

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

JAGUAR HEALTH, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

46-2956775
(I.R.S. Employer
Identification No.)

**200 Pine Street, Suite 400
San Francisco, California 94104
(415) 371-8300**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

**Lisa A. Conte
Chief Executive Officer and President
Jaguar Health, Inc.**

**200 Pine Street, Suite 400
San Francisco, California 94104 (415) 371-8300**

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies of all correspondence to:

**Donald C. Reinke, Esq.
Michael S. Lee, Esq.
Reed Smith LLP
1841 Page Mill Road, Suite 110
Palo Alto, California 94304
(650) 352-0500**

**Approximate date of commencement of proposed sale of the securities to the public:
From time to time after the effective date of this registration statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered ⁽¹⁾⁽²⁾	Proposed Maximum Offering Price per Unit ⁽³⁾⁽⁴⁾	Proposed Maximum Aggregate Offering Price ⁽³⁾⁽⁴⁾	Amount of Registration Fee ⁽⁴⁾⁽⁵⁾
Primary Offering				
Common Stock, par value \$0.0001 per share	—	—	—	—
Preferred Stock, par value \$0.0001 per share	—	—	—	—
Warrants	—	—	—	—
Subscription Rights	—	—	—	—
Units	—	—	—	—
Total Primary Offering			\$ 75,000,000	\$6,952.50
Secondary Offering				
Common Stock, par value \$0.0001 per share	309,242	\$1.52	\$ 470,047.84	\$ 43.57
Total (Primary and Secondary)	—	—	\$75,470,047.84	\$6,996.07

- (1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended, the securities being registered hereunder shall be deemed to cover additional shares of common stock and preferred stock that may be offered or issued to prevent dilution resulting from stock splits, stock dividends, anti-dilution provision or similar transactions.
- (2) With regard to the securities included in the primary offering made hereby, an indeterminate number of the securities of each identified class is being registered as may from time to time be offered hereunder at indeterminate prices, along with an indeterminate number of securities that may be issued upon exercise, settlement, exchange or conversion of securities offered or sold hereunder as shall have an aggregate initial offering price not to exceed \$75,000,000. Any securities registered hereunder may be sold separately or as units with the other securities registered hereunder. The proposed maximum offering price per unit will be determined, from time to time, by the registrant in connection with the issuance by the registrant of the securities registered hereunder. With respect to the secondary offering, there is being registered hereunder 309,242 shares of common stock that the selling stockholders may sell from time to time.
- (3) With regard to the securities included in the primary offering made hereby, the proposed maximum offering price per security will be determined from time to time by the registrant in connection with, and at the time of, the issuance of the securities and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act of 1933, as amended.
- (4) With regard to the securities included in the secondary offering made hereby, the offering price and registration fee are estimated pursuant to Rule 457(c) under the Securities Act of 1933, as amended, based on the average of the high and low prices reported for the shares of common stock as reported on The Nasdaq Capital Market on November 18, 2021.
- (5) With regard to the securities included in the primary offering made hereby, the registration fee is calculated pursuant to Rule 457(o) under the Securities Act, based on the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement consists of two prospectuses:

- a base prospectus which covers the offering, issuance and sale by us of up to \$75,000,000 of our common stock, preferred stock, warrants, subscriptions rights, and/or units; and
 - a resale prospectus covering the resale by the selling stockholders of up to 309,242 shares of our common stock.
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SUBJECT TO COMPLETION, DATED NOVEMBER 22, 2021



JAGUAR HEALTH, INC.

\$75,000,000

**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 \$75,000,000 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 November 18, 2021, the last reported sale price of our voting common stock on The Nasdaq Capital Market was \$1.45 per share.

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 _____, 2021.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer, solicitation or sale is not permitted.

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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 \$75,000,000.

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 opiod and sustainably derived prescription medicines for people and animals with gastrointestinal distress, specifically chronic, debilitating diarrhea. Our wholly-owned subsidiary, Napo Pharmaceuticals, Inc. (“Napo”), focuses on developing and commercializing proprietary human gastrointestinal pharmaceuticals for the global marketplace 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. Napo’s substantially owned Italian subsidiary, Napo EU S.p.A., focuses on expanding crofelemer access in Europe.

