common Stock to be outstanding after this offering is based on 120,471,812 shares of our Common Stock outstanding, as of December 31, 2020, on a pro forma basis, and excludes shares of Common Stock issuable upon exercise of options, warrants and other rights outstanding on December 31, 2020 on a pro forma basis.

PLAN OF DISTRIBUTION

We have entered into sales agreement (the “Sales Agreement”) with Ladenburg Thalmann & Co. Inc. (“Ladenburg” or the “Agent”) under which we may issue and sell shares of our Common Stock from time to time through Ladenburg acting as agent. Sales of our shares of Common Stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on or through the Nasdaq Capital Market or any other existing trading market for our Common Stock in the United States or to or through a market maker, subject to the limitations imposed by General Instruction I.B.6. to Form S-3, as applicable.

Each time we wish to issue and sell shares of Common Stock under the Sales Agreement, we will notify Ladenburg of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Ladenburg, subject to the terms and conditions of the Sales Agreement, Ladenburg has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Ladenburg under the Sales Agreement to sell our shares of Common Stock are subject to a number of conditions that we must meet.

The Agent will provide written confirmation to us following the close of trading on Nasdaq following each day in which shares of our Common Stock are sold under the Sales Agreement. Each confirmation will include the number of shares sold on the day, the aggregate gross sales proceeds, the net proceeds to us, and the compensation payable by us to Ladenburg with respect to the sales. The settlement of sales of shares between us and Ladenburg is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our shares of Common Stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Ladenburg may agree. There is no arrangement for funds to be received in an escrow, trust or similar arrangement. We will report at least quarterly the number of shares of Common Stock sold through Ladenburg under the Sales Agreement, the net proceeds to us and the compensation paid by us to Ladenburg in connection with the sales of Common Stock.

We will pay Ladenburg a commission equal to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of Common Stock. Because there is no minimum offering amount required as a condition of this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Ladenburg for the fees and disbursements of its counsel, payable upon execution of the Sales Agreement, in an amount not to exceed \$75,000, in addition to certain ongoing disbursements of its legal counsel up to \$3,000 per calendar quarter. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Ladenburg under the terms of the Sales Agreement, will be approximately \$95,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

In connection with the sale of the shares of Common Stock on our behalf, Ladenburg will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Ladenburg will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Ladenburg against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Ladenburg may be required to make in respect of such liabilities.

The offering of our shares of Common Stock pursuant to the Sales Agreement will terminate upon the earlier of (i) October 5, 2022 and (ii) the termination of the Sales Agreement as permitted therein. We and Ladenburg may each terminate the Sales Agreement at any time with prior written notice.

This summary of the material provisions of the Sales Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sales Agreement is filed as an exhibit to our [Current Report on Form 8-K filed under the Exchange Act on October 5, 2020](#) and incorporated by reference in this prospectus supplement. See “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” below.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by our counsel, Reed Smith LLP, Palo Alto, California. Sheppard, Mullin, Richter & Hampton LLP, New York, New York, is acting as counsel for Ladenburg in connection with this offering.

EXPERTS

The financial statements of the Company as of December 31, 2020 and 2019 and for each of the two years in the period ended December 31, 2020 incorporated by reference in this prospectus and the registration statement have been so incorporated in reliance on the report of Mayer Hoffman McCann P.C., an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. These reports, proxy statements and other information are available at the SEC's web site at <http://www.sec.gov>.

This prospectus supplement is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus supplement, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. The registration statement, including the exhibits and schedules, is available at the SEC's web site at <http://www.sec.gov>.

We also maintain a website at <https://jaguar.health>, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. This prospectus supplement omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus supplement. Statements in this prospectus supplement or the accompanying prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- : [our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 filed on March 31, 2021;](#)
- : [our preliminary proxy statement and additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders to be held on May 13, 2021, filed March 31, 2021;](#)
- Our Current Reports on Form 8-K filed on [January 8, 2021](#), [January 14, 2021](#) (as subsequently amended on [January 14, 2021](#)), [January 22, 2021](#), [March 11, 2021](#) and [April 8, 2021](#);
- : [the description of our common stock filed as Exhibit 4.26 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 filed on April 3, 2020, including any amendment or report filed for the purpose of updating such description; and](#)
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination or completion of the offering of securities under this prospectus supplement shall be deemed to be incorporated by reference in this prospectus supplement and to be a part hereof from the date of filing such reports and other documents.

