Jaguar Animal Health, Inc.
Form S-1
September 22, 2016

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As filed with the Securities and Exchange Commission on September 22, 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	**2834**	**46-2956775**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

201 Mission Street, Suite 2375
San Francisco, California 94105
(415) 371-8300

(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)

Copies to:

Donald C. Reinke, Esq.
Reed Smith LLP
101 Second Street, Suite 1800
San Francisco, California 94105

(415) 543-8700

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: ý

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. o

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. o

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. o

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 (Do not check if a smaller reporting company)	Smaller reporting company ý

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Amount to be Registered(1)**	**Proposed Maximum Offeirng Price Per Share(2)**	**Proposed Maximum Aggregate Offering Price(1)(2)**	**Amount of Registration Fee(2)**
Common Stock, par value $0.0001 per share	1,500,000	$1.21	$1,815,000.00	$182.77

(1) The registrant is registering for resale, from time to time, up to 1,500,000 additional shares of its common stock, par value $0.0001, that the registrant has issued and may sell to Aspire Capital Fund, LLC, or Aspire Capital, pursuant to a Common Stock Purchase Agreement, dated June 8, 2016, by and between Aspire Capital and the registrant. Pursuant to Rule 416 under the Securities Act, the shares of common stock registered hereby also include an indeterminate number of additional shares of common stock as may from time to time become issuable by reason of stock splits, stock dividends, recapitalizations or other similar transactions.

(2) Pursuant to Rule 457(c), calculated on the basis of the average of the high and low prices per share of the registrant's common stock on the NASDAQ Capital Market on September 20, 2016.

Pursuant to Rule 429 under the Securities Act, the prospectus contained in this Registration Statement is a combined prospectus and also relates to an aggregate of 1,321,111 shares registered and remaining unsold (the "Previously Registered Securities") under the registrant's Registration Statement on Form S-1 (File No. 333-212173), which was initially filed on June 22, 2016 and became effective on July 8, 2016 (the "Prior Registration Statement"). Upon effectiveness, this Registration Statement constitutes a post-effective amendment to the Prior Registration Statement, which post-effective amendment shall hereafter become effective concurrently with the effectiveness of this Registration Statement in accordance with Section 8(c) of the Securities Act. If any Previously Registered Securities under the Prior Registration Statement are offered and sold before the effective date of this Registration Statement, the amount of the Previously Registered Securities so sold will not be included in the prospectus hereunder. The filing fee payable in connection with the Prior Registration Statement was previously paid at the time of its initial filing.

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 this Registration Statement shall become effective on such date as the Commission, acting pursuant to

said Section 8(a), may determine.

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Explanatory Note

The registrant filed a Registration Statement on Form S-1 (File No. 333-212173), which was initially filed on June 22, 2016 and became effective on July 8, 2016 (the "Prior Registration Statement"), in order to register 3,000,000 shares of its common stock, $0.0001 par value per share, that the registrant had issued and may issue to Aspire Capital Fund, LLC, or Aspire Capital, pursuant to a Common Stock Purchase Agreement, dated as of June 8, 2016, by and between the registrant and Aspire Capital, or the Purchase Agreement.

This Registration Statement is being filed by the registrant to register 1,500,000 additional shares of the registrant's common stock that the registrant may issue to Aspire Capital pursuant to the Purchase Agreement, which were not registered pursuant to the Prior Registration Statement.

Pursuant to Rule 429(a) under the Securities Act of 1933, as amended, or the Securities Act, the prospectus included in this Registration Statement is a combined prospectus relating to an aggregate of 2,821,111 shares of the registrant's common stock that the registrant has issued and may issue to Aspire Capital, including 1,500,000 shares of the registrant's common stock being registered hereby and 1,321,111 shares that were registered under the Prior Registration Statement and remain unsold. Pursuant to Rule 429(b) under the Securities Act, upon effectiveness, this Registration Statement also constitutes a post-effective amendment to the Prior Registration Statement, which post-effective amendment shall hereafter become effective concurrently with the effectiveness of this Registration Statement and in accordance with Section 8(c) of the Securities Act. The filing fee payable in connection with the Prior Registration Statement was previously paid at the time of filing of the Prior Registration Statement on June 22, 2016.

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The information in this preliminary prospectus is not complete and may be changed. The selling stockholder 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 SEPTEMBER 22, 2016

2,821,111 Shares

Common Stock

This prospectus relates to the sale of up to 2,821,111 shares of our common stock by Aspire Capital. Aspire Capital is also referred to in this prospectus as the selling stockholder. The prices at which the selling stockholder 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 of the shares by the selling stockholder. However, we have received proceeds of approximately $1.9 million and may receive additional proceeds of up to approximately $13.1 million, for an aggregate of $15.0 million, from the sale of our common stock to the selling stockholder, pursuant to a common stock purchase agreement entered into with the selling stockholder on June 8, 2016, once the registration statement, of which this prospectus is a part, is declared effective.

The selling stockholder is an "underwriter" within the meaning of the Securities Act of 1933, as amended. We will pay the expenses of registering these shares, but all selling and other expenses incurred by the selling stockholder will be paid by the selling stockholder.

Our common stock is listed on the NASDAQ Capital Market under the ticker symbol "JAGX." On September 20, 2016, the last reported sale price per share of our common stock was $1.22 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 .

