

Jaguar Health, Inc.
Form 424B3
April 27, 2018

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[TABLE OF CONTENTS](#)

[Table of Contents](#)

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Registration No. 333-219736

PROSPECTUS

JAGUAR HEALTH, INC.

5,154,515 Shares of Common Stock

This prospectus relates to the proposed resale or other disposition from time to time of up to 5,154,515 shares of Jaguar Health, Inc. common stock, \$0.0001 par value per share, by the selling shareholder identified in this prospectus. Of these shares, 4,884,245 shares are outstanding shares of common stock held by the selling shareholder and 270,270 shares are shares of common stock issuable upon conversion of the non-voting common stock held by the selling shareholder. We are not selling any shares of common stock under this prospectus and will not receive any of the proceeds from the sale or other disposition of common stock by the selling shareholder.

The selling shareholder or its pledgees, assignees or successors-in-interest may offer and sell or otherwise dispose of the shares of common stock described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling shareholder will bear all commissions and discounts, if any, attributable to the sales of shares. We will bear all other costs, expenses and fees in connection with the registration of the shares. See "Plan of Distribution" beginning on page 12 for more information about how the selling shareholder may sell or dispose of their shares of common stock.

Our common stock is listed on the NASDAQ Capital Market, under the symbol "JAGX." On April 25, 2018, the last reported sale price of our common stock on the NASDAQ Capital Market was \$0.16 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 7 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 April 27, 2018.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	<u>1</u>
<u>PROSPECTUS SUMMARY</u>	<u>2</u>
<u>RISK FACTORS</u>	<u>7</u>
<u>CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	<u>8</u>
<u>USE OF PROCEEDS</u>	<u>9</u>
<u>SELLING SHAREHOLDER</u>	<u>10</u>
<u>PLAN OF DISTRIBUTION</u>	<u>12</u>
<u>LEGAL MATTERS</u>	<u>14</u>
<u>EXPERTS</u>	<u>14</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>14</u>
<u>INCORPORATION OF INCORPORATION BY REFERENCE</u>	<u>15</u>

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission (the "SEC") pursuant to which the selling shareholder named herein may, from time to time, offer and sell or otherwise dispose of the securities covered by this prospectus. 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, 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.

Neither we nor the selling shareholder has 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.

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

Table of Contents

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

We are a natural-products pharmaceuticals company focused on the development and commercialization of novel, sustainably derived gastrointestinal products for both human prescription use and animals on a global basis. Our wholly-owned subsidiary, Napo Pharmaceuticals, Inc. ("Napo"), focuses on the development and commercialization of 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 ("FDA") for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. In the animal health space, we focus on developing and commercializing first-in-class gastrointestinal products for companion and production animals, foals, and high value horses.

Jaguar was founded in San Francisco, California as a Delaware corporation on June 6, 2013. Napo formed Jaguar to develop and commercialize animal health products. Effective as of December 31, 2013, Jaguar was a wholly-owned subsidiary of Napo, and until May 13, 2015, Jaguar was a majority-owned subsidiary of Napo. 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.

Mytesi is a novel, first-in-class anti-secretory agent which has a basic normalizing effect locally on the gut, and this mechanism of action has the potential to benefit multiple disorders. We believe we control commercial rights for Mytesi for all indications, territories and patient populations globally, and we are pursuing a follow-on indication for Mytesi in cancer related diarrhea ("CRD"), an important supportive care indication for patients undergoing primary or adjuvant chemotherapy for cancer treatment. Mytesi is also in development for rare disease indications for infants and children with congenital diarrheal disorders and short bowel syndrome ("SBS"); for irritable bowel syndrome ("IBS") (Mytesi has demonstrated benefit to IBS-D patients in published Phase 2 studies); for supportive care for inflammatory bowel disease ("IBD"); and as a second-generation anti-secretory agent for use in cholera patients. Mytesi has received orphan-drug designation for SBS.

Our management team has significant experience in gastrointestinal product development for both humans and animals. Napo was founded 28 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 executive vice president of sustainable supply, ethnobotanical research and intellectual property, and Lisa Conte, our founder, president and CEO, have worked together for more than 28 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.