Unless otherwise noted, the SEC file number for each of the documents listed above is 001-36714.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of this prospectus supplement shall be deemed to be incorporated by reference into this prospectus supplement.

Any statement contained in this prospectus supplement, the accompanying prospectus, or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement or the accompanying prospectus will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement, the accompanying prospectus, or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement or accompanying prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Jaguar Health, Inc., 200 Pine Street, Suite 400, San Francisco, CA, 94104 or call (415) 371-8300.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.



JAGUAR HEALTH, INC.

\$40,000,000

**Common Stock
Preferred Stock
Warrants
Subscription Rights
Units**

This prospectus relates to common stock, preferred stock, warrants and subscription rights that we may sell from time to time in one or more offerings up to a total public offering price of \$40,000,000 on terms to be determined at the time of sale, which securities may be sold either individually or in units consisting of two or more of the foregoing classes of securities.

Each time we sell securities hereunder, we will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

These securities may be offered and sold in the same offering or in separate offerings, directly to purchasers, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See “Plan of Distribution” in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any sale of securities offered by us will also be included in a prospectus supplement.

Our voting common stock is listed on The Nasdaq Capital Market, under the symbol “JAGX.” On September 10, 2020, the last reported sale price of our voting common stock on The Nasdaq Capital Market was \$0.38 per share.

As of September 1, 2020, the aggregate market value of the voting and non-voting common equity held by non-affiliates was approximately \$35,155,613, which was calculated based on 43,944,516 shares of outstanding common stock held by non-affiliates and a closing price per share of \$0.80 on August 10, 2020. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million. During the 12 calendar months prior to and including the date of this prospectus, we have offered and sold \$1.8 million of securities pursuant to General Instruction I.B.6 of Form S-3. As a result, we are currently eligible to offer and sell up to an aggregate of approximately \$9.9 million of our securities pursuant to General Instruction I.B.6. of Form S-3.

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption “Risk Factors” and in the documents incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is September 23, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total public offering price of \$40,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The prospectus supplement may also add to, update or change information contained in this prospectus.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any of our securities other than the securities covered hereby, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy any securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about, and to observe, any restrictions as to the offering and the distribution of this prospectus applicable to those jurisdictions.

We further note that the representations, warranties and covenants made in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front cover of this prospectus or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or securities are sold or otherwise disposed of on a later date. It is important for you to read and consider all information contained in this prospectus, including the Information Incorporated by Reference herein, and any prospectus supplement in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions “Where You Can Find More Information” and “Incorporation of Information by Reference” in this prospectus.

Unless the context otherwise requires, references in this prospectus to “Jaguar,” the “Company,” “we,” “us,” and “our” refer to Jaguar Health, Inc.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the SEC. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Overview

Jaguar is a commercial stage pharmaceuticals company focused on developing novel, plant-based, non-opioid, and sustainably derived prescription medicines for people and animals with GI distress, specifically chronic, debilitating diarrhea. Our wholly-owned subsidiary, Napo Pharmaceuticals, Inc. (“Napo”), focuses on developing and commercializing proprietary plant-based human gastrointestinal pharmaceuticals from plants used traditionally in rainforest areas. Our Mytesi (“crofelemer”) product is approved by the U.S. Food and Drug Administration for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy and is the only oral plant-based prescription medicine approved under FDA Botanical Guidance. In the animal health space, we focus on developing and commercializing first-in-class gastrointestinal products for companion and production animals, foals, and high value horses.

Jaguar was founded in San Francisco, California as a Delaware corporation on June 6, 2013. Napo formed Jaguar to develop and commercialize animal health products. Effective as of December 31, 2013, Jaguar was a wholly-owned subsidiary of Napo, and Jaguar was a majority-owned subsidiary of Napo until the close of the Company’s initial public offering on May 18, 2015. On July 31, 2017, the merger of Jaguar Animal Health, Inc. and Napo became effective, at which point Jaguar Animal Health’s name changed to Jaguar Health, Inc. and Napo began operating as a wholly-owned subsidiary of Jaguar focused on human health and the ongoing commercialization of, and development of follow-on indications for, Mytesi. Most of the activities of the Company are now focused on the commercialization of Mytesi and development of follow-on indications for crofelemer and a second-generation anti-secretory product, lechlemer. In the field of animal health, we have limited activities which are focused on developing and commercializing first-in-class gastrointestinal products for dogs, dairy calves, foals, and high value horses.