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Neither we nor the selling stockholder 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 stockholder is 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 stockholder 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 the treatment of various forms of diarrhea in dogs. We completed a canine proof-of-concept study in February 2015, suggesting that Canalevia treatment is superior to placebo. 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 intend to address the important unmet medical need of Chemotherapy Induced Diarrhea (CID) with a pilot program later this year for supportive care management. In June 2015 we completed a multi-site pilot safety study involving the anticipated commercial formulation of Canalevia for CID. We have received MUMS designation for Canalevia for the treatment of CID in dogs and are planning to bring the product to market in 2017. SB-300 is Jaguar's prescription drug product candidate for the treatment of gastrointestinal ulcers in horses, specifically equine athletes. Canalevia and SB-300 contain ingredients isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Neonorm Foal and Neonorm Calf are our lead 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. Jaguar has nine active investigational new animal drug applications, or INADs, filed with the FDA and intends to develop species-specific formulations of Neonorm in six additional target species, SB-300 for ulcers in horses, and Canalevia for cats and dogs, and potentially for diarrhea associated with acute colitis in horses, which can cause sudden, massive fluid loss and severe electrolyte imbalances that can result in death in a matter of hours. In December 2015 we completed a pilot safety study to evaluate crofelemer in adult horses, the first step in the development program for diarrhea associated with acute colitis in horses.

Crofelemer is the active pharmaceutical ingredient, or API, in Canalevia. 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.

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 this investigational new animal drug, SB-300, for the treatment of gastrointestinal ulcers in horses. In April 2016, we announced that standard drug testing in race horses having received SB-300 did not detect any substances commonly disallowed by horse racing authorities. The results of this initial study show that SB-300 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 May 2016 we initiated a dose determination study of the target commercial paste formulation of SB-300, with both a placebo control arm and a positive control comparator, omeprazole.

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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, SB-300 has the potential to address ulcers in horses, as well as diarrhea. We are initially developing this product for 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 SB-300. 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 SB-300 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 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 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

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double-blinded, randomized study involves 40 Holstein bull calves affected with naturally occurring diarrhea. The study results 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.

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 SB-300 drug product candidate for EGUS. We believe SB-300 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.

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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 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.

In September 2016, we entered into 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.

The piglet studies were sponsored by Integrated Animal Nutrition and Health Inc., involved more than 1,000 animals, and took place earlier this year at pig farms in China. The results indicate resolution and cure rates ranging from 60-99%, and a benefit on prophylaxis of diarrhea.

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.

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 SmithKline Beecham Corporation, now GlaxoSmithKline LLC, Zoetis Inc., Novartis International AG, 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 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
				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 2017
Species-specific formulations of crofelemer	Horses	Diarrhea associated with acute colitis		
			Completed pilot safety study in December 2015	Product development in 2017
	Horses	Ulcers		
			INAD opened in October 2015	Results from dose confirmation study
			Proof-of-concept safety and effectiveness results in January 2016	Commence pivotal field trial in second half of 2016
			Product development meeting with FDA in first half of 2016	
			Initiated dose confirmation study with positive control	
	Cats	Acute diarrhea		
			INAD opened in 2014	

				Initiate safety and proof-of-concept in 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	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
				Business development activities
			Shipped $660,041 of product to distributors since commercial launch	Further analysis of prophylactic data
			Analysis completed in October 2015 supports prebiotic effect	
			Field study completed in September 2015 supports beneficial effect of on prewean weight gain	
			Positive prophylactic results	
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	
Other farm/production animals	Supports gut health normalizing fecal formation	Entered exclusive distribution agreement for pigs and dairy calves in China	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, intended for the treatment of various forms of diarrhea in dogs. SB-300 is our prescription drug product candidate for the treatment of gastrointestinal ulcers in horses. Canalevia and SB-300 contain ingredients isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Neonorm Calf and Neonorm Foal are our lead 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,

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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.

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

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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 SB-300 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.

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

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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

Although we have no present commitments or agreements for any specific acquisitions or investments, 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. As of September 1, 2016, Napo owns 22.8% 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.

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, SB-300 and Canalevia, and non-prescription product, Neonorm, and cannot be certain that necessary approvals will be received for Canalevia or SB-300 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.

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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.

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 stockholder	2,821,111 shares
Common stock outstanding	11,821,408 (as of September 15, 2016)
Use of proceeds	The selling stockholder 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 stockholder. However, we have received proceeds of approximately $1.9 million, and may receive up to approximately $13.1 million in additional proceeds, for an aggregate of $15.0 million from the sale of our common stock to the selling stockholder under the common stock purchase agreement described below. Any proceeds from the selling stockholder that we receive under the purchase agreement are expected be used to for working capital, general corporate purposes and business development activities. 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 11,821,408 shares outstanding as of September 15, 2016, but excludes:

- 1,679,016 shares of common stock issuable upon exercise of outstanding options as of September 15, 2016, at a weighted average exercise price of $3.29 per share, of which 813,018 shares are vested as of such date;
- 932,192 shares of common stock reserved for future issuance under the 2014 Stock Incentive Plan;
- 715,539 shares of common stock issuable upon exercise of warrants outstanding as of September 15, 2016;
- 20,789 shares issuable upon vesting of outstanding restricted stock unit awards, or RSUs, as of September 15, 2016; and
- 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 September 15, 2016.

