Jaguar Animal Health, Inc.
Form 424B3
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Filed Pursuant to Rule 424(b)(3)
Registration No. 333-214956

6,666,672 Shares

Common Stock

This prospectus relates to the sale of up to 6,666,672 shares of our common stock, $0.0001 par value per share, by the selling stockholders identified in this prospectus. Of these shares, 1,666,668 shares are outstanding shares of common stock held by the selling stockholders and 5,000,004 shares are shares of common stock issuable upon the exercise of warrants held by the selling stockholders. The prices at which the selling stockholders may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions. We will not receive proceeds from the sale or other disposition of the shares by the selling stockholders. We will, however, receive the net proceeds from any warrants exercised for cash.

The selling stockholders or their 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 stockholders 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 57 for more information about how the selling stockholders may sell or dispose of their shares of common stock.

Our common stock is listed on the NASDAQ Capital Market under the ticker symbol "JAGX." On December 16, 2016, the last reported sale price per share of our common stock was $0.76 per share.

You should read this prospectus and any prospectus supplement, together with additional information described under the headings "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information," carefully before you invest in any of our securities.

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.

The date of this prospectus is December 19, 2016.

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Neither we nor the selling stockholders 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 selling stockholders 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 selling stockholders has 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.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in or incorporated by reference into 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 incorporated by reference herein, 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, foals, and high value horses. Canalevia is our lead prescription drug product candidate, intended for treatment of various forms of diarrhea in dogs. We achieved statistically significant results in a multicenter canine proof-of-concept study completed in February 2015, supporting the conclusion that Canalevia treatment is superior to placebo. As we announced in December 2015, the pivotal clinical field study to evaluate the safety and effectiveness of Canalevia for acute diarrhea in dogs is underway. An estimated 200 dogs will be enrolled in the Canalevia pivotal study, which is expected to complete enrollment around the end of 2016. Jaguar has received Minor Use in a Minor Species (MUMS) designation for Canalevia for Chemotherapy-Induced Diarrhea (CID) in dogs. Canalevia is a canine-specific formulation of crofelemer, an active pharmaceutical ingredient isolated and purified from the Croton lechleri tree, which is sustainably harvested. A human-specific formulation of crofelemer, Mytesi (formerly known as 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, which was Jaguar's parent company until May 13, 2015. The reception among users of our lead nonprescription products Neonorm Calf and Neonorm Foal, an anti-diarrheal product we launched for newborn horses early this year has been quite positive. The clinically-proven performance of Neonorm Foal, in combination with our heightened understanding of market needs within the global equine space, is driving our increased focus on equine product development. Equilevia (formerly referred to as SB-300) is Jaguar's prescription drug product candidate for treatment of gastrointestinal ulcers in horses. Equilevia is a pharmaceutical formulation of a standardized botanical extract. Neonorm is a standardized botanical extract derived from the Croton lechleri tree. We launched Neonorm Calf in the United States at the end of 2014 for preweaned dairy calves. Canalevia, Equilevia and Neonorm are distinct products formulated to address specific species and market channels. We have filed nine investigational new animal drug applications, or INADs, with the FDA and intend to develop species-specific formulations of Neonorm in six additional target species, and Canalevia for both cats and dogs. We recently released data from two China-based studies sponsored by Fresno, California-based Integrated Animal Nutrition and Health Inc. showing remarkable resolution of diarrhea and cure of piglets afflicted with diarrhea following treatment with a Croton lechleri botanical extract administered in water. As we announced in September 2016, we have signed an exclusive supply and distribution agreement for this botanical extract with Integrated Animal Nutrition and Health Inc. for dairy cattle and pigs in the Chinese marketplace. According to the Minnesota-based Institute for Agriculture and Trade Policy, swine production was expected to reach 723 million head in 2014 in China, where pork is still the main protein source for many consumers. In 2015 there were an estimated 15.6 million dairy cattle in China, according to Index Muni.