We believe Jaguar is poised to realize a number of synergistic, value adding benefits — an expanded pipeline of potential blockbuster human follow-on indications, a second-generation anti-secretory agent, as well as a pipeline of important animal indications for crofelemer — upon which to build global partnerships. As previously announced, Jaguar, through Napo, now holds extensive global rights for Mytesi, and crofelemer manufacturing is being conducted at a multimillion-dollar commercial manufacturing facility that has been FDA-inspected and approved. Additionally, several of the drug product candidates in Jaguar’s Mytesi pipeline are backed by what we believe are strong Phase 2 and proof of concept evidence from completed human clinical trials.

Mytesi is a novel, first-in-class anti-secretory agent which has a basic normalizing effect locally on the gut, and this mechanism of action has the potential to benefit multiple disorders. Mytesi is in development for multiple possible follow-on indications, including cancer therapy-related diarrhea; orphan-drug indications for infants and children with congenital diarrheal disorders and short bowel syndrome (SBS); supportive care for inflammatory bowel disease (IBD); irritable bowel syndrome (IBS); and for idiopathic/functional diarrhea. In addition, a second-generation anti-secretory agent, lechlemer, is in development for cholera. Mytesi previously received orphan-drug designation for SBS.

In September 2020, Jaguar launched the Entheogen Therapeutics initiative to support the discovery and development of novel, natural medicines derived from psychoactive plant compounds for treatment of mood disorders, neuro-degenerative diseases, addiction, and other mental health disorders. The initiative will initially focus on plants with the potential to treat depression and will leverage Napo’s proprietary library of approximately 2,300 plants with medicinal properties. According to statistics available from the National Institute of Mental Health Disorders, part of the National Institutes of Health, approximately 9.5% of American adults ages 18 and over will suffer from a depressive illness (major depression, bipolar disorder, or dysthymia) each year.

While Jaguar and Napo remain steadfastly focused on the commercial success of Mytesi and on the development of potential crofelemer follow-on indications in the area of gastrointestinal health, the Company believes the same competencies and multi-disciplinary scientific strategy that led to the development of crofelemer will support collaborative efforts with potential partners to develop novel first-in-class prescription medicines derived from psychoactive plants.

Our management team has significant experience in gastrointestinal product development for both humans and animals. Napo was founded 30 years ago to perform drug discovery and development by leveraging the knowledge of traditional healers working in rainforest areas. Ten members of the Jaguar and Napo team have been together for more than 15 years. Dr. Steven King, our chief sustainable supply, ethnobotanical research and intellectual property officer, and Lisa Conte, our founder, president and CEO, have worked together for more than 30 years. Together, these dedicated personnel successfully transformed crofelemer, which is extracted from trees growing in the rainforest, to Mytesi, which is a natural, sustainably harvested, FDA-approved drug available from essentially any pharmacy in the United States.

Corporate Information

We were incorporated in the State of Delaware on June 6, 2013. Our principal executive offices are located at 201 Mission Street, Suite 2375, San Francisco, CA 94015 and our telephone number is (415) 371-8300. Our website address is <https://jaguar.health>. The information contained on, or that can be accessed through, our website is not part of this prospectus. Our common stock is listed on The Nasdaq Capital Market and trades under the symbol "JAGX."

On June 3, 2019, we filed an amendment to our Third Amended and Restated Certificate of Incorporation to effect on June 7, 2019, a 1-for-70 reverse split of our voting common stock. Accordingly, all of the stock figures and related market, conversion and exercise prices in this prospectus have been adjusted to reflect the reverse split.

Jaguar Health, our logo, Napo Pharmaceuticals, Mytesi, Canalevia, Equilevia and Neonorm are our trademarks that are used in this prospectus. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ©, ® or ™ symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

The Offering

This prospectus relates to the offer by us of up to \$40,000,000 of common stock, preferred stock, warrants, subscription rights or units in one or more offerings and in any combination.