On June 8, 2016, we entered into a common stock purchase agreement, or the Purchase Agreement, with Aspire Capital Fund, LLC, an Illinois limited liability company, or Aspire Capital or the selling stockholder, which provides that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital is committed to purchase up to an aggregate of $15.0 million of our shares of common stock over the approximately 30-month term of the Purchase Agreement. In consideration for entering into the Purchase Agreement, concurrently with the execution of the Purchase Agreement, we issued to Aspire Capital 456,667 shares of our common stock as a commitment fee, or the Commitment Shares. Upon execution of the Purchase Agreement, we agreed to sell to Aspire Capital 222,222 shares of common stock, or the Initial Purchase Shares, at $2.25 per

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share for proceeds of $500,000. Concurrently with entering into the Purchase Agreement, we also entered into a registration rights agreement with Aspire Capital, or the Registration Rights Agreement, in which we agreed to file one or more registration statements, including the registration statement of which this prospectus is a part, as permissible and necessary to register under the Securities Act of 1933, as amended, or the Securities Act, the sale of the shares of our common stock that have been and may be issued to Aspire Capital under the Purchase Agreement.

On June 22, 2016, we registered up to 3,000,000 shares of our common stock that have been or may be issued to Aspire Capital under the Purchase Agreement in a registration statement, which we refer to as the Prior Registration Statement. Through September 15, 2016, we have sold an aggregate of 1,678,889 shares of our common stock to Aspire Capital under the Purchase Agreement for aggregate gross proceeds of approximately $1.9 million. After the Securities and Exchange Commission, or the SEC, has declared effective the registration statement of which this prospectus is a part, on any trading day on which the closing sale price of our common stock exceeds $0.50, we have the right, in our sole discretion, to present Aspire Capital with a purchase notice, or each a Purchase Notice, directing Aspire Capital (as principal) to purchase up to 100,000 shares of our common stock per trading day, up to $15.0 million of our common stock in the aggregate at a per share price, or the Purchase Price, calculated by reference to the prevailing market price of our common stock (as more specifically described below).

In addition, on any date on which we submit a Purchase Notice for 100,000 shares to Aspire Capital, we also have the right, in our sole discretion, to present Aspire Capital with a volume-weighted average price purchase notice, or each a VWAP Purchase Notice, directing Aspire Capital to purchase an amount of stock equal to up to 30% of the aggregate shares of our common stock traded on the NASDAQ Capital Market on the next trading day, or the VWAP Purchase Date, subject to a maximum number of shares we may determine, or the VWAP Purchase Share Volume Maximum, and a minimum trading price, or the VWAP Minimum Price Threshold (as more specifically described below). The purchase price per Purchase Share pursuant to such VWAP Purchase Notice, or the VWAP Purchase Price, is calculated by reference to the prevailing market price of our common stock (as more specifically described below).

The Purchase Agreement provides that we and Aspire Capital shall not effect any sales under the Purchase Agreement on any purchase date where the closing sale price of our common stock is less than $0.50 per share, or the Floor Price. This Floor Price and the respective prices and share numbers in the preceding paragraphs shall be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction. There are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Aspire Capital. Aspire Capital has no right to require any sales by us, but is obligated to make purchases from us as we direct in accordance with the Purchase Agreement. There are no limitations on use of proceeds, financial or business covenants, restrictions on future fundings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement. Aspire Capital may not assign its rights or obligations under the Purchase Agreement. The Purchase Agreement may be terminated by us at any time, at our discretion, without any penalty or cost to us.

Although the Purchase Agreement provides that we may sell up to $15.0 million of our common stock to Aspire Capital, only 2,821,111 shares of our common stock are being offered under this prospectus, which represents (i) 1,321,111 shares registered and remaining unsold under the Prior Registration Statement and issued or issuable to Aspire Capital under the Purchase Agreement and (ii) an additional 1,500,000 shares which may be issued to Aspire Capital in the future under the Purchase Agreement. As of September 15, 2016, there were 11,821,408 shares of our common stock outstanding (7,135,716 shares held by non-affiliates including Aspire Capital), which includes 1,678,889 shares of our common stock that have already been issued to Aspire Capital under the Purchase

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Agreement, but excludes the 2,821,111 shares of common stock that we may issue to Aspire Capital in the future under the terms of the Purchase Agreement. If all of such 2,821,111 shares of our common stock offered hereby were issued and outstanding as of the date hereof, such shares would represent 19.3% of the total common stock outstanding or 28.3% of the non-affiliate shares of common stock outstanding as of the date hereof. The number of shares of our common stock ultimately offered for sale by Aspire Capital is dependent upon the number of shares purchased by Aspire Capital under the Purchase Agreement.

The aggregate number of shares that we may issue to Aspire Capital under the Purchase Agreement may in no case exceed 2,027,490 shares of our common stock (which is equal to approximately 19.99% of the common stock outstanding on the date of the Purchase Agreement), unless (i) shareholder approval is obtained to issue more, in which case this 2,027,490 share limitation, will not apply, or (ii) shareholder approval has not been obtained and at any time the 2,027,490 share limitation is reached and at all times thereafter the average price paid for all shares issued under the Common Stock Purchase Agreement (including the Commitment Shares) is equal to or greater than $1.32, the Minimum Price, a price equal to the closing sale price of our common stock on the date of the execution of the Purchase Agreement; provided that at no one point in time shall Aspire Capital (together with its affiliates) beneficially own more than 19.99% of our common stock.