Since inception, we have been primarily focused on designing and conducting studies of Canalevia to treat diarrhea in dogs and of Neonorm to help retain fluid in calves and to function as an anti-diarrheal in foals. We are also focused on developing a full suite of equine products to support and

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improve gastrointestinal health in foals and adult horses. Gastrointestinal conditions such as acute diarrhea, ulcers and diarrhea associated with acute colitis can be extremely debilitating for horses, and present a significant economic and emotional burden for veterinarians and owners around the world. A portion of our activities has also been focused on other efforts associated with being a recently formed company, including securing necessary intellectual property, recruiting management and key employees, and financing activities.

In January 2016 we announced positive topline results from the proof-of-concept study we initiated in November 2015 to evaluate the safety and effectiveness of Equilevia, our investigational new animal drug for treatment of gastrointestinal ulcers in horses. In April 2016, we announced that standard drug testing in race horses having received Equilevia did not detect any substances commonly disallowed by horse racing authorities. The results of this initial study show that Equilevia may offer horse owners an additional advantage in the competition horse world, where requirements exist for animals to compete free from the effect of any drugs. Future work is being planned to confirm these results. The study also provided visual evidence suggesting that feed does not interfere with the product candidate's local availability in the gut. In November 2016 we completed a dose determination study of the target commercial paste formulation of Equilevia, with both a placebo control arm and a positive control comparator, Merial's GASTROGARD® product. The randomized, blinded, controlled, multisite dose determination study enrolled 121 racehorses two years of age or older. All enrolled horses were diagnosed with glandular and squamous gastric ulcers. The primary objective of the study was to select the minimally effective dose of Equilevia for the treatment of equine gastric ulcers in a future pivotal field study.

Horses on treatment with Equilevia in the dose determination study had higher average winnings as a percent of purse in races during the study treatment period compared with the period in which they raced prior to the study. Horses on placebo or on the positive control had a reduction in their average winnings as a percent of purse during the study treatment period compared with the period in which they raced prior to the study.

Additionally, horses on treatment with Equilevia had higher average total dollar winnings in races during the study period compared with the period in which they raced prior to the study. However, horses on placebo had a reduction in total earnings in races during the study period compared with the period in which they raced prior to the study, whereas horses on GASTROGARD® had essentially no change in their earnings in races compared with the period in which they raced prior to the study.

When analyzing data according to whether or not a horse finished a race in the top 3 or in the top 5, there was also an improvement seen for horses treated with Equilevia during the study treatment period compared with the period in which they raced prior to the study. Horses treated with placebo, however, had a reduction in frequency of finishing in the top 3 or in the top 5 in the study period compared with the period in which they raced prior to the study.

No statistically significant comparisons were generated for the aforementioned exploratory analyses. Racing results in horses treated with Equilevia during our dose determination study are of interest because ulcers are a particular problem in equine athletes. This study was not powered for this type of result nor would we expect to have such a result listed in a product label.

A full analysis of the dose determination study data with scoring of squamous and glandular ulcers is awaiting an independent, blinded review by an equine veterinarian experienced in gastric ulcer disease, and is expected to be available in early January 2017.

Ulcers are lesions of the lining of the digestive tract and are very common in horses used for many competitive activities. We believe that because *Croton lechleri*-derived products have been shown to act locally in the gut and have traditional use and rodent model benefit for ulcers, Equilevia has the potential to address ulcers in horses, as well as diarrhea. We are initially developing this product for

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the indication of equine gastric ulcer syndrome (EGUS), and we plan to potentially investigate the possible efficacy of this product candidate for treatment of colonic ulcers in horses as a potential follow on indication following the anticipated launch of Equilevia. EGUS results from both squamous and glandular gastric ulceration. Ulcers can negatively impact the performance of horses which are expected to perform at peak efficiency, including show horses and race horses. We believe a significant market exists for a product that treats both squamous and glandular ulcers in horses without altering stomach pH. According to a 2005 study, 54% of performance horses have both colonic and gastric ulcers and 97% of performance horses have either a gastric (87%) or a colonic (63%) ulcer. Data from the American Horse Council states that there are currently 9.2 million horses in the U.S., a population that includes 844,531 race horses, more than 2.7 million show horses, and more than 3.9 million recreational horses. Data from the Food and Agriculture Organization of the United Nations indicate that there were approximately 5.7 million horses in Europe in 2013 and nearly 60.0 million horses in 2013 worldwide. Our goal is to see Equilevia serve as an important tool in the standard of care for equine ulcers.