The active ingredient in Mytesi is the basis for our eleven different animal health products across eight different species, all of which work by the same mechanism of action, which is highly conserved across all mammals. In the animal health space, we focus on developing and commercializing first-in-class gastrointestinal products for companion and production animals, foals, and high value horses. Portfolio planning for the animal health space is of utmost importance to us, given the wide

Table of Contents

array of potential species-specific products and because we do not want animal-related research and development activities to divert significant financial resources while we are focusing on growing Mytesi sales and seeking to move the company towards profitability. Canalevia is our lead veterinary prescription drug product candidate, intended for treatment of various forms of diarrhea in dogs. We have received minor use in a minor species ("MUMS") designation for Canalevia for chemotherapy-induced diarrhea ("CID") and EID in dogs. If Canalevia is approved for CID and EID in dogs, we expect to conduct the commercial launch of Canalevia for these indications in the first half of 2018. We have completed the pivotal trial for acute diarrhea in dogs and are in discussions with the CVM with respect to our plans for this indication of Canalevia.

The equine athlete business continues to be a major focus area for the animal health side of our business. The demand, particularly in the Middle East, for a "total gut health" product for high performance equine athletes appears to be quite strong, and we believe this is indicative of an unmet medical need. Based on this demand, and with support from studies we conducted in horses with gastric ulcers a prevalent problem in competing horses and also horses with diarrhea, we have transitioned development of Equilevia to a create a non-prescription, personalized, premium proprietary product for total gut health in equine athletes. Gut health is of critical importance in horses, as conditions such as colic can lead to the death of an otherwise healthy horse in a matter of hours. We continue to assess the size of the opportunity represented by this program and potential partnerships that would increase access to relevant competitive stables and trainers.

We will consider additional animal formulations and additional animal product expenditures from time to time as part of portfolio planning and prioritization in the context of the combined company.

There are significant barriers to entry for Mytesi (crofelemer). Through Napo, we hold an extensive global patent portfolio. At the present time we hold 110 issued worldwide patents, with coverage in many cases that extends until 2031. These issued patents cover multiple indications including HIV-AIDS diarrhea, IBS, IBD, manufacturing, enteric protection from gastric juices, among others. We also have 68 pending patent applications worldwide in the human and animal health areas that are being prosecuted.

Mytesi is the first oral drug approved by the FDA under botanical guidance, which provides another barrier to entry from potential generic competition. The FDA requires that the manufacturer of crofelemer use a validated proprietary bioassay to release the drug substance and drug product of Mytesi. While most generic products are fashioned to meet chemical release specifications that are in the public domain, the specifics of this assay are not publicly available. In addition, Mytesi is not systemically absorbed, so the classic approach of creating a generic drug by matching pharmacokinetic blood levels is not possible. A generic player would have to conduct costly and risky clinical trials.

Crofelemer is extracted from the Croton lechleri tree, which we sustainably harvest and manage through programs that we have been developing over the past 28 years. This process has involved working with communities to plant trees, obtaining permits for export, and creating a supply network that is robust and reliable.

We continue to have working relationships with partners that began in the 1990s. Additionally, through the establishment of a nonprofit called the Healing Forest Conservancy (HFC), our team has created a long-term mechanism for benefit sharing that recognizes the intellectual contribution of indigenous populations. This program is intended to contribute to the continued strength and effectiveness of the valued and strategically important relationships we have carefully cultivated over the past 28 years.

We, through Napo, own the intellectual property rights and technology related to our products and product candidates, including rights to a library of over 2,300 medicinal plants, for all veterinary treatment uses and indications for all species of animals. This includes rights to Neonorm, Canalevia,

Table of Contents

and other distinct prescription drug product candidates in our pipeline along with the corresponding existing preclinical and clinical data packages. We also recently expanded this intellectual property portfolio to include combinations of our proprietary anti-secretory product lines, Canalevia and Neonorm, with the non-absorbed antibiotic, rifaximin, for gastrointestinal indications in all animals.