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 equine athletes.

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, FDA-compliant 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 and proof of concept evidence from completed human clinical trials.

Crofelemer 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. Crofelemer 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 for short bowel syndrome with intestinal failure with “SB-IFS”; supportive care for diarrhea relief in inflammatory bowel diseases (“IBD”); diarrhea-predominant irritable bowel syndrome (“IBS-D”); and for idiopathic/functional diarrhea. In addition, a second-generation anti-secretory agent, lechlemer, is in development for cholera. Crofelemer previously received orphan-drug designation for SBS in the U.S.

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.

Description of the Offering

Under this prospectus, we may offer up to \$75,000,000 of common stock, preferred stock, warrants, subscription rights or units from time to time in one or more offerings and in any combination. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

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. 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 (as amended, restated, or modified, the "Certificate of Incorporation") to effect on June 7, 2019, a 1-for-70 reverse split of our voting common stock (the "2019 Reverse Split"). On September 3, 2021, we filed the fifth amendment to the Certificate of Incorporation to effect on September 8, 2021, a 1-for-3 reverse stock split of our voting common stock (the "2021 Reverse Split" and, together with the "2019 Reverse Split" the "Reverse Splits"). Accordingly, all of the stock figures and related market, conversion and exercise prices in this prospectus have been adjusted to reflect the Reverse Splits.

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.

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 those described 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 or include in any applicable prospectus supplement. 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, the documents that we incorporate by reference and any free writing prospectuses that we may authorize for use in connection with this offering 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”). These forward-looking statements can generally be identified as such because the context of the statement will include words such as “may,” “will,” “intend,” “plan,” “believe,” “anticipate,” “expect,” “estimate,” “predict,” “potential,” “continue,” “likely,” or “opportunity,” the negative of these words or words of similar import. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the “Business” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC.

These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those noted in “Risk Factors” above and in any applicable prospectus supplement or free writing prospectus, and those included in the documents that we incorporate by reference herein and therein.

In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this prospectus or any applicable prospectus supplement or free writing prospectus, or documents incorporated by reference herein and therein, that include forward-looking statements.

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 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 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 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 3,150-for-one basis (i) upon transfers to non-affiliates of Nantucket Investments Limited 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, there are no shares of 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 ⅔% 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 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 reallowed 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 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, 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, 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 Exchange Act 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, 2020 filed on March 31, 2021;](#)
- [our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders held on May 13, 2021, filed on April 13, 2021;](#)
- our [Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2021 filed on May 17, 2021](#), our [Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2021 filed on August 13, 2021](#), and our [Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2021 filed on November 17, 2021;](#)
- our Current Reports on Form 8-K filed on [January 8, 2021](#), [January 11, 2021](#) (excluding Item 7.01), [January 14, 2021](#) (as subsequently amended on [January 14, 2021](#)), [January 22, 2021](#), [March 11, 2021](#) (excluding Item 7.01), [March 31, 2021](#) (excluding Item 2.02), [April 8, 2021](#), [April 15, 2021](#), [April 30, 2021](#), [May 11, 2021](#) (excluding Item 7.01), [May 14, 2021](#), [May 17, 2021](#) (excluding Item 2.02), [June 4, 2021](#), [June 11, 2021](#), [July 15, 2021](#), [July 23, 2021](#) (excluding Item 7.01), [August 6, 2021](#), [August 24, 2021](#) (excluding Item 7.01), [September 3, 2021](#) (excluding Item 7.01), and [September 17, 2021](#) (excluding Item 7.01); and
- [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.](#)

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

In addition, all documents that the Company files pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, subsequent to the filing of this Registration Statement and prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing of such documents, except as to any document or portion of any document that is deemed furnished and not filed.

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., 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 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.