RISK FACTORS

Please carefully consider the risk factors described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus. Additional risks and uncertainties not presently known to us or that we deem currently immaterial may also impair our business operations or adversely affect our results of operations or financial condition.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, including the documents incorporated by reference into this prospectus and any accompanying prospectus supplement, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in or incorporated by reference into this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing of receipt of clinical trial, field study and other study data, and likelihood of success, commercialization plans and timing, other plans and objectives of management for future operations, and future results of current and anticipated products are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

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 prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions including those listed in the “Risk Factors” incorporated by reference into this prospectus from our Annual Report on Form 10-K, as updated by subsequent reports. Forward-looking statements are subject to inherent risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do 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.

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of the securities offered by us for working capital and other general corporate purposes, and possibly acquisitions of other companies, products or technologies. Working capital and other general corporate purposes may include research and development expenditures, capital expenditures, operating and administrative expenditures, and any other purpose that we may specify in any prospectus supplement. While we have no current plans for any specific acquisitions at this time, we believe opportunities may exist from time to time to expand our current business through strategic alliances or acquisitions with other companies, products or technologies. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of the securities offered by us. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities. Our plans to use the estimated net proceeds from the sale of the securities offered by us may change, and if they do, we will update this information in a prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the most important terms of our capital stock. Because it is only a summary of the provisions of our Third Amended and Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), and amended and restated bylaws, it does not contain all of the information that may be important to you. For a complete description of the matters set forth in this "Description of Capital Stock," you should refer to our Certificate of Incorporation and our amended and restated bylaws, each of which are included as exhibits to the registration statement of which this prospectus is a part, and to the applicable provisions of Delaware law. Our authorized capital stock consists of 204,475,074 shares of capital stock, which consists of (i) 150,000,000 shares of voting common stock, \$0.0001 par value per share, (ii) 50,000,000 shares of convertible non-voting common stock, \$0.0001 par value per share, and (iii) 4,475,074 shares of preferred stock, \$0.0001 par value per share.

Common Stock

We have two classes of common stock: voting common stock and non-voting common stock. Holders of both classes of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock or that we may designate or issue in the future. In the event of our liquidation, dissolution or winding up, the holders of both classes of our common stock are entitled to share ratably in all assets remaining after the payment of liabilities, subject to the prior distribution rights of preferred stock then outstanding. There are no preemptive, conversion or subscription rights applicable to either class of common stock. There are no redemption or sinking fund provisions applicable to either class of common stock. The rights, preferences, and privileges of the holders of both classes of common stock are subject to and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future. All of our outstanding shares of voting common stock and non-voting common stock are, and the shares of common stock to be issued pursuant to this offering, when paid for, will be fully paid and nonassessable.

Voting Common Stock

The holders of our voting common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders.

Non-Voting Common Stock

The holders of our non-voting common stock do not have any cumulative voting rights and are not entitled to vote, except on an as-converted basis with respect to any Change of Control (as defined in the Certificate of Incorporation). Shares of non-voting common stock are convertible into shares of voting common stock on a 1,050-for-one basis (i) upon transfers to non-affiliates of Nantucket Investments Limited ("Nantucket") and (ii) at any time at the option of the respective holders thereof.

Quotation on The Nasdaq Capital Market

Our voting common stock is quoted on The Nasdaq Capital Market under the symbol "JAGX".

Transfer Agent

The transfer agent of our common stock is American Stock Transfer & Trust Company, LLC. Their address is 6201 15th Avenue, Brooklyn, New York, 11219.

Preferred Stock

Under our Certificate of Incorporation, our board of directors is authorized to issue up to 4,475,074 shares of preferred stock from time to time, in one or more classes or series, without stockholder approval. As of the date of this prospectus, we have 7,534 shares of Series B-2 Convertible Preferred Stock ("Series B-2 Preferred Stock") outstanding, 842,500 shares of Series C Perpetual Preferred Stock ("Series C Preferred Stock") and 842,500 shares of Series D Perpetual Preferred Stock ("Series D Preferred Stock") outstanding.

Prior to the issuance of shares of each class or series, our board of directors is required by the Delaware General Corporation Law (“DGCL”) and our Certificate of Incorporation to adopt resolutions and file a certificate of designation with the Delaware Secretary of State. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions of that class or series, including the following:

- the number of shares constituting each class or series;
- voting rights;
- rights and terms of redemption, including sinking fund provisions;
- dividend rights and rates;
- terms concerning the distribution of assets;
- conversion or exchange terms;
- redemption prices; and
- liquidation preferences.

