Jaguar Animal Health, Inc. Form S-1 January 07, 2016

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As filed with the Securities and Exchange Commission on January 7, 2016.

Registration No. 333-

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

JAGUAR ANIMAL HEALTH, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

2834

(Primary Standard Industrial Classification Code Number) 201 Mission Street, Suite 2375 San Francisco, California 94105 (415) 371-8300 46-2956775

(I.R.S. Employer Identification Number)

(Address, including zip code, and telephone number, including area code, of registrant's principal executive office)

Lisa A. Conte Chief Executive Officer and President Jaguar Animal Health, Inc. 201 Mission Street, Suite 2375 San Francisco, California 94105 (415) 371-8300

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement is declared effective.

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 check the following box: o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please 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 post-effective amendment filed pursuant to Rule 462(d) 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.

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

Large accelerated filer o Accelerated filer o Non-accelerated filer o Smaller reporting company ý

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common Stock, par value \$0.0001 per share(2)	\$12,650,000	\$1,273.86

- (1) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(o) of the Securities Act of 1933, as amended.
- (2) Includes shares of common stock the underwriters have the option to purchase to cover over-allotments, if any.

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, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary 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 preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS SUBJECT TO COMPLETION DATED JANUARY 7, 2016

Shares Common Stock

(1)

This is a firm commitment public offering of shares of our common stock by Jaguar Animal Health, Inc. Our common stock is listed on The NASDAQ Capital Market under the symbol "JAGX." On January 6, 2016, the last reported sale price of our common stock was \$2.45 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Our business and an investment in our securities involve a high degree of risk. See "Risk Factors" beginning on page 14 of this prospectus for a discussion of information that you should consider before investing in our securities.

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.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

See "Underwriting" beginning on page 138 of this prospectus for a description of compensation payable to the underwriters.

We have granted a 45-day option to the underwriters to purchase up to additional shares of common stock solely to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment therefor on or about , 2016.

Aegis Capital Corp

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under the circumstances and in the jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date. We are not, and the underwriters are not, making an offer of these securities in any jurisdiction where such offer is not permitted.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of securities and the distribution of this prospectus outside the United States.

Jaguar Animal Health, our logo, Canalevia 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.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the section in this prospectus titled "Risk Factors" and our financial statements and related notes appearing elsewhere in this prospectus, before making an investment decision.

As used in this prospectus, references to "Jaguar," "we," "us" or "our" refer to Jaguar Animal Health, Inc.

Overview

We are an animal health company focused on developing and commercializing first-in-class gastrointestinal products for companion and production animals, and high value horses. Canalevia is our lead prescription drug product candidate for the treatment of various forms of diarrhea in dogs. We achieved statistically significant results in a canine proof-of-concept study completed in February 2015, suggesting that Canalevia treatment is superior to placebo, with 91% of the Canalevia-treated dogs achieving a formed stool during the study versus 50% of the placebo-treated dogs. In December 2015 we initiated a pivotal trial to evaluate the safety and effectiveness of Canalevia for the treatment of acute diarrhea in dogs. Additionally, we are seeking a first to market introduction of Canalevia with a conditional approval for the indication of chemotherapy induced diarrhea, or CID. In June 2015 we completed a multi-site pilot safety study involving the anticipated commercial formulation of Canalevia for CID, and in August 2015 we completed submission of all required major technical sections for a conditional approval new animal drug application, or CNADA, for CID to the Food and Drug Administration, or FDA, for a phased review. Canalevia is a canine-specific formulation of crofelemer, an active pharmaceutical ingredient isolated and purified from the Croton lechleri tree. A human-specific formulation of crofelemer, Fulyzaq, was approved by the FDA in 2012 for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. Members of our management team developed crofelemer while at Napo Pharmaceuticals, Inc., or Napo. Neonorm is our lead non-prescription product to support gut health thereby normalizing fecal formation in animals suffering from watery diarrhea, or scours. We launched Neonorm in the United States at the end of 2014 for preweaned dairy calves under the brand name Neonorm Calf, and in 2015 we launched Neonorm in the United States for foals under the brand name Neonorm Foal. We expect to launch additional formulations of Neonorm in the coming years. Through December 31, 2015, we have shipped approximately \$611,000 of Neonorm Calf to distributors. Neonorm is a standardized botanical extract also derived from the Croton lechleri tree. Canalevia and Neonorm are distinct products that are formulated to address specific species and market channels. We have submitted nine active investigational new animal drug applications, or INADs, to the FDA and intend to develop species-specific formulations of Neonorm in six additional target species.