\$75,000,000

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

PROSPECTUS

, 2021

SUBJECT TO COMPLETION, DATED NOVEMBER 22, 2021

**JAGUAR HEALTH, INC.****309,242 Shares of Common Stock**

Pursuant to this prospectus, the selling stockholders identified herein (the “Selling Stockholders”) are offering on a resale basis from time to time an aggregate of up to 309,242 shares (the “Shares”) of voting common stock, par value \$0.0001 per share of Jaguar Health, Inc. (“Jaguar,” “we,” “our” or the “Company”), a Delaware corporation. We are not selling any shares of common stock under this prospectus and will not receive any of the proceeds from the sale by the Selling Stockholders of the Shares.

The Selling Stockholders or their pledgees, assignees or successors in interest may sell or otherwise dispose of the Shares covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the Selling Stockholders may sell or otherwise dispose of the Shares covered by this prospectus in the section entitled “Plan of Distribution” on page 14. Discounts, concessions, commissions and similar selling expenses attributable to the sale of Shares covered by this prospectus will be borne by the Selling Stockholders. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the Shares with the Securities and Exchange Commission.

Our voting common stock is listed on The Nasdaq Capital Market, under the symbol “JAGX.” On November 18, 2021, the last reported sale price of our voting common stock on The Nasdaq Capital Market was \$1.45 per share.

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 5 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 _____, 2021.

The information in this prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer, solicitation or sale is not permitted.

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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, the Selling Stockholders may, over time, offer and sell the Shares described in this prospectus in one or more offerings or resales.

This prospectus provides you with a general description of the Shares. Each time a Selling Stockholder sells the Shares, such Selling Stockholder may provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add to, update or change information contained in this prospectus.

We and the Selling Stockholders 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 opiod and sustainably derived prescription medicines for people and animals with gastrointestinal distress, specifically chronic, debilitating diarrhea. Our wholly-owned subsidiary, Napo Pharmaceuticals, Inc. (“Napo”), focuses on developing and commercializing proprietary human gastrointestinal pharmaceuticals for the global marketplace 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. Napo’s substantially owned Italian subsidiary, Napo EU S.p.A., focuses on expanding crofelemer access in Europe.

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 equine athletes.

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, FDA-compliant 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 and proof of concept evidence from completed human clinical trials.

Crofelemer 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. Crofelemer 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 for short bowel syndrome with intestinal failure with “SB-IFS”; supportive care for diarrhea relief in inflammatory bowel diseases (“IBD”); diarrhea-predominant irritable bowel syndrome (“IBS-D”); and for idiopathic/functional diarrhea. In addition, a second-generation anti-secretory agent, lechlemer, is in development for cholera. Crofelemer previously received orphan-drug designation for SBS in the U.S.

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.

Description of the Issuance of the Shares Pursuant to the PIPE Purchase Agreement

On September 13, 2021, the Company entered into a securities purchase agreement (the “PIPE Purchase Agreement”) with certain investors named therein (the “Investors”), pursuant to which the Company agreed to issue and sell the Shares to the Investors in a private placement, for an aggregate purchase price of approximately \$776,197 (the “Private Placement”) or \$2.51 per share, a \$0.01 premium to market price (defined as the Minimum Price under Nasdaq Listing Rule 5635(d)). The Investors in the Private Placement include (i) Lisa Conte, Chief Executive Officer of the Company, and Carol Lizak, Chief Financial Officer of the Company, who each invested approximately \$20,000 in the Private Placement and (ii) Joshua Mailman, the sponsor of Dragon SPAC S.p.A. The Company intends to use the proceeds from the Private Placement for working capital and general corporate purposes.

The PIPE Purchase Agreement includes representations, warranties, and covenants customary for a transaction of this type. In addition, the Company agreed to file a registration statement on Form S-3 with the U.S. Securities and Exchange Commission no later than 90 calendar days following the closing of the Private Placement to register the resale of the Shares issued and sold to the Investors. Such Shares were offered and sold to the Investors in reliance upon exemptions from registration pursuant to Section 4(a)(2) under the Securities Act of 1933, as amended (the “Securities Act”), and Rule 506 of Regulation D promulgated thereunder.