All shares of preferred stock offered, when issued and paid for, will be validly issued, fully paid and nonassessable and will not have any preemptive or subscription rights.

We will specify the following terms relating to any class or series of preferred stock offered by us:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;
- voting rights, if any, of the preferred stock;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Delaware Law

Certain provisions of Delaware law and our Certificate of Incorporation and amended and restated bylaws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed in part to encourage anyone seeking to acquire control of us to negotiate with our board of directors. We believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Third Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our Certificate of Incorporation and amended and restated bylaws include provisions that:

- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairman of our board of directors, the chief executive officer or the president;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms;
- specify that no stockholder is permitted to cumulate votes at any election of our board of directors; and
- require approval of the stockholders of at least 75% of the shares and a majority of the board of directors to amend certain of the above-mentioned provisions.

Exclusive Jurisdiction

Under the provisions of our Certificate of Incorporation and amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of us; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our Certificate of Incorporation or amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our Certificate of Incorporation or amended and restated bylaws; or (v) any action asserting a claim against us governed by the internal affairs doctrine; provided that, if and only if the Court of Chancery of the State of Delaware does not have subject matter jurisdiction, then any such action may be brought in another state or federal court sitting in the State of Delaware. This exclusive forum provision would not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our Certificate of Incorporation or amended and restated bylaws to be inapplicable or unenforceable in such action. Our amended and restated bylaws provide that if any part of the exclusive forum provision is held to be invalid, illegal or unenforceable, as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such part in any other circumstance and of the remaining parts of the exclusive forum provision and the application of such provision to other persons or entities and circumstances will not in any way be affected or impaired thereby.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon the closing of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers, and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 $\frac{2}{3}$ % of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage business combinations or other attempts that might result in the payment of a premium over the market price for the shares of common stock held by our stockholders.

The provisions of Delaware law and our Certificate of Incorporation and amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock or preferred stock. Warrants may be issued independently or together with common stock or preferred stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of warrants or beneficial owners of warrants. This summary of some provisions of the warrants is not complete. You should refer to the warrant agreement, including the forms of warrant certificate representing the warrants, relating to the specific warrants being offered for the complete terms of the warrant agreement and the warrants. That warrant agreement, together with the terms of the warrant certificate and warrants, will be filed with the SEC in connection with the offering of the specific warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;
- the price at which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants will commence and the date on which such right shall expire;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;
- if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax considerations.

Warrants for the purchase of common stock or preferred stock will be offered and exercisable for U.S. dollars only. Securities warrants will be issued in registered form only.

Each warrant will entitle its holder to purchase the number of shares of common stock or preferred stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised warrants will become void. We will specify the place or places where, and the manner in which, warrants may be exercised in the applicable prospectus supplement.

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Prior to the exercise of any warrants to purchase common stock or preferred stock, holders of the warrants will not have any of the rights of holders of common stock or preferred stock purchasable upon exercise, including the right to vote or to receive any payments of dividends on the common stock or preferred stock purchasable upon exercise.

DESCRIPTION OF SUBSCRIPTION RIGHTS

The following is a general description of the terms of the subscription rights we may issue from time to time. Particular terms of any subscription rights we offer will be described in the prospectus supplement or free writing prospectus relating to such subscription rights, and may differ from the terms described herein.

We may issue subscription rights to purchase our securities. These subscription rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering. The applicable prospectus supplement will describe the specific terms of any offering of subscription rights for which this prospectus is being delivered, including the following:

- whether common stock, preferred stock or warrants for those securities will be offered under the stockholder subscription rights;
- the price, if any, for the subscription rights;
- the exercise price payable for each security upon the exercise of the subscription rights;
- the number of subscription rights issued to each stockholder;
- the number and terms of the securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities;
- if appropriate, a discussion of material U.S. federal income tax considerations; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the SEC if we offer subscription rights.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, warrants, or subscription rights in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under “Description of Capital Stock,” “Description of Warrants,” and “Description of Subscription Rights” will apply to each unit, as applicable, and to any common stock, preferred stock, warrant, or subscription right included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