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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. If we fail to achieve or maintain profitability, then we may be unable to continue our operations at planned levels and be forced to reduce or cease operations.

Our independent registered public accounting firm has included an explanatory paragraph in its audit report on our financial statements for the year ended December 31, 2015, regarding our assessment of substantial doubt about our ability to continue as a going concern. Our financial statements do not include any adjustments that may result from the outcome of this uncertainty. If we are unable to continue as a viable entity, our stockholders may lose their entire investment.

We have never generated any material revenue from operations and may not generate any material revenue from our operations in the foreseeable future.

We are an animal health company focused on developing and commercializing prescription drug and non-prescription products for companion and production animals, foals, and high value horses. Since inception in June 2013, we have not generated any material revenue from operations. There is no guarantee that our recent commercial launch of Neonorm Calf for preweaned dairy calves in the

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United States will be successful or that we will be able to sell any products in the future. Further, in order to commercialize our prescription drug product candidates, we must receive regulatory approval from the FDA in the United States and other regulatory agencies in various jurisdictions. We have not yet received any regulatory approvals for our prescription drug product candidates. In addition, certain of our non-prescription products, such as Neonorm Calf, may be subject to regulatory approval outside the United States prior to commercialization. Accordingly, until and unless we receive any necessary regulatory approvals, we cannot market or sell our products. Moreover, even if we receive the necessary approvals, we may not be successful in generating revenue from sales of our products as we do not have any meaningful experience marketing or distributing our products. Accordingly, we may never generate any material revenue from our operations.

We expect to incur significant additional costs as we continue commercialization efforts for Neonorm, and undertake the clinical trials necessary to obtain regulatory approvals for Canalevia and SB-300, which will increase our losses.

We commenced sales of Neonorm for preweaned dairy calves in the United States under the brand name Neonorm Calf at the end of 2014. We will need to continue to invest in developing our internal and third-party sales and distribution network and outreach efforts to key opinion leaders in the dairy industry, including veterinarians. We will also need to conduct clinical trials for SB-300 and Canalevia in order to obtain necessary initial regulatory approvals and to subsequently broaden Canalevia to additional indications and additional species. We will also need to conduct species-specific testing with Neonorm to expand to additional animal populations.

We are actively identifying additional products for development and commercialization, and will continue to expend substantial resources for the foreseeable future to develop SB-300, Canalevia and Neonorm and develop products from the library of over 2,300 medicinal plants that we have licensed. These expenditures will include costs associated with:

- identifying additional potential prescription drug product candidates and non-prescription products;
- formulation studies;
- conducting pilot, pivotal and toxicology studies;
- completing other research and development activities;
- payments to technology licensors;
- maintaining our intellectual property;
- obtaining necessary regulatory approvals;
- establishing commercial supply capabilities; and
- sales, marketing and distribution of our commercialized products.

We also may incur unanticipated costs in connection with developing and commercializing our products. Because the outcome of our development activities and commercialization efforts is inherently uncertain, the actual amounts necessary to successfully complete the development and commercialization of our current or future products and product candidates may be greater than we anticipate.

Because we anticipate incurring significant costs for the foreseeable future, if we are not successful in broadly commercializing any of our current or future products or product candidates or raising additional funding to pursue our research and development efforts, we may never realize the benefit of our development efforts and our business may be harmed.

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We will need to raise substantial additional capital in the future to fund our operations and we may be unable to raise such funds when needed and on acceptable terms, which would force us to delay, limit, reduce or terminate one or more of our product development programs or future commercialization efforts.

We are forecasting continued losses and negative cash flows as we continue to fund our operating and marketing activities and research and development programs, and we will not have sufficient cash on hand to fund our operating plan through December 2016 and to complete the development of all the current products in our pipeline, or any additional products we may identify. We will need to seek additional funds sooner than planned through public or private equity or debt financings or other sources such as strategic collaborations. We do not expect that the net proceeds from this offering will be sufficient to complete the development of all the current products in our pipeline, or any additional products we may identify. We may need to raise additional capital to fund these activities. Other than the loan and security agreement (which provided for an initial loan commitment of $6.0 million) and the Purchase Agreement (which committed Aspire Capital to purchase up to an aggregate of $15.0 million of our shares of common stock over the term of the Purchase Agreement), we have no current agreements or arrangements with respect to any such financings or collaborations, and any such financings or collaborations may result in dilution to our stockholders, the imposition of debt covenants and repayment obligations or other restrictions that may harm our business or the value of our common stock. We may also seek from time to time to raise additional capital based upon favorable market conditions or strategic considerations such as potential acquisitions.

Our future capital requirements depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching and developing our current and future prescription drug product candidates and non-prescription products;
- the timing of, and the costs involved in, obtaining any regulatory approvals for our current and any future products;
- the number and characteristics of the products we pursue;
- the cost of manufacturing our current and future products and any products we successfully commercialize;
- the cost of commercialization activities for Neonorm, SB-300 and Canalevia, if approved, including sales, marketing and distribution costs;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- our ability to establish and maintain strategic collaborations, distribution or other arrangements and the financial terms of such agreements; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing possible patent claims, including litigation costs and the outcome of any such litigation.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate one or more of our product development programs or future commercialization efforts.