The descriptions of the PIPE Purchase Agreement are not complete and is qualified in their entirety by reference to the PIPE Purchase Agreement, which have been filed as exhibits to the registration statement of which this prospectus is a part. See “Where You Can Find More Information” and “Incorporation of Information by Reference.” The representations, warranties and covenants made in such agreements and instruments were made solely for the benefit of the parties to such agreements and instruments, including, in some cases, for the purpose of allocating risk among the parties thereto, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were made as of an earlier date. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

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. 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 (as amended, restated, or modified, the “Certificate of Incorporation”) to effect on June 7, 2019, a 1-for-70 reverse split of our voting common stock (the “2019 Reverse Split”). On September 3, 2021, we filed the fifth amendment to the Certificate of Incorporation to effect on September 8, 2021, a 1-for-3 reverse stock split of our voting common stock (the “2021 Reverse Split” and, together with the “2019 Reverse Split” the “Reverse Splits”). Accordingly, all of the stock figures and related market, conversion and exercise prices in this prospectus have been adjusted to reflect the Reverse Splits.

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

Shares to be offered by the Selling Stockholders	Up to 309,242 shares of our common stock
Use of Proceeds	We will not receive any proceeds from the sale of the Shares by the Selling Stockholders. See “Use of Proceeds” in this prospectus.
Risk Factors	This investment involves a high degree of risk. See “Risk Factors” for a discussion of factors you should consider carefully before making an investment decision.
The Nasdaq Capital Market symbol	“JAGX”.

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 those described 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 the documents that we incorporate by reference 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”). These forward-looking statements can generally be identified as such because the context of the statement will include words such as “may,” “will,” “intend,” “plan,” “believe,” “anticipate,” “expect,” “estimate,” “predict,” “potential,” “continue,” “likely,” or “opportunity,” the negative of these words or words of similar import. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the “Business” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC.

These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those noted in “Risk Factors” above and in any applicable prospectus supplement or free writing prospectus, and those included in the documents that we incorporate by reference herein and therein.

In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this prospectus or any applicable prospectus supplement or free writing prospectus, or documents incorporated by reference herein and therein, that include forward-looking statements.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the Shares in this offering. The Selling Stockholders will receive all of the proceeds from this offering.

Pursuant to the PIPE Purchase Agreement, all fees and expenses incurred in effecting the registration of the Shares covered by this prospectus, including all registration and filing fees, fees and expenses of our counsel, and our independent registered public accountants shall be borne by the Company.

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 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 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 3,150-for-one basis (i) upon transfers to non-affiliates of Nantucket Investments Limited 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, there are no shares of 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 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.

SELLING STOCKHOLDERS

The Shares being offered by the Selling Stockholders are those previously issued to the Selling Stockholders pursuant to the PIPE Purchase Agreement. For additional information regarding the issuances of the Shares and the relationship between the Selling Stockholders and us, see “Prospectus Summary — Description of the Issuance of the Shares Pursuant to the PIPE Purchase Agreement” above. We are registering the Shares in order to permit the Selling Stockholders to offer the Shares for resale from time to time.

The following table sets forth:

- the Selling Stockholders and other information regarding the beneficial ownership of the shares of common stock held by the Selling Stockholders;
- the number of shares of common stock beneficially owned by each Selling Stockholder, based on their respective ownership of the shares of common stock, as of November 7, 2021;
- the number of Shares that may be offered by each Selling Stockholder pursuant to this prospectus;
- the number of shares of common stock to be beneficially owned by the Selling Stockholders and their respective affiliates following the sale of any of the Shares covered by this prospectus; and
- the percentage of our issued and outstanding common stock to be beneficially owned by the Selling Stockholders and their respective affiliates following the sale of all the Shares covered by this prospectus.

This prospectus generally covers the resale of all the Shares purchased by the Selling Stockholders in connection with the transactions contemplated by the PIPE Purchase Agreement.

To our knowledge, none of the Selling Stockholders is either a broker-dealer or an affiliate of a broker-dealer.

The Selling Stockholders may sell all, some or none of its Shares in this offering. See “Plan of Distribution.”