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 to our knowledge there are currently no FDA-approved anti-secretory agents to treat canine diarrhea. We estimate that in the United States, veterinarians see approximately 6.0 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 have received MUMS designation for Canalevia for the treatment of CID in dogs. We plan to market Canalevia in 2017, 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 USDA, almost one in four preweaned dairy heifers, 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 Calf has the potential to effectively meet this need.

A challenge clinical study was completed in May 2014 by researchers from Cornell, and published in 2015 in the official journal of the American Dairy Science Association, *Journal of Dairy Science*. The results of this 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.

A further analysis, completed in October 2015, of the above-referenced Cornell study supports a 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.

In January 2016 we announced the initiation of 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 and dehydration in preweaned dairy calves and investigate the possible prebiotic benefit of the product. This double-blinded, randomized study involves 40 Holstein bull calves affected with naturally occurring diarrhea. The study results, announced in June and September of 2016, show that calves under prophylactic administration of Neonorm Calf had significantly lower water content in fecal samples at multiple measurement points, lower incidence of diarrhea, and had fewer fluid therapy interventions.

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In November 2015 we completed an initial proof-of-concept study (NEO101) of Neonorm Foal that involved 60 foals. The objective of this randomized, multi-site, blinded, placebo-controlled study was to evaluate the safety and performance of the product for treatment of foals suffering from secretory diarrhea, and the treated animals received Neonorm Foal in combination with a third-party probiotic. In December 2015 we announced positive results for an exploratory, investigator-initiated follow-up study (ARG102) which assessed the safety and performance of Neonorm Foal, without inclusion of a probiotic, in preweaned foals with watery diarrhea. 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 placebo-treated foals 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.

The reception among users of Neonorm Foal, the anti-diarrheal for newborn horses that we launched early this year with a nationwide campaign offering samples, has been overwhelmingly positive. User feedback regarding Neonorm Calf also continues to be very favorable. Commercialization of these two non-prescription products has provided numerous benefits that we intend to leverage during our expected introductions of high value, first-in-class prescription drug products into the U.S. marketplace and beyond. The commercialization process has allowed us to extend to animals the clinical utility of the novel mechanism of action of *Croton lechleri*-derived anti-secretory products, refine messaging to veterinarians, fine-tune internal processes, forge commercial manufacturing relationships, and develop commercial infrastructure with important distributors relevant to both prescription and non-prescription products.

The clinically-proven performance of Neonorm Foal, in combination with our heightened understanding of the vast and unmet need for novel and differentiated ulcer treatment within the equine athlete space, is driving our increased focus on equine product and market development. Data from the American Horse Council states that there are an estimated 9.2 million horses in the U.S. alone, a population that includes nearly 845,000 race horses, more than 2.7 million show horses, and more than 3.9 million recreational horses. We expect the ongoing promotion of both Neonorm Foal and Neonorm Calf to drive awareness regarding the utility of our first-in-class anti-secretory *Croton lechleri*-derived products, including our prescription product candidate for acute diarrhea in dogs, Canalevia. The positive reception to Neonorm Foal by early users is helping establish the Jaguar brand among horse owners, horse breeders and equine veterinarians the expected future customers of the equine drug product candidates in our pipeline. As part of our equine franchise, we will continue commercial efforts around Neonorm Foal, and focus on preparations for the expected commercial launch of our Equilevia drug product candidate for EGUS. We believe Equilevia will be an important product introduction, with performance attributes differentiated from proton pump inhibitors such as omeprazole. We are also focusing resources on the expected commercial launch of Canalevia for acute diarrhea in dogs.