The extent to which we utilize the Purchase Agreement with Aspire Capital as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, the volume of trading in our common stock and the extent to which we are able to secure funds from other sources. The number of shares that we may sell to Aspire Capital under the Purchase Agreement on any given day and

during the term of the agreement is limited. See "The Aspire Capital Transaction"

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section of this prospectus for additional information. Additionally, we and Aspire Capital may not effect any sales of shares of our common stock under the Purchase Agreement during the continuance of an event of default or on any trading day that the closing sale price of our common stock is less than $0.50 per share. Even if we are able to access the full $15 million under the Purchase Agreement, we will still need additional capital to fully implement our business, operating and development plans.

We are substantially dependent on the success of SB-300, Canalevia and Neonorm and cannot be certain that SB-300 or Canalevia will be approved or that we can successfully commercialize these products.

We currently do not have regulatory approval for any of our prescription drug product candidates, including SB-300 and Canalevia. Our current efforts are primarily focused on the commercial launch of Neonorm Calf and Neonorm Foal in the United States, and development efforts related to Canalevia. We are focused on expanding Canalevia's proposed indications to cover acute diarrhea in dogs and full FDA approval for CID for dogs. Accordingly, our near-term prospects, including our ability to generate material product revenue, obtain any new financing if needed to fund our business and operations or enter into potential strategic transactions, will depend heavily on the success of Neonorm and, if approved, SB-300 and Canalevia.

Substantial time and capital resources have been previously devoted by third parties in the development of crofelemer, the active pharmaceutical ingredient, or API, in Canalevia, and the botanical extract used in Neonorm. Both crofelemer and the botanical extract used in Neonorm were originally developed at Shaman Pharmaceuticals, Inc., or Shaman, by certain members of our management team, including Lisa A. Conte, our Chief Executive Officer and President, and Steven R. King, Ph.D., our Executive Vice President, Sustainable Supply, Ethnobotanical Research and Intellectual Property and Secretary. Shaman spent significant development resources before voluntarily filing for bankruptcy in 2001 pursuant to Chapter 11 of the U.S. Bankruptcy Code. The rights to crofelemer and the botanical extract used in Neonorm, as well as other intellectual property rights, were subsequently acquired by Napo from Shaman in 2001 pursuant to a court approved sale of assets. Ms. Conte founded Napo in 2001 and is the current interim chief executive officer of Napo and a member of its board of directors. While at Napo, certain members of our management team, including Ms. Conte and Dr. King, continued the development of crofelemer. In 2005, Napo entered into license agreements with Glenmark Pharmaceuticals Ltd., or Glenmark, and Luye Pharma Group Limited for rights to various human indications of crofelemer in certain territories as defined in the respective license agreements with these licensees. Subsequently, after expending significant sums developing crofelemer, including trial design and on-going patient enrollment in the final pivotal Phase 3 trial for crofelemer for non-infectious diarrhea in adults with HIV/AIDS on antiretroviral therapy, in late 2008, Napo entered into a collaboration agreement with Salix Pharmaceuticals, Inc., or Salix, for development and commercialization rights to certain indications worldwide and certain rights in North America, Europe, and Japan, to crofelemer for human use. In January 2014, we entered into the Napo License Agreement pursuant to which we acquired an exclusive worldwide license to Napo's intellectual property rights and technology, including crofelemer and the botanical extract used in Neonorm, for all veterinary treatment uses and indications for all species of animals. In February 2014, most of the executive officers of Napo, and substantially all Napo's employees, became our employees. If we are not successful in the development and commercialization of Neonorm and Canalevia, our business and our prospects will be harmed.

The successful development and commercialization of Neonorm and, if approved, Canalevia will depend on a number of factors, including the following:

- the successful completion of the pivotal trials and toxicology studies for Canalevia, which may take significantly longer than we currently anticipate and will depend, in part, upon the satisfactory performance of third-party contractors;

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- our ability to demonstrate to the satisfaction of the FDA and any other regulatory bodies, the safety and efficacy of Canalevia;
- our ability and that of our contract manufacturers to manufacture supplies of Neonorm and Canalevia and to develop, validate and maintain viable commercial manufacturing processes that are compliant with current good manufacturing practices, or cGMP, if required;
- the success of Neonorm field studies and acceptance of their results by dairy producers;
- our ability to successfully launch Neonorm, whether alone or in collaboration with others;
- our ability to successfully launch Canalevia assuming approval is obtained, whether alone or in collaboration with others;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of our prescription drug product candidates and non-prescription products compared to alternative and competing treatments;
- the acceptance of our prescription drug product candidates and non-prescription products as safe and effective by veterinarians, animal owners and the animal health community;
- our ability to achieve and maintain compliance with all regulatory requirements applicable to our business; and
- our ability to obtain and enforce our intellectual property rights and obtain marketing exclusivity for our prescription drug product candidates and non-prescription products, and avoid or prevail in any third-party patent interference, patent infringement claims or administrative patent proceedings initiated by third parties or the U.S. Patent and Trademark Office, or USPTO.