Diarrhea is one of the most common reasons for veterinary office visits for dogs and is the second most common reason for visits to the veterinary emergency room, yet there are no FDA-approved anti-secretory products for the treatment of diarrhea in animals. We estimate that in the United States, veterinarians see approximately six million annual cases of acute and chronic watery diarrhea in dogs, approximately two-thirds of which are acute diarrhea. We believe that Canalevia will be effective in treating acute diarrhea because it acts at the last physiological step, conserved across mammalian species, in the manifestation of acute diarrhea, regardless of cause, by normalizing ion and water flow in the intestinal lumen. We are first seeking a minor use, minor species, or MUMS, designation with the FDA for Canalevia for CID in dogs which will shorten the time frame to commercialization if we are granted MUMS designation. If we receive conditional approval pursuant to MUMS designation, we expect to commercialize Canalevia for CID in dogs in the second half of 2016. We completed a canine proof-of-concept study in February 2015, with statistically significant results, in support of protocol

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concurrence discussions with the FDA regarding expansion of labeled indications of watery diarrhea beyond CID, to include acute diarrhea as a secondary indication. We plan to market Canalevia, if approved, through our focused direct sales force and to complement our relationships with distribution partners.

According to the Dairy 2007 study conducted by the United States Department of Agriculture, or USDA, almost one in four preweaned dairy heifer, or female, calves suffers from diarrhea or other digestive problems. The preweaning period is generally the first 60 days after birth. Scours, diarrhea or other digestive problems are responsible for more than half of all preweaned heifer calf deaths, and result in impaired weight gain and long-term reduction in milk production. We believe that the incidence rate of scours and its corresponding financial impact represent a health and business opportunity and that Neonorm has the potential to effectively meet this need. A challenge clinical study was completed in May 2014 by researchers from Cornell University College of Veterinary Medicine, or Cornell, and published in 2015 in the official journal of the American Dairy Science Association, *Journal of Dairy Science*. The results of this 2013 study suggest that Neonorm Calf can significantly increase the fecal dry matter of neonatal calves with experimentally-induced enterotoxigenic *E. coli* diarrhea, and suggest a potential benefit of Neonorm Calf in supporting weight gain in calves. The results of our field study in Wisconsin completed in 2015 further support the benefits of Neonorm Calf in reducing water loss associated with diarrhea and enabling weight gain in preweaned dairy calves.

A further analysis of the Cornell study completed in October 2015 supports the benefit of Neonorm Calf on the optimization of the intestinal microbiome profile in preweaned dairy calves, a potential prebiotic benefit. The microbiome is a community of microorganisms that live normally in the gut and are vital to maintenance of gut health. We recently initiated a placebo-controlled study in conjunction with researchers from Cornell to evaluate the efficacy of the prophylactic use of a second-generation formulation of Neonorm Calf administered in liquid on naturally occurring diarrhea in preweaned dairy calves and investigate the possible prebiotic benefit of the product. This double-blinded, randomized study will involve 40 Holstein bull calves affected with naturally occurring diarrhea. The study will compare prophylactic use against a placebo (water), and either the placebo or the Neonorm will be administered twice daily. Data regarding fecal dry matter will be used to measure water loss due to secretory diarrhea. Body weight measurements will be performed daily to determine average daily weight gain during the 25-day study. Blood and fecal samples will also be collected, along with data related to bacterial genus prevalence.