About Mytesi

Mytesi (crofelemer) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy (ART). Mytesi is not indicated for the treatment of infectious diarrhea. Rule out infectious etiologies of diarrhea before starting Mytesi. If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen. In clinical studies, the most common adverse reactions occurring at a rate greater than placebo were upper respiratory tract infection (5.7%), bronchitis (3.9%), cough (3.5%), flatulence (3.1%), and increased bilirubin (3.1%).

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

Description of the Private Placement and Transfer of Shares in Connection with the Merger

On July 31, 2017, we completed the acquisition of Napo Pharmaceuticals, Inc. ("Napo") pursuant to the Agreement and Plan of Merger, dated March 31, 2017, by and among the Company, Napo, Napo Acquisition Corporation ("Merger Sub"), and Napo's representative (the "Merger Agreement"). In accordance with the terms of the Merger Agreement, Merger Sub merged with and into Napo, with Napo surviving as our wholly-owned subsidiary.

In order to induce us to enter into the Merger Agreement, on March 31, 2017, Napo entered into a Settlement and Discounted Payoff Agreement with Nantucket Investments Limited ("Nantucket") and the lenders named therein (the "Settlement Agreement"), pursuant to which, among other things, Napo agreed, simultaneously with the consummation of the merger, (a) to make a cash payment to Nantucket of no less than \$8 million, which reduced the outstanding principal obligations under the Financing Agreement, dated October 10, 2014, by and between Napo and Nantucket (the "Financing Agreement"), and (b) in satisfaction as a compromise for the outstanding obligations under the Financing Agreement and the release of any lien or security interest in respect of such outstanding obligations, (x) to transfer to Nantucket 2,666,666 shares of our common stock (the "Initial Tranche C Shares") owned by Napo and (y) pursuant to the Merger Agreement, to cause us to issue to Nantucket (i) 2,217,579 shares of our common stock (the "Remaining Tranche C Shares" and, together with the Initial Tranche C Shares, the "Tranche C Shares"), (ii) 18,479,826 shares of our non-voting common stock (the "Tranche A Shares") and (iii) 19,700,625 shares of our non-voting common stock (the "Tranche B Shares"), all of which shares are subject to the terms of the Investor Rights Agreement described below.

In connection with the execution of the Merger Agreement and the Settlement Agreement, we and Nantucket entered into an Investor Rights Agreement, dated March 31, 2017 (the "Investor Rights Agreement"), pursuant to which, among other things, we agreed to pay Nantucket's expenses incurred in connection with the transactions contemplated by the Investor Rights Agreement, Settlement Agreement and Merger Agreement, which, pursuant to the Investor Rights Agreement, we have elected to pay by issuing 270,270 additional shares of our non-voting common stock (the "Expense Reimbursement Shares") to Nantucket. We also agreed to register on one or more registration statements the resale of the Tranche C Shares and the shares of common stock issuable upon

Table of Contents

conversion of the Expense Reimbursement Shares, the Tranche A Shares and, to the extent certain conditions are met, the Tranche B Shares.

The Investor Rights Agreement also imposes certain restrictions on the transfer and sale of the shares of common stock and non-voting common stock issued to Nantucket in connection with the Settlement Agreement, including (but not limited to) the following: (a) first, the Tranche B Shares are to be held in escrow and will be released to either Nantucket or the former Napo stockholders, depending on whether the resale of the Tranche A Shares to third parties provides Nantucket with cash returns at or exceeding a specified amount over a specified period of time (the "Hurdle Amounts"); (b) second, we are restricted from paying any dividends on any shares of our capital stock or redeeming any shares, except in limited circumstances, without the prior written consent of Nantucket; (c) third, until the earlier of (i) April 1, 2020 and (ii) the date on which the applicable Hurdle Amount is achieved, in the event that any potential purchaser approaches Nantucket to acquire some or all of the Tranche A Shares, Nantucket agrees to promptly sell some or all of its Tranche A Shares as requested by such party, provided all such sales are above a certain minimum share price for the relevant time period specified in the Investor Rights Agreement; and (d) lastly, if the applicable Hurdle Amount is achieved before all of the Tranche A Shares are sold, Nantucket is required to surrender 50% of the unsold Tranche A Shares, which will be exchanged for shares of common stock and distributed pro rata among holders of certain contingent rights that were issued in connection with the merger and holders of Napo restricted stock units.