Canalevia utilizes the same mechanism of action as Neonorm Foal and Neonorm Calf and of Mytesi (formerly known as Fulyzaq), the human drug approved by the FDA in 2012 for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. Each of these products normalizes ion and water flow into the intestinal lumen. Because this is a

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physiological pathway generally present in mammals, we have validated our low risk strategy of extending the clinical success in humans to preweaned dairy calves, foals, and dogs; and we believe these clinical benefits will continue to be confirmed in other mammalian species.

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 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 Zoetis Inc., Novartis International AG, Merial Inc., the animal health division of Sanofi S.A., Morris Animal Foundation, Virbac Animal Health, Pfizer 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 products to address unmet needs in animal health. Our pipeline currently includes prescription drug product candidates for nine indications across multiple species, and non-prescription products targeting seven species.

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Prescription Drug Product Candidates

Product Candidates	Species	Indication	Recent Developments	Anticipated Near-Term Milestones
Canalevia	Dogs	CID		
			Completed safety study with commercial formulation in June 2015	Initiate pilot study for longer-term management
				Commercial launch in 2017
	Dogs	Acute diarrhea		
			Concurred protocol	Complete clinical development program fourth quarter of 2016
			Initiated pivotal trial to evaluate safety and effectiveness in December 2015	Initiate NADA in 2016
				Commercial launch in 2018
Species-specific formulations of crofelemer	Horses	Diarrhea/associated with acute colitis		
			Completed pilot safety study in December 2015	Product development in 2017
Equilevia	Horses	Ulcers		
			Proof-of-concept safety and effectiveness results in January 2016	Results from dose confirmation study
			Product development meeting with FDA in first half of 2016	Commence pivotal field trial under CVM concurred protocols
			Completed dose confirmation study with positive control	

	Cats	Acute diarrhea		
			INAD opened in 2014	Initiate safety and proof-of-concept in first half of 2017
Virend (topical)	Cats	Herpes virus		
			INAD opened in 2014	Initiate safety and proof of concept in 2017
Species-specific formulations of NP-500	Dogs	Obesity-related metabolic dysfunction	INAD opened in 2014	
	Horses	Metabolic syndrome	INAD opened in 2014	
	Cats	Type II diabetes	INAD opened in 2014	

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Non-Prescription Products

Products	Species	Use	Recent Developments	Anticipated Near-Term Milestones
Neonorm Calf	Dairy calves	Helps proactively retain fluid in calves aiding the animals in avoiding debilitating, dangerous levels of dehydration	Positive prophylactic results	Launch second generation formulation for administration in liquid
			Initiated study in December, 2015 to investigate possible prophylactic and prebiotic benefits	Commercial launch in South America
			Shipped $667,236 of product to distributors since commercial launch	Business development activities
			Analysis completed in October 2015 supports prebiotic effect	
			Field study completed in September 2015 supports beneficial effect on prewean weight gain	
Species-specific formulations of Neonorm	Horse foals	Anti-diarrheal for newborn horses	Completed proof-of-concept study in November 2015	
			Soft-launched product in December 2015 and conducted commercial launch in first quarter of 2016	
			Shipped $40,152 of product to distributors since commercial launch	

Pigs and dairy calves	Helps proactively retain fluid in pigs and calves, aiding the animals in avoiding debilitating, dangerous levels of dehydration	Entered exclusive distribution agreement for pigs and dairy calves in China	
Other farm/production animals	Supports gut health normalizing fecal formation		Initiate proof-of-concept studies and partnering discussions based on market research

Canalevia is our lead prescription drug product candidate, intended for the treatment of various forms of diarrhea in dogs. Equilevia is our prescription drug product candidate for the treatment of gastrointestinal ulcers in horses. Canalevia and Equilevia contain ingredients isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Neonorm Calf and Neonorm Foal are our lead

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non-prescription products. Neonorm is a standardized botanical extract derived from the *Croton lechleri* tree. Canalevia and Neonorm are distinct products that act at the same last step in a physiological pathway generally present in mammals.