PLAN OF DISTRIBUTION

We may offer and sell the securities from time to time in one or more of the following transactions:

- to or through underwriters, brokers or dealers (acting as agent or principal);
- on The Nasdaq Capital Market, in the over-the-counter market or on any other national securities exchange on which our shares are then listed or traded;
- directly to one or more other purchasers;
- upon the exercise of rights distributed or issued to our security holders;
- through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- in “at the market” offerings within the meanings of Rule 415(a)(4) under the Securities Act of 1933 or through a market maker or into an existing market, on an exchange, or otherwise;
- directly to purchasers, through a specific bidding or auction process, on a negotiated basis or otherwise;
- in ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- through the writing or settlement of options (including put or call options), whether the options are listed on an options exchange or otherwise;
- through agents on a best-efforts basis;

- through any other method permitted pursuant to applicable law; or
- otherwise through a combination of any of the above methods of sale.

In addition, we may enter into option, share lending or other types of transactions that require us to deliver shares of common stock to an underwriter, broker or dealer, who will then resell or transfer the shares of common stock under this prospectus. We may also enter into hedging transactions with respect to our securities. For example, we may:

- enter into transactions involving short sales of the shares of common stock by underwriters, brokers or dealers;
- sell shares of common stock short and deliver the shares to close out short positions;
- enter into option or other types of transactions that require us to deliver shares of common stock to an underwriter, broker or dealer, who will then resell or transfer the shares of common stock under this prospectus; or
- loan or pledge the shares of common stock to an underwriter, broker or dealer, who may sell the loaned shares or, in the event of default, sell the pledged shares.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

If we use any underwriter, we will provide a prospectus supplement that will name any underwriter involved in the offer and sale of the securities. The prospectus supplement will also set forth the terms of the offering, including:

- the purchase price of the securities and the proceeds we will receive from the sale of the securities;
- any underwriting discounts and other items constituting underwriters' compensation;
- any public offering or purchase price and any discounts or commissions allowed or re-allowed or paid to dealers;
- any commissions allowed or paid to agents;
- any securities exchanges on which the securities may be listed;
- the method of distribution of the securities;
- the terms of any agreement, arrangement or understanding entered into with the underwriters, brokers or dealers; and
- any other information we think is important.

If underwriters or dealers are used in the sale, the securities will be acquired by the underwriters or dealers for their own account. The securities may be sold from time to time by us in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices;
- at varying prices determined at the time of sale; or
- at negotiated prices.

Such sales may be effected:

- in transactions on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in transactions in the over-the-counter market;
- in block transactions in which the broker or dealer so engaged will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction, or in crosses, in which the same broker acts as an agent on both sides of the trade;
- through the writing of options; or
- through other types of transactions.

The securities may be offered to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more of such firms. Unless otherwise set forth in the prospectus supplement, the obligations of underwriters or dealers to purchase the securities offered will be subject to certain conditions precedent and the underwriters or dealers will be obligated to purchase all the offered securities if any are purchased. Any public offering price and any discount or concession allowed or reallocated or paid by underwriters or dealers to other dealers may be changed from time to time.

We may also make direct sales through subscription rights distributed to our existing stockholders on a pro rata basis, which may or may not be transferable. In any distribution of subscription rights to our stockholders, if all of the underlying securities are not subscribed for, we may then sell the unsubscribed securities directly to third parties or may engage the services of one or more underwriters, dealers or agents, including standby underwriters, to sell the unsubscribed securities to third parties. In addition, whether or not all of the underlying securities are subscribed for, we may concurrently offer additional securities to third parties directly or through underwriters, dealers or agents.

The securities may be sold directly by us through agents designated by us, as applicable, from time to time. Any agent involved in the offer or sale of the securities in respect of which this prospectus is delivered will be named, and any commissions payable by us, as applicable, to such agent will be set forth in, the prospectus supplement. Unless otherwise indicated in the prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

Offers to purchase the securities offered by this prospectus may be solicited, and sales of the securities may be made by us directly to institutional investors or others, who may be deemed to be underwriters within the meaning of the Securities Act of 1933 with respect to any resale of the securities. The terms of any offer made in this manner will be included in the prospectus supplement relating to the offer.