For the avoidance of doubt, none of the restrictions on the transfer and sale of shares by Nantucket applies to the Tranche C Shares or the Expense Reimbursement Shares registered hereunder. The Company is restricted from redeeming the Tranche C Shares, as described above.

The description of the Merger Agreement, Settlement Agreement and Investor Rights Agreement are not complete and are qualified in their entirety by reference to the Merger Agreement, Settlement Agreement and Investor Rights Agreement, each of which has been filed as an exhibit 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 were made solely for the benefit of the parties to such agreements, 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 201 Mission Street, Suite 2375, San Francisco, CA 94015 and our telephone number is (415) 371-8300. Our website address is www.jaguaranimalhealth.com. 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."

Jaguar Health, our logo, Canalevia, Neonorm and Myesi 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.

Table of Contents

THE OFFERING

This prospectus relates to the resale of to 5,154,515 shares of our common stock, of which 4,884,245 shares are outstanding shares of common stock held by the selling shareholder and 270,270 shares are shares of common stock issuable upon conversion of the shares of non-voting common stock held by the selling shareholder identified in this prospectus, including its transferees, pledgees, donees or successors. See "Selling Shareholder."

The selling shareholder may offer to sell the shares being offered in this prospectus at fixed prices, at prevailing market prices at the time of sale, at varying prices or at negotiated prices. Our common stock is listed on the NASDAQ Capital Market under the symbol "JAGX."

We have agreed to register the offer and sale of the common stock to satisfy registration rights we have granted to the selling shareholder. We will not receive any proceeds from the sale of the securities by the selling shareholder.

Table of Contents

RISK FACTORS

Please carefully consider the risk factors described 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.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions including those listed in the "Risk Factors" incorporated by reference into this prospectus from our Annual Report on Form 10-K, as updated by subsequent reports. Forward-looking statements are subject to inherent risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Table of Contents

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares of our common stock in this offering. The selling shareholder will receive all of the proceeds from this offering.

The selling shareholder will pay any underwriting discounts and commissions and expenses incurred by the selling shareholder for brokerage, accounting, tax or legal services or any other expenses incurred by the selling shareholder in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, fees and expenses of our counsel, certain expenses of counsel to the selling shareholder and our independent registered public accountants.

Table of Contents

SELLING SHAREHOLDER

The shares of common stock being offered by the selling shareholder are those previously issued to the selling shareholder, and those issuable to the selling shareholder, upon conversion of the non-voting common stock. For additional information regarding the issuances of those shares of common stock and non-voting common stock and the relationship between the selling shareholder and us, see "Prospectus Summary Description of the Private Placement and Transfer of Shares in Connection with the Merger" above. We are registering the shares of common stock in order to permit the selling shareholder to offer the shares for resale from time to time.

The following table sets forth:

the selling shareholder and other information regarding the beneficial ownership of the shares of common stock by the selling shareholder;

the number of shares of common stock beneficially owned by the selling shareholder, based on its ownership of the shares of common stock and non-voting common stock, as of April 23, 2018, assuming the conversion of the non-voting common stock held by the selling shareholder on that date, without regard to any limitations on exercises prior to the sale of the shares covered by this prospectus;

the number of shares that may be offered by the selling shareholder pursuant to this prospectus;

the number of shares to be beneficially owned by the selling shareholder and its affiliates following the sale of any shares covered by this prospectus; and

the percentage of our issued and outstanding common stock to be beneficially owned by the selling shareholder and its affiliates following the sale of all shares covered by this prospectus.

In accordance with the terms of the Investor Rights Agreement, this prospectus generally covers the resale of all shares received by the selling shareholder in connection with the transactions contemplated by the Investor Rights Agreement and the Settlement Agreement, including any shares of common stock issued or issuable upon the conversion of any shares of non-voting common stock received by the selling shareholder, but excluding the Tranche B Shares currently held in escrow in accordance with the terms of the Investor Rights Agreement and the Tranche A Shares.

The selling shareholder may sell all, some or none of their shares in this offering. See "Plan of Distribution."