This study will elucidate the mechanism by which the prophylactic use of the second-generation formulation of Neonorm Calf may support the gut health of preweaned calves herd-wide during the onset of naturally occurring diarrhea. Additionally, characterization of the fecal microbiome throughout the preweaning period will allow us to demonstrate that, under natural conditions, the product may positively alter the intestinal microbiome to the benefit of the host. We expect results from this study to be available in 2016.

We launched Neonorm for preweaned dairy calves in the United States under the brand name Neonorm Calf in 2014. Our commercialization activities are focused on large commercial dairy operations and include active ongoing education and outreach to dairy industry key opinion leaders, such as academics involved in dairy cattle research or who advise the dairy cattle industry, as well as veterinarians. We intend to augment these commercialization efforts by working with regional distributors to leverage the geographic concentration of the dairy market in the United States as well as national distributors to provide wider geographic access to our products. In February 2015 we signed a distribution agreement with Biogenesis Bagó, a veterinary biotechnology company in Latin America, a region that contains approximately 401 million dairy and beef cattle and produces approximately 11% of the world's milk supply. The distribution agreement provides Biogenesis Bagó with exclusive distribution rights for Neonorm Calf in Argentina, Brazil, Paraguay, Uruguay, and Bolivia. In addition, where appropriate, we intend to explore other international and distribution partnership arrangements.

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In August 2014, we entered into our first regional distribution agreement with Animart, Inc. for the Upper Midwest region and, together with this partner, launched Neonorm Calf at the 2014 World Dairy Expo, and in September 2014, entered into an agreement with Vedco, Inc., a national master distributor, who also distributes prescription products for the companion animal market.

In December 2015 we announced positive results for an exploratory, investigator-initiated follow-up study which assessed the safety and performance of Neonorm Foal, without inclusion of a probiotic, in preweaned foals with watery diarrhea. In November 2015 we completed an initial proof-of-concept study (NEO101) of Neonorm Foal that involved 60 foals. The objective of this earlier, randomized, multi-site, blinded, placebo-controlled study was to evaluate the safety and performance of the product for use in foals suffering from secretory diarrhea, wherein animals received Neonorm Foal in combination with a third-party probiotic. The results of a meta-analysis between the two studies demonstrated a significantly higher percentage of foals with clinical response and resolution of diarrhea for Neonorm Foal, from either ARG102 or NEO101, compared with the placebo group in NEO101.

During the 72-hour administration period, 35% of foals receiving the placebo in NEO101 were identified as clinical responders, compared with 85% of foals treated with Neonorm Foal in ARG102. For the purposes of both studies, clinical responders were defined as foals that achieved a formed stool by the end of the reported period.

During the 72-hour administration period, resolution of diarrhea was observed in 41% of foals receiving a placebo in NEO101 compared with 85% of foals receiving Neonorm Foal in ARG102. For the purposes of both studies, resolution of diarrhea was defined as a foal that produced a formed stool at any point during the reported period.

In December 2015 we conducted a soft launch of Neonorm Foal at the American Association of Equine Practitioners Annual Convention in Las Vegas. The convention was attended by more than 7,394 veterinary professionals, students, exhibitors and other industry professionals. There was a positive interest in the product from the many attending equine veterinarians who visited our booth at this event, and we received approximately 130 requests for free samples of Neonorm Foal.

We expect the ongoing launch of Neonorm Calf and Neonorm Foal to drive awareness among veterinarians regarding the utility of our first-in-class anti-secretory *Croton lechleri* -derived products, including our prescription product, Canalevia.

We have an exclusive worldwide license to Napo's intellectual property rights and technology related to our products and product candidates, including rights to its library of over 2,300 medicinal plants, for all veterinary treatment uses and indications for all species of animals. This license includes rights to Neonorm, Canalevia, and other distinct prescription drug product candidates in our pipeline along with the corresponding existing preclinical and clinical data packages. We also recently expanded our 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.