We are developing Canalevia as a prescription drug product and Neonorm as a non-prescription product due to differences between the companion, horse and production animal markets. Owners of companion animals and equine athletes 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.

For our prescription product line, we are seeking protocol concurrences with the FDA where appropriate. 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 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.

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, and the markets for foals and high-value horses. 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 production and companion animals, and horses.

Our management team collectively has more than 100 years of experience in the development of gastrointestinal prescription drug and non-prescription products. This experience covers all aspects of product development, including discovery, preclinical and clinical development and regulatory strategy.

In addition to our near-term development efforts advancing Canalevia for dogs, Neonorm Calf for preweaned dairy calves, and Neonorm Foal for young horses, we are developing formulations of Canalevia and Neonorm to address the unmet medical need for the treatment of acute diarrhea and to support fluid retention across multiple animal species and market channels. The development of a full suite of products to support and improve gastrointestinal health in adult horses is one of our core focus areas. Gastrointestinal conditions such as acute diarrhea, ulcers and diarrhea associated with acute colitis can be extremely debilitating for horses, and present a significant economic and emotional burden for veterinarians and horse owners around the world. Our products are designed with a thorough understanding of not only species-specific health issues, but also market practices, the economics of current treatment strategies, competitive dynamics, government initiatives such as concern about extensive antibiotic usage, and effective channels for new product introductions. Many of our products are being formulated into separate and distinct gastrointestinal products accounting for multiple specific species, markets and regulatory dynamics.

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Establish commercial capabilities, including third-party sales and distribution networks and our own targeted commercial efforts, through the launch and ongoing marketing of Neonorm Calf and Neonorm Foal.

In 2014 we launched Neonorm in the United States under the brand name Neonorm Calf. In December 2015 we conducted the soft launch of Neonorm Foal, and we conducted the commercial launch in the first quarter of 2016. We intend to establish a focused direct sales force. We will direct our sales and marketing efforts on educational activities and outreach to key opinion leaders and decision makers at targeted regional and global accounts and also plan to continue to partner with leading distributors to commercialize our products. We expect that our current and future distribution partners will have the presence, name recognition, reputation and reach in the veterinary markets and in both key urban and rural centers, as appropriate. We believe this overall approach is scalable and transferable as we expand our commercialization efforts to companion animals, as well as when we expand internationally.

Launch Canalevia and our other product candidates for companion animals and horses, if approved, leveraging the commercial capabilities and brand awareness we are currently building.

We have nine active INADs filed with the FDA and intend to develop species-specific formulations of Neonorm in six additional target species, formulations of Equilevia in horses, and Canalevia for cats and dogs, and potentially for diarrhea associated with acute colitis in horses.

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. As an example, in February 2015 we signed a distribution agreement with Biogenesis Bagó, a large veterinary biotechnology company in Latin America, a region that contained approximately 401 million dairy and beef cattle in 2009 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.

Additionally, in September 2016, we entered an exclusive supply and distribution agreement for *Croton lechleri* botanical extract with Fresno, California-based Integrated Animal Nutrition and Health Inc. for dairy cattle and pigs in the Chinese marketplace. The agreement was executed following the positive results, which we announced in July 2016, of two studies to evaluate the safety and effectiveness of the botanical extract in piglets. The terms of the agreement specify annual minimum purchase amounts that are required to maintain exclusivity, and state that Integrated Animal Nutrition and Health Inc. is responsible for all activities and costs to obtain all required product registrations, marketing authorizations, and customs clearances for the Chinese market.