Name of Selling Shareholder	Number of shares of Common Stock Owned Prior to Offering(1)	Maximum Number of shares of Common Stock to be Sold Pursuant to this Prospectus(2)	Number of shares of Common Stock Owned After Offering(3)	
			Number	Percent
Nantucket Investments Limited(4)	23,634,341	5,154,515	18,479,826	12.2

(1) Excludes 19,700,625 Tranche B Shares issued in the name of the selling shareholder that are currently held in escrow pursuant to the terms of the Investor Rights Agreement.

(2) Assumes the conversion of all shares of non-voting common stock held by the selling shareholder into shares of common stock. Excludes (x) 18,479,826 Tranche A Shares issued in the name of the selling shareholder that are currently subject to certain restrictions on transfer and sale under the Investor Rights Agreement and (y) 19,700,625 Tranche B Shares issued in the name of the

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selling shareholder that are currently held in escrow pursuant to the terms of the Investor Rights Agreement.

Table of Contents

- (3) Assumes that the selling shareholder sells all shares of common stock registered under this prospectus held by such selling shareholder.
- (4) The securities listed herein are held by Nantucket. Burford Capital LLC, a Delaware limited liability company, is the investment adviser to Nantucket. Burford Capital Holdings (UK) Limited, a company organized under the laws of the United Kingdom, is the sole owner of Burford Capital LLC and is majority owned by Burford Capital Limited, a company organized under the laws of Guernsey and publicly traded on the London Stock Exchange. Each of Nantucket, Burford Capital Holdings (UK) Limited and Burford Capital Limited disclaim beneficial ownership of the securities listed herein.

Table of Contents

PLAN OF DISTRIBUTION

The selling shareholder of the securities and any of its pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their securities covered hereby on the Nasdaq Stock Market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling shareholder may use any one or more of the following methods when selling securities:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the securities 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;

in transactions through broker-dealers that agree with the selling shareholder to sell a specified number of such securities at a stipulated price per security;

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 shareholder may also sell securities under Rule 144 under the Securities Act of 1933, as amended (the "Securities Act"), if available, or pursuant to other available exemptions rather than under this prospectus.

Broker-dealers engaged by the selling shareholder may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling shareholder (or, if any broker-dealer acts as agent for the purchaser of securities, 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 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

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

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The selling shareholder and any broker-dealers or agents that are involved in selling the securities 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 securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling shareholder has informed the Company that it does not have any

Table of Contents

written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

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

We agreed to keep this prospectus effective until the earlier of (i) the date on which all registrable securities covered by this prospectus have been sold hereunder in accordance with the plan and method of distribution disclosed herein or otherwise cease to be registrable securities under the Investor Rights Agreement, and (ii) the date on which either (x) the selling shareholder and its affiliates cease to hold any registrable securities or (y) we consummate a merger, consolidation or other business combination of the Company with any entity in which the stockholders of the Company immediately prior to such transaction in the aggregate cease to own at least 50% of the voting power of the voting securities of the entity surviving or resulting from such transaction (or the ultimate parent thereof) or a sale of all or substantially all of our assets. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities 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 resale securities 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 shareholder 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 the common stock by the selling shareholder or any other person. We will make copies of this prospectus available to the selling shareholder 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).

Table of Contents

LEGAL MATTERS

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

EXPERTS

The financial statements of the Company as of December 31, 2017 and 2016 and for each of the two years in the period ended December 31, 2017 incorporated by reference in this prospectus and the registration statement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm (the reports on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

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

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

We also maintain a website at www.jaguaranimalhealth.com, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus.

Table of Contents

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, 2017 filed on April 9, 2018;

our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders to be held on May 18, 2018, filed on April 24, 2018;

our Current Reports on Form 8-K filed on January 2, 2018, February 16, 2018, February 28, 2018, March 2, 2018, March 12, 2018, March 27, 2018, April 2, 2018 and April 18, 2018;

the description of our common stock contained in our registration statement on Form 8-A filed on October 30, 2014 (Registration No. 001-36714) with the SEC, including any amendment or report filed for the purpose of updating such description; and

all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

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

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

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

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

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

Table of Contents

5,154,515 Shares of Common Stock

PROSPECTUS

April 27, 2018