If indicated in the applicable prospectus supplement, underwriters, dealers or agents will be authorized to solicit offers by certain institutional investors to purchase securities from us pursuant to contracts providing for payment and delivery at a future date. Institutional investors with which these contracts may be made include, among others:

- commercial and savings banks;
- insurance companies;
- pension funds;
- investment companies; and
- educational and charitable institutions.

In all cases, these purchasers must be approved by us. Unless otherwise set forth in the applicable prospectus supplement, the obligations of any purchaser under any of these contracts will not be subject to any conditions except that (a) the purchase of the securities must not at the time of delivery be prohibited under the laws of any jurisdiction to which that purchaser is subject, and (b) if the securities are also being sold to underwriters, we must have sold to these underwriters the securities not subject to delayed delivery. Underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

Some of the underwriters, dealers or agents used by us in any offering of securities under this prospectus may be customers of, engage in transactions with, and perform services for us or affiliates of ours in the ordinary course of business. Underwriters, dealers, agents and other persons may be entitled under agreements which may be entered into with us to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, and to be reimbursed by us for certain expenses.

Any securities initially sold outside the U.S. may be resold in the U.S. through underwriters, dealers or otherwise.

Any underwriters to which offered securities are sold by us for public offering and sale may make a market in such securities, but those underwriters will not be obligated to do so and may discontinue any market making at any time.

The anticipated date of delivery of the securities offered by this prospectus will be described in the applicable prospectus supplement relating to the offering.

In compliance with the guidelines of the Financial Industry Regulatory Authority ("FINRA"), the aggregate maximum discount, commission, agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the offering proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

No FINRA member may participate in any offering of securities made under this prospectus if such member has a conflict of interest under FINRA Rule 5121, including if 5% or more of the net proceeds, not including underwriting compensation, of any offering of securities made under this prospectus will be received by a FINRA member participating in the offering or affiliates or associated persons of such FINRA members, unless a qualified independent underwriter has participated in the offering or the offering otherwise complies with FINRA Rule 5121.

To comply with the securities laws of some states, if applicable, the securities may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the securities may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities.

We agreed to keep this prospectus effective until the date on which all registrable securities covered by this prospectus have been sold hereunder.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon for us by our counsel, Reed Smith LLP, Palo Alto, California.

EXPERTS

The financial statements of the Company as of December 31, 2019 and for the fiscal year ended December 31, 2019 incorporated by reference in this prospectus and the registration statement have been so incorporated in reliance on the report of Mayer Hoffman McCann P.C., an independent registered public accounting firm (the report on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

The financial statements of the Company as of December 31, 2018 and for the fiscal year ended December 31, 2018 incorporated by reference in this prospectus and the registration statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm (the report on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at <http://www.sec.gov>.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at <https://jaguar.health>, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus.

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement and any prospectus supplement filed hereafter, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 filed on April 3, 2020;](#)
- [our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders held on May 15, 2020, filed on April 13, 2020;](#)
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020 filed on [May 15, 2020](#) and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2020 filed on [August 13, 2020](#);
- our Current Reports on Form 8-K filed on [January 27, 2020](#), [February 27, 2020](#), [February 28, 2020](#), [March 6, 2020](#), [March 23, 2020](#), [March 26, 2020](#), [April 10, 2020](#) (as subsequently amended on Form 8-K/A on [May 13, 2020](#)), [April 16, 2020](#), [May 8, 2020](#), [May 18, 2020](#), [May 21, 2020](#), [May 22, 2020](#), [May 28, 2020](#), [June 19, 2020](#), [June 26, 2020](#), [July 14, 2020](#), [July 21, 2020](#), [August 21, 2020](#), [September 2, 2020](#), [September 2, 2020](#), [September 9, 2020](#) and [September 11, 2020](#) (in each case, except for information contained therein which is furnished rather than filed);
- [the description of our common stock contained in our registration statement on Form 8-A filed on October 30, 2014 \(Registration No. 001-36714\) with the SEC, including any amendment or report filed for the purpose of updating such description; and](#)
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

Unless otherwise noted, the SEC file number for each of the documents listed above is 001-36714.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Jaguar Health, Inc., 201 Mission Street, Suite 2375, San Francisco, CA, 94105 or call (415) 371-8300.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.



Up to \$15,300,000 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Ladenburg Thalmann

April 9, 2021