According to the Minnesota-based Institute for Agriculture and Trade Policy, swine production was expected to reach 723 million head in 2014 in China, where pork is still the main protein source for many consumers. In 2015 there were an estimated 15.6 million dairy cattle in China, according to Index Muni. China, with the world's largest population, has been experiencing an increase in demand for dairy products as a result of sharply increasing income levels, fast-changing food habits, the desire of parents to feed their babies high-protein formula, and the loosening in 2015 of China's longstanding one-child policy, among other factors.

As we work to expand our commercialization efforts, we intend to seek out additional opportunities to enter key international markets. Certain markets, such as high performance horses, have strong international synergies benefiting market awareness and demand. We may also enter into partnerships that include payment of upfront licensing fees for our products and product candidates for markets outside the United States where appropriate.

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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 anti-secretory gastrointestinal product development efforts, we have expanded the depth of our gastrointestinal pipeline product candidates 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 also plan to develop products such as Virend for feline herpes and NP-500 for Type II diabetes and metabolic syndrome. Both of these product candidates have been through Phase 2 human clinical testing. In addition, we have exclusive worldwide rights to Napo's library of over 2,300 medicinal plants for veterinary use in all species. We believe we have the product candidates and expertise to address many unmet animal health needs for companion and production animals and horses. We believe our extensive library of medicinal plants will enable us to develop first-in-class products that address significant health issues and concerns of many markets and geographies.

Discussions with Napo

We have been engaged in exploratory discussions with Napo since February 2016 regarding a potential merger and/or other ways to cooperate with our respective business endeavors. On October 6, 2016, we announced that we had entered into a non-binding letter of intent, or LOI, with Napo potentially to merge the two companies. The LOI contemplates a 3-to-1 Napo-to-Jaguar value ratio (inclusive only of in-the-money convertible securities of Jaguar at the time a definitive agreement is entered into) to calculate the relative ownership of the merged entity. The LOI also outlines capitalization requirements that Napo would be required to satisfy to proceed with a potential merger.

The LOI is non-binding and any agreement is subject to the negotiation and execution of a definitive transaction agreement, which may vary from the terms set forth in the LOI. A final transaction also is anticipated to be subject to material conditions, including, but not limited to, the approval of: (i) the respective boards of directors of Jaguar and Napo, (ii) the shareholders of each company, (iii) the Nasdaq Stock Market, and (iv) other customary conditions for a transaction of this nature. Accordingly, there can be no assurance that a definitive agreement will be reached by the companies, or that any agreement will result in the completion of a merger transaction.

As of December 1, 2016, Napo owns 19.0% of our outstanding shares. Napo took over ownership of the new drug application, or NDA, and commercial rights for human applications of crofelemer in May 2016 from Valeant Pharmaceuticals International Inc., which acquired those rights from Salix Pharmaceuticals, Inc. in April 2016.

2016 Private Placement of Common Stock and Warrants

On November 22, 2016, we entered into a Securities Purchase Agreement, or the 2016 Purchase Agreement, with certain institutional investors, pursuant to which we sold securities to such investors in a private placement transaction, which we refer to herein as the 2016 Private Placement. In the 2016 Private Placement, we sold an aggregate of 1,666,668 shares of our common stock at a price of $0.60 per share for gross proceeds of approximately $1.0 million. The investors in the 2016 Private Placement also received (i) warrants to purchase up to an aggregate of 1,666,668 shares of our common stock, at an exercise price of $0.75 per share, or the Series A Warrants, (ii) warrants to purchase up to an aggregate 1,666,668 shares of our common stock, at an exercise price of $0.90 per share, or the Series B Warrants, and (iii) warrants to purchase up to an aggregate 1,666,668 shares of our common stock, at an exercise price of $1.00 per share, or the Series C Warrants and, together with the Series A Warrants and the Series B Warrants, the 2016 Warrants.