Name of Selling Stockholder ⁽¹⁾	Number of shares of Common Stock Owned Prior to Offering	Maximum Number of shares of Common Stock to be Sold Pursuant to this Prospectus	Number of shares of Common Stock Owned After Offering ⁽²⁾	
			Number	Percent
Joshua Mailman ⁽³⁾	865,869	199,203	666,666	1.45%
IdB Holding S.p.A.	94,103	94,103	—	—
Lisa Conte ⁽⁴⁾	463,787	7,968	455,819	*
Carol Lizak ⁽⁵⁾	47,511	7,968	39,543	*

* Represents less than 1% of the issued and outstanding shares of common stock as of November 7, 2021.

(1) The address for Mr. Mailman is 115 Tower Hill Road, West Tuxedo Park, NY 10987. The address for IdB Holding S.p.A. is Vitale Ortles, 12 20139 Milan, Italy. The address for each Ms. Conte and Ms. Lizak is 200 Pine Street, Suite 400, San Francisco, CA 94104.

(2) Assumes that the applicable Selling Stockholder sells all the Shares registered under this prospectus held by such Selling Stockholder.

(3) Represents (i) 865,869 shares of common stock.

(4) Represents (i) 7,976 shares of common stock, (ii) 443,311 shares of common stock issuable to Ms. Conte under stock options that are exercisable or will become exercisable in the 60 days subsequent to November 7, 2021, and (iii) 12,500 shares of common stock issuable upon exercise of warrants held by Ms. Conte. The weighted average exercise price of the 443,311 stock options is \$16.14.

(5) Represents (i) 7,968 shares of common stock and (ii) 39,543 shares of common stock issuable to Ms. Lizak under stock options that are exercisable or will become exercisable in the 60 days subsequent to November 7, 2021. The weighted average exercise price of the 39,543 stock options is \$4.25.

PLAN OF DISTRIBUTION

Each Selling Stockholder of the common stock and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their Shares covered hereby on any stock exchange, market or trading facility on which the Shares are traded or in private transactions. These sales may be at fixed or negotiated prices. A Selling Stockholder may use any one or more of the following methods when selling the Shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the Shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such Shares at a stipulated price per share;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell the Shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of Shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2121.

In connection with the sale of the Shares or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The Selling Stockholders may also sell the Shares of the common stock short and deliver the Shares to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these Shares. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities that require the delivery to such broker-dealer or other financial institution of the Shares offered by this prospectus, which Shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The Selling Stockholders and any broker-dealers or agents that are involved in selling the Shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the Shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each Selling Stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the Shares. In no event shall any broker-dealer receive fees, commissions and markups which, in the aggregate, would exceed eight percent.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the Shares. The Company has agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Because Selling Stockholders may be deemed to be “underwriters” within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act including Rule 172 thereunder. The Selling Stockholders have advised us that there is no underwriter or coordinating broker acting in connection with the proposed sale of the Shares by the Selling Stockholders.

We agreed to keep this prospectus effective until all of the Shares continuing to have registration rights have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The Shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the Shares covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the Shares may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of the common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

LEGAL MATTERS

The validity of the Shares 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, 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 Exchange Act 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, 2020 filed on March 31, 2021;](#)
- [our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders held on May 13, 2021, filed on April 13, 2021;](#)
- our [Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2021 filed on May 17, 2021](#), our [Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2021 filed on August 13, 2021](#) and our [Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2021 filed on November 17, 2021;](#)
- our Current Reports on Form 8-K filed on [January 8, 2021](#), [January 11, 2021](#) (excluding Item 7.01), [January 14, 2021](#) (as subsequently amended on [January 14, 2021](#)), [January 22, 2021](#), [March 11, 2021](#) (excluding Item 7.01), [March 31, 2021](#) (excluding Item 2.02), [April 8, 2021](#), [April 15, 2021](#), [April 30, 2021](#), [May 11, 2021](#) (excluding Item 7.01), [May 14, 2021](#), [May 17, 2021](#) (excluding Item 2.02), [June 4, 2021](#), [June 11, 2021](#), [July 15, 2021](#), [July 23, 2021](#) (excluding Item 7.01), [August 6, 2021](#), [August 24, 2021](#) (excluding Item 7.01), [September 3, 2021](#) (excluding Item 7.01), and [September 17, 2021](#) (excluding Item 7.01); and
- [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.](#)

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

In addition, all documents that the Company files pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, subsequent to the filing of this Registration Statement and prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing of such documents, except as to any document or portion of any document that is deemed furnished and not filed.