Our management team has significant experience in gastrointestinal and animal health product development. This experience includes the development of crofelemer for human use, from discovery and preclinical and clinical toxicity studies, including the existing animal studies to be used for Canalevia regulatory approvals, through human clinical development. Our team also includes individuals who have prior animal health experience at major pharmaceutical companies including SmithKline Beecham Corporation, now GlaxoSmithKline LLC, Zoetis Inc., Vétoquinol S.A., Merial Inc., the animal health division of Sanofi S.A., Morris Animal Foundation, Virbac Animal Health and Merck Animal Health, as well as management experience at major veterinary hospital institutions and experience at the FDA's Center for Veterinary Medicine.

Product Pipeline

We are developing a pipeline of prescription drug product candidates and non-prescription (non-drug) products to address unmet needs in animal health. Our pipeline currently includes prescription drug product candidates for eight indications across multiple species, and non-prescription products targeting seven species.

Prescription Drug Product Candidates

Product Candidates Canalevia	Species Dogs	Indication CID	Recent Developments	Anticipated Near-Term Milestones
			Completed safety study with commercial formulation in June 2015	Possible conditional approval in second half of 2016
Species-specific formulations of crofelemer	Dogs	Acute diarrhea	Submitted all required major technical sections of a new animal drug application, or NADA, in August 2015	
			Product development meeting with FDA in 2015	Complete clinical development program fourth quarter of 2016
	Horses	Acute colitis	Initiated pivotal trial to evaluate safety and effectiveness in December 2015	Initiate NADA in 2016
			Completed pilot safety study in December 2015	Product development meeting with FDA first half of 2016
				Possible MUMS designation in fourth quarter of 2016
	Horses	Colonic and gastric ulcers		Commence clinical development program under CVM concurred protocols first half of 2016
			INAD opened in October 2015	Proof-of-concept safety and effectiveness results in first quarter of 2016
			Initiated proof-of-concept safety and effectiveness study in November 2015	Product development meeting with FDA in first half of 2016

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	Cats	Acute diarrhea	Completed enrollment in proof-of-concept safety and effectiveness study in December 2015	Commence clinical development program under CVM concurred protocols second half of 2016
	Cuis	Tioute diamine		
W. I.a. i. D.	G.		INAD opened in 2014	Safety and proof-of-concept results first half of 2016
Virend (topical)	Cats	Herpes virus		
	5		INAD opened in 2014	Safety and proof-of-concept results in 2016
Species-specific formulations of	Dogs	Obesity-related		
NP-500		metabolic dysfunction		
	**	36 . 1 . 1!	INAD opened in 2014	
	Horses	Metabolic syndrome		
	Cats	Type II diabetes	INAD opened in 2014	
			INAD opened in 2014 4	

Non-Prescription Products

Products Neonorm Calf	Species Dairy calves	Use Supports gut health and normalizing fecal formation in preweaned dairy calves with scours	Recent Developments	Anticipated Near-Term Milestones
			Initiated study in December, 2015 to investigate possible prophylactic and prebiotic benefits	Launch second generation formulation for administration in liquid
			South American distribution agreement signed in first quarter of 2015	Commercial launch in South America
			Approximately \$611,000 of product shipped to distributors since commercial launch	
			Analysis completed in October 2015 supports prebiotic effect	
Species-specific formulations of Neonorm	Horse foals Other farm/production animals	Supports gut health normalizing fecal formation Supports gut health normalizing fecal formation	Field study completed in September 2015 supports beneficial effect of on prewean weight gain	
			Completed proof-of-concept study in November 2015	Commercial launch in first quarter of 2016
			Soft-launched product in December 2015	
			Conducted market research in 2015 which was initiated in New Zealand and China in 2014 for global market opportunities	Initiate proof-of-concept studies and partnering discussions based on market research within the next 12 months

Canalevia is our lead prescription drug product candidate for CID and general watery diarrhea in dogs. Neonorm Calf and Neonorm Foal are our lead non-prescription products to improve gut health and normalize stool formation for preweaned dairy calves with scours, and to promote normal fecal formation and reduce fluid loss in foals, respectively. Both Canalevia and Neonorm are derived from the *Croton lechleri* tree and act at the same last step in a physiological pathway generally present in mammals. However, they are distinct products based on species-specific formulations of such derivatives and have distinct chemical compositions as well as different levels of purification. Canalevia is a canine-specific formulation of crofelemer, an active pharmaceutical ingredient that is an isolated and purified compound. Neonorm is a formulation of a standardized botanical extract that is less refined than crofelemer and includes other constituents.