Many of these factors are beyond our control. Accordingly, we may not be successful in developing or commercializing Neonorm, Canalevia or any of our other potential products. If we are unsuccessful or are significantly delayed in developing and commercializing Neonorm, Canalevia or any of our other potential products, our business and prospects will be harmed and you may lose all or a portion of the value of your investment in our common stock.

If we are not successful in identifying, licensing, developing and commercializing additional product candidates and products, our ability to expand our business and achieve our strategic objectives could be impaired.

Although a substantial amount of our efforts are focused on the commercial launch of Neonorm and the continued development and potential approvals of SB-300 and Canalevia, a key element of our strategy is to identify, develop and commercialize a portfolio of products to serve the animal health market. Most of our potential products are based on our knowledge of medicinal plants. Our current focus is primarily on product candidates and products for animals whose active pharmaceutical ingredient or botanical extract has been successfully commercialized or demonstrated to be safe and effective in human trials. In some instances, we may be unable to further develop these potential products because of perceived regulatory and commercial risks. Even if we successfully identify potential products, we may still fail to yield products for development and commercialization for many reasons, including the following:

- competitors may develop alternatives that render our potential products obsolete;
- potential products we seek to develop may be covered by third-party patents or other exclusive rights;

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a potential product may on further study be shown to have harmful side effects in animals or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;

a potential product may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and

a potential product may not be accepted as safe and effective by veterinarians, animal owners, key opinion leaders and other decision-makers in the animal health market.

While we are developing species-specific formulations, including flavors, methods of administration, new patents and other strategies with respect to our current potential products, we may be unable to prevent competitors from developing substantially similar products and bringing those products to market earlier than we can. If such competing products achieve regulatory approval and commercialization prior to our potential products, our competitive position may be impaired. If we fail to develop and successfully commercialize other potential products, our business and future prospects may be harmed and we will be more vulnerable to any problems that we encounter in developing and commercializing our current potential products.

Our animal health products face significant competition from other pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The development and commercialization of animal health products is highly competitive and our success depends on our ability to compete effectively with other products in the market. We expect to compete with the animal health divisions of major pharmaceutical and biotechnology companies such as Merck Animal Health, Merial Inc., Elanco Animal Health, Bayer Animal Health GmbH, Novartis Animal Health Inc. and Boehringer Ingelheim Animal Health, as well as specialty animal health medicines companies such as Zoetis Inc., Phibro Animal Health Corporation and, in Europe, Virbac S.A., Vétoquinol S.A., Ceva Animal Health S.A. and Dechra Pharmaceuticals PLC. We are also aware of several early-stage companies that are developing products for use in the animal health market, including Aratana Therapeutics, Inc., Kindred Biosciences, Inc., Parnell Pharmaceuticals Holdings Ltd, Nexvet Biopharma and ImmuCell Corporation. We also compete with academic institutions, governmental agencies and private organizations that are conducting research in the field of animal health products.

Although there are currently no FDA-approved anti-secretory products to treat acute diarrhea in dogs, we anticipate that Canalevia, if approved, will face competition from various products, including products approved for use in humans that are used extra-label in animals. Extra-label use is the use of an approved drug outside of its cleared or approved indications in the animal context. All of our potential products could also face competition from new products in development. These and other potential competing products may benefit from greater brand recognition and brand loyalty than our products and product candidates may achieve.

Many of our competitors and potential competitors have substantially more financial, technical and human resources than we do. Many also have more experience in the development, manufacture, regulation and worldwide commercialization of animal health products, including animal prescription drugs and non-prescription products.

For these reasons, we cannot be certain that we and our products can compete effectively.

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We may be unable to obtain, or obtain on a timely basis, regulatory approval for our existing or future prescription drug product candidates under applicable regulatory requirements, which would harm our operating results.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of animal health products are subject to extensive regulation. We are usually not permitted to market our prescription drug product candidates in the United States until we receive approval of an NADA from the FDA. To gain approval to market an animal prescription drug for a particular species, we must provide the FDA with safety and efficacy data from pivotal trials that adequately demonstrate that our prescription drug product candidates are safe and effective in the target species (*e.g.* dogs, cats or horses) for the intended indications. In addition, we must provide manufacturing data evidencing that we can produce our product candidates in accordance with cGMP. For the FDA, we must also provide data from toxicology studies, also called target animal safety studies, and in some cases environmental impact data. In addition to our internal activities, we will partially rely on contract research organizations, or CROs, and other third parties to conduct our toxicology studies and for certain other development activities. The results of toxicology studies and other initial development activities, and of any previous studies in humans or animals conducted by us or third parties, may not be predictive of future results of pivotal trials or other future studies, and failure can occur at any time during the conduct of pivotal trials and other development activities by us or our CROs. Our pivotal trials may fail to show the desired safety or efficacy of our prescription drug product candidates despite promising initial data or the results in previous human or animal studies conducted by others, and success of a prescription drug product candidate in prior animal studies, or in the treatment of humans, does not ensure success in subsequent studies. Clinical trials in humans and pivotal trials in animals sometimes fail to show a benefit even for drugs that are effective because of statistical limitations in the design of the trials or other statistical anomalies. Therefore, even if our studies and other development activities are completed as planned, the results may not be sufficient to obtain a required regulatory approval for a product candidate.