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., 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 and any prospectus supplement. Neither we nor the Selling Stockholders have 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.



309,242 Shares of Common Stock

PROSPECTUS

, 2021

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an itemization of the various expenses, all of which we will pay, in connection with the issuance and distribution of the securities being registered. All of the amounts shown are estimated except the SEC registration fee.

SEC Registration Fee	\$6,996.07
Legal Fees and Expenses	*
Accounting Fees and Expenses	*
Miscellaneous	*
Total	\$ *

* These fees will be dependent on the type of securities offered and number of offerings and, therefore, cannot be estimated at this time. In accordance with Rule 430B under the Securities Act, additional information regarding estimated fees and expenses will be provided at the time information as to an offering is included in a prospectus supplement.

Item 15. Indemnification of Directors and Officers

Section 102(b)(7) of the DGCL authorizes a corporation in its certificate of incorporation to eliminate or limit personal liability of directors of the corporation for violations of the directors' fiduciary duty of care. However, directors remain liable for breaches of duties of loyalty, failing to act in good faith, engaging in intentional misconduct, knowingly violating a law, paying a dividend or approving a stock repurchase which was illegal under DGCL Section 174 or obtaining an improper personal benefit. In addition, equitable remedies for breach of fiduciary duty of care, such as injunction or recession, are available.

Our current certificate of incorporation eliminates the personal liability of the members of our board of directors to the fullest extent permitted by the DGCL. Any repeal or modification of that provision by the stockholders of the corporation will not adversely affect any right or protection of a director of the corporation existing at the time of such repeal or modification.

Section 145 of the DGCL provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our current bylaws provide for indemnification of its officers and directors to the fullest extent permitted by the DGCL.

We have entered into indemnification agreements with each of our directors and officers, pursuant to which we agreed, to the maximum extent permitted by applicable law and subject to the specified terms and conditions set forth in each agreement, to indemnify a director or officer who acts on our behalf and is made or threatened to be made a party to any action or proceeding against expenses, judgments, fines and

amounts paid in settlement that are incurred by such officer or director in connection with the action or proceeding. The indemnification provisions apply whether the action was instituted by a third party or by us.

We have purchased and maintain insurance on behalf of our officers and directors that provides coverage for expenses and liabilities incurred by them in their capacities as officers and directors.

Item 16. Exhibits

The exhibits to this registration statement are listed in the Exhibit Index to this registration statement, which Exhibit Index is hereby incorporated by reference.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a)

of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
4.1	<u>Specimen Voting Common Stock Certificate of Jaguar Health, Inc. (f/k/a Jaguar Animal Health, Inc.) (incorporated by reference to Exhibit 4.1 to the Registration Statement on Form S-1/A (No. 333-198383) filed on October 10, 2014).</u>
4.2*	Form of Warrant Agreement (together with form of Warrant Certificate).
4.3*	Form of Rights Agreement (together with form of Rights Certificate).
5.1**	<u>Opinion of Reed Smith LLP as to validity of the securities being registered.</u>
10.1	<u>Securities Purchase Agreement, dated September 13, 2021, by and between Jaguar Health, Inc. and the Investors named therein. (incorporated by reference to Ex. 10.1 to the Current Report on Form 8-K filed on September 17, 2021).</u>
23.1**	<u>Consent of Mayer Hoffman McCann P.C., independent registered public accounting firm.</u>
23.2**	<u>Consent of Reed Smith LLP (included in Exhibit 5.1).</u>
24.1**	<u>Power of Attorney (included on the signature page hereto).</u>

* To be subsequently filed, if applicable, by an amendment to the Registration Statement or by a Current Report on Form 8-K.