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We are developing Canalevia as a prescription drug product and Neonorm as a non-prescription product due to differences between the companion and production animal markets. Companion animal owners generally visit veterinarians, who prescribe a product to treat a disease or condition. We believe the ability to make a disease treatment claim is important in this market, and such a claim is only possible with FDA approval as a prescription product. In contrast, dairy farmers and other production animal owners generally make purchasing decisions based on a product's ability to demonstrate an economic benefit from health endpoints, such as weight gain.

We are initially pursuing conditional FDA approval for Canalevia for CID in dogs pursuant to MUMS designation, and are conducting studies to broaden the Canalevia label to include acute diarrhea in dogs as a secondary indication. A MUMS designation is a status similar to the orphan drug designation in humans. In the case of major animal species such as dogs, cats and high value horses, MUMS designations are typically limited to drugs that are used to treat a small number of animals each year. For dogs and cats that number is no more than 70,000 and 120,000 animals, respectively. MUMS designation can potentially expedite the process of product approval and therefore availability to the patient. A sponsor of a MUMS drug can apply for conditional approval, which allows the sponsor to make the drug commercially available before collecting all necessary effectiveness data, but after proving the drug is safe and showing that there is a reasonable expectation of effectiveness.

We also plan to expand our gastrointestinal product line to other animals by developing species-specific formulations including formulations of Neonorm for sheep and other farm animals. We are seeking protocol concurrences from the FDA where appropriate. For example, we are planning a trial to develop a formulation of crofelemer for acute diarrhea in cats, and in December 2015 we completed a pilot safety study to evaluate the safety of crofelemer in adult high value horses, the first step in a planned development program for acute colitis.

A protocol concurrence in animal drug development means that the FDA agrees that the design and analyses proposed in a protocol are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied and will not change its view of these matters, unless public or animal health concerns arise that were not recognized at the time of concurrence or we change the protocol. We plan to seek concurrence on all major regulatory trials.

We have licensed intellectual property from Napo to develop prescription drug product candidates for diabetes and metabolic syndrome for dogs, cats and high value horses, as well as a topical herpes product for cats. Similar to our lead prescription drug product candidate, these products were tested in animals for safety to support their development for use in humans. We recently expanded our gastrointestinal product line to include combinations of our proprietary anti-secretory products derived from *Croton lechleri* with the non-absorbed antibiotic, rifaximin, a human approved product, for gastrointestinal indications in all animals. We are leveraging the data and knowledge gained during the development of human therapeutics into veterinary applications.

Novel Mechanism of Action

Our anti-secretory gastrointestinal products and product candidates act by normalizing the flow of ions and water in the intestinal lumen, the dysregulation of which is the last step common to the manifestation of watery diarrhea. As a result, we believe that our products and product candidates may be effective in addressing watery diarrhea, regardless of cause. In addition, the channels that regulate this ion and water flow, including channels known as CFTR and CaCC (the sites of action of our gastrointestinal products), are generally present in mammals. We therefore expect that the clinical benefit shown in humans, preweaned dairy calves, foals and dogs will be confirmed in multiple other species, including cats and adult horses. Accordingly, we believe we can bring to market multiple products for a range of species that are first-in-class and effective in preventing the debilitating and devastating ramifications of watery diarrhea in companion and production animals. The following

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diagram illustrates the mechanism of action of our gastrointestinal products and product candidates, which normalize chloride and water flow and transit time of fluids within the intestinal lumen.