Regulatory authorities can delay, limit or deny approval of any of our prescription drug product candidates for many reasons, including:

- if they disagree with our interpretation of data from our pivotal studies or other development efforts;
- if we are unable to demonstrate to their satisfaction that our product candidate is safe and effective for the target indication and in the target species;
- if they require additional studies or change their approval policies or regulations;
- if they do not approve of the formulation, labeling or the specifications of our current and future product candidates; and
- if they fail to approve the manufacturing processes of our third-party contract manufacturers.

Further, even if we receive a required approval, such approval may be for a more limited indication than we originally requested, and the regulatory authority may not approve the labeling that we believe is necessary or desirable for successful commercialization.

Any delay or failure in obtaining any necessary regulatory approval for the intended indications of our product candidates would delay or prevent commercialization of such product candidates and would harm our business and our operating results.

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The results of our earlier studies of Neonorm may not be predictive of the results in any future species-specific formulation studies, and we may not be successful in our efforts to develop or commercialize line extensions of Neonorm.

Our product pipeline includes a number of species-specific formulations of Neonorm, our lead non-prescription product. The results of our dairy calf studies and other initial development activities and of any previous studies in humans or animals conducted by us or third parties may not be predictive of future results of these formulation studies. Failure can occur at any time during the conduct of these trials and other development activities. Even if our species-specific formulation studies and other development activities are completed as planned, the results may not be sufficient to pursue a particular line extension for Neonorm. Further, even if we obtain promising results from our species-specific formulation studies, we may not successfully commercialize any line extension. Because line extensions are developed for a particular species market, we may not be able to leverage our experience from the commercial launch of Neonorm Calf and Neonorm Foal in new animal species markets. If we are not successful in developing and successfully commercializing these line extension products, we may not be able to grow our revenue and our business may be harmed.

Development of prescription drug products is inherently expensive, time-consuming and uncertain, and any delay or discontinuance of our current or future pivotal trials would harm our business and prospects.

Development of prescription drug products for animals remains an inherently lengthy, expensive and uncertain process, and our development activities may not be successful. We do not know whether our current or planned pivotal trials for any of our product candidates will begin or conclude on time, and they may be delayed or discontinued for a variety of reasons, including if we are unable to:

address any safety concerns that arise during the course of the studies;

complete the studies due to deviations from the study protocols or the occurrence of adverse events;

add new study sites;

address any conflicts with new or existing laws or regulations; or

reach agreement on acceptable terms with study sites, which can be subject to extensive negotiation and may vary significantly among different sites.

Further, we may not be successful in developing species-specific formulations for Neonorm, and Neonorm may be subject to the same regulatory regime as prescription drug products in jurisdictions outside the United States. Any delays in completing our development efforts will increase our costs, delay our development efforts and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects. In addition, factors that may cause a delay in the commencement or completion of our development efforts may also ultimately lead to the denial of regulatory approval of our product candidates which, as described above, would harm our business and prospects.

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We will partially rely on third parties to conduct our development activities. If these third parties do not successfully carry out their contractual duties, we may be unable to obtain regulatory approvals or commercialize our current or future product candidates on a timely basis, or at all.

We will partially rely upon CROs to conduct our toxicology studies and for other development activities. We intend to rely on CROs to conduct one or more of our planned pivotal trials. These CROs are not our employees, and except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our programs or manage the risks associated with their activities on our behalf. We are responsible for ensuring that each of our studies is conducted in accordance with the development plans and trial protocols presented to regulatory authorities. Any deviations by our CROs may adversely affect our ability to obtain regulatory approvals, subject us to penalties or harm our credibility with regulators. The FDA and foreign regulatory authorities also require us and our CROs to comply with regulations and standards, commonly referred to as good clinical practices, or GCPs, or good laboratory practices, or GLPs, for conducting, monitoring, recording and reporting the results of our studies to ensure that the data and results are scientifically valid and accurate.

Agreements with CROs generally allow the CROs to terminate in certain circumstances with little or no advance notice. These agreements generally will require our CROs to reasonably cooperate with us at our expense for an orderly winding down of the CROs' services under the agreements. If the CROs conducting our studies do not comply with their contractual duties or obligations, or if they experience work stoppages, do not meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised, we may need to secure new arrangements with alternative CROs, which could be difficult and costly. In such event, our studies also may need to be extended, delayed or terminated as a result, or may need to be repeated. If any of the foregoing were to occur, regulatory approval, if required, and commercialization of our product candidates may be delayed and we may be required to expend substantial additional resources.

Even if we obtain regulatory approval for Canalevia or our other product candidates, they may never achieve market acceptance. Further, even if we are successful in commercially launching Neonorm, it may not achieve commercial success.

If we obtain necessary regulatory approvals for Canalevia or our other product candidates, such products may still not achieve market acceptance and may not be commercially successful. Market acceptance of Canalevia, SB-300, Neonorm and any of our other products depends on a number of factors, including:

- the safety of our products as demonstrated in our target animal studies;
- the indications for which our products are approved or marketed;
- the potential and perceived advantages over alternative treatments or products, including generic medicines and competing products currently prescribed by veterinarians, and products approved for use in humans that are used extra-label in animals;
- the acceptance by veterinarians, companion animal owners and production animal owners, including in the dairy industry, of our products as safe and effective;
- the cost in relation to alternative treatments and willingness on the part of veterinarians and animal owners to pay for our products;
- the prevalence and severity of any adverse side effects of our products;
- the relative convenience and ease of administration of our products; and
- the effectiveness of our sales, marketing and distribution efforts.