** Filed herewith.



Reed Smith LLP
 101 Second Street
 Suite 1800
 San Francisco, CA 94105-3659
 Tel +1 415 543 8700
 Fax +1 415 391 8269
 reedsmith.com

November 22, 2021

Jaguar Health, Inc.
 200 Pine Street, Suite 400
 San Francisco, California 94104

Ladies and Gentlemen:

This opinion is furnished to you in connection with the Registration Statement on Form S-3 (the "Registration Statement") filed by Jaguar Health, Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission (the "Commission") on the date hereof in connection with the registration under the Securities Act of 1933, as amended (the "Securities Act"), for:

(a) the offer and sale by the Company from time to time on a delayed or continuous basis pursuant to Rule 415 of the Securities Act of up to \$75,000,000 in aggregate amount of (i) shares (the "Primary Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock"), (ii) shares of the Company's preferred stock, par value \$0.0001 per share (the "Preferred Stock"), which may be issued in one or more series, (iii) warrants for the purchase of Common Stock and/or Preferred Stock (the "Warrants"), which may be issued under warrant agreements, to be dated on or about the date of the first issuance of the applicable Warrants thereunder, by and between the Company and a warrant agent to be selected by the Company (each, a "Warrant Agreement"), (iv) subscription rights to purchase Common Stock and/or Preferred Stock (the "Rights"), which may be issued pursuant to a rights agreement and certificates issued thereunder, to be dated on or about the date of the first issuance of the applicable Rights thereunder, by and between the Company and a rights agent to be selected by the Company (each, a "Rights Agreement"), and (v) units comprised of one or more securities described in clauses (a)(i) through (iv) above in any combination (the "Units" and, together with the Primary Shares, the Preferred Stock, the Warrants and the Rights, collectively being referred to herein as the "Primary Securities"), which may be issued under unit agreements, to be dated on or about the date of first issuance of the applicable Units thereunder, by and between the Company and a unit agent selected by the Company (each, a "Unit Agreement"); and

(b) the resale by the selling stockholders named in the Registration Statement (the "Selling Stockholders") of a total of 309,242 shares of the Common Stock (the "Secondary Shares") issued to the Selling Stockholders. The Primary Securities and the Secondary Shares are collectively referred to herein as the "Securities."

We are acting as counsel for the Company in connection with the registration of the Securities by the Company.

ABU DHABI ATHENS AUSTIN BEIJING BRUSSELS CENTURY CITY CHICAGO DALLAS DUBAI
 FRANKFURT HONG KONG
 HOUSTON KAZAKHSTAN LONDON LOS ANGELES MIAMI MUNICH NEW YORK PARIS PHILADELPHIA
 PITTSBURGH PRINCETON
 RICHMOND SAN FRANCISCO SHANGHAI SILICON VALLEY SINGAPORE TYSONS WASHINGTON, D.C.
 WILMINGTON

In rendering the opinion set forth herein, we have examined originals or copies, certified or otherwise identified to our satisfaction, of such documents, corporate records, certificates of public officials and other instruments as we have deemed necessary or advisable.

In such examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all items submitted to us as originals, the conformity with originals of all items submitted to us as copies, and the authenticity of the originals of such copies. As to any facts material to the opinions expressed herein that we did not independently establish or verify, we have relied upon statements and representations of officers and other representatives of the Company and public officials.