We have recently supplemented our anti-secretory product line by filing intellectual property for combinations with rifaximin, a non-absorbed antibiotic. Rifaximin is approved for human use for the treatment of traveler's diarrhea and for reduction of the risk of recurrence of hepatic encephalopathy. It is now approved for oral administration in veterinary health, and provides another opportunity for local drug administration (*i.e.*, non-systemic) in the gut of the animal to target bacterial causes of watery diarrhea coincident with an anti-secretory approach to normalization of ion and water flow associated with watery diarrhea.

Business Strategy

Our goal is to become a leading animal health company with first-in-class products that address unmet medical needs in both the companion and production animal markets. To accomplish this goal, we plan to:

Leverage our significant gastrointestinal knowledge, experience and intellectual property portfolio to develop a line of Croton lechleri-derived products for both production and companion animals. In addition to Canalevia for dogs and Neonorm for preweaned dairy calves, we are developing formulations of these products across multiple animal species and market channels.

Establish commercial capabilities, including third-party sales and distribution networks and our own targeted commercial efforts, through the launch of Neonorm. We recently launched Neonorm in the United States under the brand name Neonorm Calf. We intend to establish a focused direct sales force for both the companion and production animal markets, as well as continue to partner with leading distributors to commercialize our products.

Launch Canalevia and our other product candidates for companion animals, if approved, leveraging the commercial capabilities and brand awareness we are currently building. We believe the ongoing Neonorm launch will allow us to establish sales and marketing capabilities in advance of the planned launch of Canalevia for both CID (early 2016) and general watery diarrhea (2016) in dogs, to build corporate brand identity awareness, and to establish distributor relationships relevant to both our non-prescription and prescription drug product lines.

Expand to international markets. We intend to leverage our proprietary product development in the United States to international markets, with meaningful partnerships to address international requirements for product development, registration, and access to commercialization in relevant markets for each of our prescription and non-prescription products. We may also enter into

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partnerships that include payment of upfront licensing fees for our products and product candidates for markets outside the United States where appropriate.

Identify market needs that can be readily accessed and develop species-specific products by leveraging our broad intellectual property portfolio, deep pipeline and extensive botanical library. In addition to our gastrointestinal pipeline product candidates, both *Croton lechleri* and rifaximin-based, we are also developing products such as Virend for feline herpes and NP-500 for Type II diabetes and metabolic syndrome, both of which have been through Phase 2 human clinical testing. We have exclusive worldwide rights to a library of over 2,300 medicinal plants for all veterinary treatment uses and indications for all species of animals.

Risks Related to Our Business

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

We have a limited operating history, have not yet generated any material revenues, expect to continue to incur significant research and development and other expenses, and may never become profitable. Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

We have never generated any material revenue from operations and may need to raise additional capital to achieve our goals.

We are substantially dependent on the success of our current lead prescription drug product candidate, Canalevia, and non-prescription product, Neonorm, and cannot be certain that necessary approvals will be received for Canalevia or that these products will be successfully commercialized, either by us or any of our partners.

We are dependent upon our license agreement with Napo, and if this agreement is terminated, we will be unable to commercialize our products and our business will be harmed.

The results of earlier studies may not be predictive of the results of our pivotal trials or other future studies, and we may be unable to obtain any necessary regulatory approvals for our existing or future prescription drug product candidates under applicable regulatory requirements.

Development of prescription drug products, and to a lesser extent, non-prescription products, for the animal health market is inherently expensive, time-consuming and uncertain, and any delay or discontinuance of our current or future pivotal trials, or dosage or formulation studies, would harm our business and prospects.

Even if we obtain any required regulatory approvals for our current or future prescription drug product candidates, they may never achieve market acceptance or commercial success.

We are dependent upon contract manufacturers for supplies of our current prescription drug product candidates and non-prescription products and intend to rely on contract manufacturers for commercial quantities of any of our commercialized products.

If we are not successful in identifying, developing and commercializing additional prescription drug product candidates and non-prescription products, our ability to expand our business and achieve our strategic objectives would be impaired.