On November 22, 2016, we also entered into a Registration Rights Agreement with the investors in the 2016 Private Placement, pursuant to which we are required to file a registration statement on

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Form S-1 within 10 business days of November 22, 2016 to cover the resale of the shares of common stock sold to such investors pursuant to the 2016 Purchase Agreement and the shares of common stock underlying the 2016 Warrants. Our failure to satisfy certain deadlines described in the Registration Rights Agreement may subject us to payment of certain monetary penalties. See "2016 Private Placement of Common Stock and Warrants" for a more detailed description of the 2016 Private Placement.

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 candidates, Equilevia and Canalevia, and non-prescription product, Neonorm, and cannot be certain that necessary approvals will be received for Canalevia or Equilevia 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.

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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.

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The Offering

Common stock offered by the selling stockholders	Up to 6,666,672 shares of common stock, consisting of (1) 1,666,668 issued and outstanding shares issued to investors in the 2016 Private Placement and (2) 5,000,004 shares underlying the 2016 Warrants issued to the investors in the 2016 Private Placement.
Common stock outstanding	14,007,132 shares (as of December 1, 2016)
Use of proceeds	The selling stockholders will receive all of the proceeds from the sale of the shares offered for sale by it under this prospectus. We will not receive proceeds from the sale of the shares by the selling stockholders. We may, however, receive the net proceeds of any warrant exercised for cash. If the selling stockholders exercise, on a cash basis, all of the warrants underlying the shares being registered, we would receive gross proceeds of approximately $4.4 million. We intend to use such proceeds, if any, for working capital and general corporate purposes. See "Use of Proceeds" for a more detailed description of the intended use of proceeds from this offering.
NASDAQ Capital Market symbol	"JAGX"
Risk factors	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.

The number of shares of our common stock to be outstanding following this offering is based on an aggregate of 14,007,132 shares outstanding as of December 1, 2016, but excludes:

2,426,596 shares of common stock issuable upon exercise of outstanding options as of December 1, 2016, at a weighted average exercise price of $2.60 per share, of which 939,056 shares are vested as of such date;

184,612 shares of common stock reserved for future issuance under the 2014 Stock Incentive Plan;

5,968,876 shares of common stock issuable upon exercise of warrants outstanding as of December 1, 2016 (including common stock issuable upon exercise of the 2016 Warrants);

20,789 shares issuable upon vesting of outstanding restricted stock unit awards, or RSUs, as of December 1, 2016; and

up to 67,655 shares of common stock issuable upon conversion of outstanding convertible promissory notes in the aggregate principal amount of $150,000 issued as of December 1, 2016.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information contained in or incorporated by reference in this prospectus, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, as updated in our Quarterly Reports on Form 10-Q, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may harm our business, financial condition, results of operations and prospects.

Risks Related to Our Business and Need for Additional Capital

We have a limited operating history, expect to incur further losses as we grow and may be unable to achieve or sustain profitability. Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

Since formation in June 2013, our operations have been primarily limited to the research and development of our lead prescription drug product candidate, Canalevia, to treat various forms of diarrhea in dogs, and our non-prescription product, Neonorm Calf, to help dairies and calf farms proactively retain fluid in calves helping the animals avoid debilitating, dangerous levels of dehydration, and the recent commercial launch of Neonorm Foal. As a result, we have limited meaningful historical operations upon which to evaluate our business and prospects and have not yet demonstrated an ability to broadly commercialize any of our products, obtain any required marketing approval for any of our prescription drug product candidates or successfully overcome the risks and uncertainties frequently encountered by companies in emerging fields such as the animal health industry. We also have not generated any material revenue to date, and expect to continue to incur significant research and development and other expenses. Our net loss and comprehensive loss for the year ended December 31, 2015 was $16,291,550. As of December 31, 2015, we had total stockholders' equity of $4,399,097. We expect to continue to incur losses for the foreseeable future, which will increase significantly from historical levels as we expand our product development activities, seek necessary approvals for our product candidates, conduct species-specific formulation studies for our non-prescription products and begin commercialization activities. Even if we succeed in developing and broadly commercializing one or more of our products or product candidates, we expect to continue to incur losses for the foreseeable future, and we may never become profitable. I