We have assumed that the Warrant Agreement, Rights Agreement and Unit Agreement will each be duly authorized, executed, and delivered by the warrant agent, rights agent, and unit agent, respectively, thereunder. With respect to our opinion as to the Primary Shares and Primary Securities convertible into or exercisable for shares of Common Stock, we have assumed that, at the time of issuance and sale, a sufficient number of shares of Common Stock are authorized and available for issuance under the Company's certificate of incorporation as then in effect and that the consideration for the issuance and sale of the Common Stock (or Warrants or Rights exercisable for, or Preferred Stock convertible into, Common Stock) is in an amount that is not less than the par value of the Common Stock. With respect to our opinion as to the Preferred Stock and Primary Securities convertible into or exercisable for shares of Preferred Stock, we have assumed that, at the time of issuance and sale, a sufficient number of shares of Preferred Stock are authorized and available for issuance under the Company's certificate of incorporation as then in effect and that the consideration for the issuance and sale of the Preferred Stock (or Warrants or Rights exercisable for Preferred Stock) is in an amount that is not less than the par value of the Preferred Stock. We have also assumed that any Warrants, Rights or Units offered under the Registration Statement, and the related Warrant Agreement, Rights Agreement and Unit Agreement, as applicable, will be executed in the forms to be filed as exhibits to the Registration Statement or incorporated by reference therein. We have not independently verified any of the foregoing assumptions.

This opinion is based solely on the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, we express no opinion with respect to (i) the qualification of the Securities under the securities or blue sky laws of any state or any foreign jurisdiction or (ii) the compliance with any federal or state law, rule or regulation relating to securities, or to the sale or issuance thereof.

Based upon and subject to the foregoing, we are of the opinion that:

1. With respect to the Primary Shares, when (i) specifically authorized for issuance by the Company's board of directors or an authorized committee thereof (the "Authorizing Resolutions"), (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) an appropriate prospectus supplement with respect to the Primary Shares has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (iv) if the Primary Shares are to be sold pursuant to a purchase, underwriting or similar agreement (an "Underwriting Agreement"), such Underwriting Agreement with respect to the Primary Shares in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto, or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (v) the terms of the sale of the Primary Shares have been duly established in conformity with the Company's certificate of incorporation and bylaws, as then in effect, and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding on the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vi) the Primary Shares have been issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (vii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Primary Shares will be validly issued, fully paid and nonassessable.

2. With respect to the Preferred Stock, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) an appropriate prospectus supplement with respect to the Preferred Stock has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (iv) if the applicable shares of Preferred Stock are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable shares of Preferred Stock in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto, or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (v) an appropriate certificate or certificates of amendment or designation relating to a class or series of Preferred Stock to be sold under the Registration Statement has been duly authorized, adopted and filed with the Secretary of State of the State of Delaware prior to the issuance of the Preferred Stock; (vi) the terms of the sale of such class or series of Preferred Stock have been duly established in conformity with the Company's certificate of incorporation and bylaws, as then in effect, and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding on the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) shares of such class or series of Preferred Stock have been issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Preferred Stock will be validly issued, fully paid and nonassessable.

3. With respect to the Warrants, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Warrant Agreement relating to the Warrants has been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Warrants has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Warrants are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Warrants in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Warrants and of their issuance and sale have been duly established in conformity with the Warrant Agreement and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Warrants have been duly executed and countersigned in accordance with the Warrant Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Warrants will constitute valid and legally binding obligations of the Company.

4. With respect to the Rights, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Rights Agreement and any certificates relating to the Rights have been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Rights has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Rights are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Rights in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Rights and of their issuance and sale have been duly established in conformity with the Rights Agreement and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Rights have been duly executed and countersigned in accordance with the Rights Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Rights will constitute valid and legally binding obligations of the Company.

5. With respect to the Units, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Unit Agreement relating to the Units has been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Units has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Units are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Units in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Units and of their issuance and sale have been duly established in conformity with the Unit Agreement and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Units have been duly executed and countersigned in accordance with the Unit Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Units will constitute valid and legally binding obligations of the Company.

6. The Secondary Shares are validly issued, fully paid and nonassessable.

We consent to the inclusion of this opinion as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act and further consent to all references to us under the caption "Legal Matters" in the Registration Statement. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the applicable rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ REED SMITH LLP

REED SMITH LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-3 dated November 22, 2021, of our report dated March 31, 2021, relating to the consolidated financial statements of Jaguar Health, Inc. as of December 31, 2020 and 2019, and the related consolidated statements of operations, changes in convertible preferred stock and stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2020. We also consent to the reference to our Firm under the caption "Experts."

/s/ Mayer Hoffman McCann P.C.
San Diego, California
November 22, 2021