Corporate Information

We were founded in San Francisco, California as a Delaware corporation on June 6, 2013. Napo formed our company to develop and commercialize animal health products. Effective as of December 31, 2013, we were a wholly-owned subsidiary of Napo, and until May 13, 2015, we were a majority-owned subsidiary of Napo. See "Certain Relationships and Related Person Transactions Transactions with Napo" and "Napo Arrangements" for information regarding our transactions with Napo.

Our executive offices are located at 201 Mission Street, Suite 2375, San Francisco, California 94105, 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, and is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from specified disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;

not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

reduced disclosure obligations regarding executive compensation; and

exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We can take advantage of these provisions until December 31, 2020 (the fiscal year-end following the fifth anniversary of the closing of our initial public offering, which occurred on May 18, 2015) or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we were to generate more than \$1.0 billion in annual revenues, have more than \$700.0 million in market value of our capital stock held by non-affiliates or issue more than \$1.0 billion of non-convertible debt over a three-year period. As an emerging growth company, we may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

The Offering

Common stock offered by us shares (or shares if the underwriters exercise their option to purchase additional

shares in full) Common stock to be outstanding after this shares if the underwriters exercise their option to purchase additional shares (or shares in full)

Option to purchase additional shares We have granted the underwriters a 45-day option to purchase up to additional shares of

our common stock to cover over-allotments, if any. The net proceeds from this offering after deducting estimated underwriting discounts and

commissions and offering expenses payable by us will be approximately \$ \$ million if the underwriters exercise in full their option to purchase additional shares of common stock from us), assuming an offering price per share of \$, the last reported sale price of our common stock on The NASDAQ Capital Market on January , 2016. We intend to use the net proceeds from this offering for development work for Canalevia and our other prescription drug products, for commercial activities related to Neonorm, for formulation costs and establishing contract manufacturing capabilities, and for other research and product development activities, working capital and general corporate purposes. See "Use of Proceeds" for a more detailed description of the intended use of proceeds from this offering. See "Risk Factors" and other information included in this prospectus for a discussion of factors

that you should consider carefully before deciding to invest in our common stock.

"JAGX"

offering

Use of proceeds

Risk factors

NASDAO Capital Market symbol

The number of shares of common stock to be outstanding after this offering is based on 8,124,923 shares of common stock outstanding as of December 31, 2015, and excludes as of such date:

> 143,000 shares of common stock issuable upon exercise of outstanding warrants issued as of December 31, 2015 at an exercise price of \$8.75 per share;

207,664 shares of common stock issuable upon exercise of outstanding warrants as of December 31, 2015 with an exercise price of \$2.5281 per share;

16,666 shares of common stock issuable upon exercise of an outstanding warrant as of December 31, 2015 with an exercise price of \$6.30 per share;

269,938 shares of our common stock issuable upon exercise of outstanding warrants as of December 31, 2015 with an exercise price of \$5.60 per share;

111,605 shares of common stock issuable upon exercise of outstanding warrants issued after December 31, 2015 with an exercise price of \$5.60 per share;

919,506 shares issuable upon exercise of outstanding options as of December 31, 2015 with a weighted-average exercise price of \$3.87 per share;

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55,536 shares issuable upon vesting of outstanding restricted stock unit awards, or RSUs, as of December 31, 2015;

up to 26,785 shares of common stock issuable upon conversion of outstanding convertible promissory notes in the aggregate principal amount of \$150,000 issued as of December 31, 2015; and

106,833 shares of common stock reserved for future issuance under our 2014 Stock Incentive Plan as of December 31, 2015.

Unless otherwise indicated, the information in this prospectus assumes the following:

no exercise of outstanding options or warrants, or issuance of shares upon the vesting of restricted stock units;

a public offering price of \$, which was the last reported sale price of our common stock on The NASDAQ Capital Market on January , 2016; and

no exercise by the underwriters of their option to purchase additional shares of common stock.