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Any failure by Canalevia, SB-300, Neonorm or any of our other products to achieve market acceptance or commercial success would harm our financial condition and results of operations.

The dairy industry is subject to conditions beyond our control and the occurrence of any such conditions may harm our business and impact the demand for our products.

The demand for production animal health products, such as Neonorm Calf, is heavily dependent on factors that affect the dairy market that are beyond our control, including the following, any of which may harm our business:

- cost containment measures within the dairy industry, in response to international, national and local general economic conditions, which may affect the market adoption of our products;
- state and federal government policies, including government-funded programs or subsidies whose discontinuance or modification could erode the demand for our products;
- a decline in demand for dairy products due to changes in consumer diets away from dairy products, which could adversely affect the demand for production animal health products;
- adverse weather conditions and natural disasters, such as floods, droughts, and pestilence, which can lower dairy yields; and
- disease or other conditions beyond our control.

Animal products, like human products, are subject to unanticipated post-approval safety or efficacy concerns, which may harm our business and reputation.

The success of our commercialization efforts will depend upon the perceived safety and effectiveness of animal health products, in general, and of our products, in particular. Unanticipated safety or efficacy concerns can subsequently arise with respect to approved prescription drug products, or non-prescription products, such as Neonorm, which may result in product recalls or withdrawals or suspension of sales, as well as product liability and other claims. Any safety or efficacy concerns, or recalls, withdrawals or suspensions of sales of our products, or human products derived from *Croton lechleri*, if any, could harm our reputation and business, regardless of whether such concerns or actions are justified.

Future federal and state legislation may result in increased exposure to product liability claims, which could result in substantial losses.

Under current federal and state laws, companion and production animals are generally considered to be the personal property of their owners and, as such, the owners' recovery for product liability claims involving their companion and production animals may be limited to the replacement value of the animal. Companion animal owners and their advocates, however, have filed lawsuits from time to time seeking non-economic damages such as pain and suffering and emotional distress for harm to their companion animals based on theories applicable to personal injuries to humans. If new legislation is passed to allow recovery for such non-economic damages, or if precedents are set allowing for such recovery, we could be exposed to increased product liability claims that could result in substantial losses to us if successful. In addition, some horses can be worth millions of dollars or more, and product liability for horses may be very high. While we currently have product liability insurance, such insurance may not be sufficient to cover any future product liability claims against us.

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If we fail to retain current members of our senior management, or to identify, attract, integrate and retain additional key personnel, our business will be harmed.

Our success depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We are highly dependent upon our senior management, particularly Lisa A. Conte, our president and Chief Executive Officer. The loss of services of any of our key personnel would cause a disruption in our ability to develop our current or future product pipeline and commercialize our products and product candidates. Although we have offer letters with these key members of senior management, such agreements do not prohibit them from resigning at any time. For example, the resignation of our former Chief Financial Officer, Charles O. Thompson, in September 2014, and the mutually agreed departure of our former Chief Veterinary Officer, Serge Martinod, D.V.M., Ph.D. in February 2015, caused us to incur additional expenses and expend resources to ensure a smooth transition with their respective successors, which diverted management attention away from executing our operational plan during this period. We currently do not maintain "key man" life insurance on any of our senior management team. The loss of Ms. Conte or other members of our current senior management could adversely affect the timing or outcomes of our current and planned studies, as well as the prospects for commercializing our products.

In addition, competition for qualified personnel in the animal health field is intense, because there are a limited number of individuals who are trained or experienced in the field. Further, our headquarters are located in San Francisco, California, and the dairy and agriculture industries are not prevalent in urban areas such as San Francisco. We will need to hire additional personnel as we expand our product development and commercialization activities. Even if we are successful in hiring qualified individuals, as we are a growing organization, we do not have a track record for integrating and retaining individuals. If we are not successful in identifying, attracting, integrating or retaining qualified personnel on acceptable terms, or at all, our business will be harmed.

We are dependent on two suppliers for the raw material used to produce the active pharmaceutical ingredient in Canalevia and the botanical extract in Neonorm. The termination of either of these contracts would result in a disruption to product development and our business will be harmed.

The raw material used to manufacture Canalevia and Neonorm is crude plant latex, or CPL, derived from the *Croton lechleri* tree, which is found in countries in South America, principally Peru. The ability of our contract suppliers to harvest CPL is governed by the terms of their respective agreements with local government authorities. Although CPL is available from multiple suppliers, we only have contracts with two suppliers to obtain CPL and arrange the shipment to our contract manufacturer. Accordingly, if our contract suppliers do not or are unable to comply with the terms of our respective agreements, and we are not able to negotiate new agreements with alternate suppliers on terms that we deem commercially reasonable, it may harm our business and prospects. The countries from which we obtain CPL could change their laws and regulations regarding the export of the natural products or impose or increase taxes or duties payable by exporters of such products. Restrictions could be imposed on the harvesting of the natural products or additional requirements could be implemented for the replanting and regeneration of the raw material. Such events could have a significant impact on our cost and ability to produce Canalevia, Neonorm and anticipated line extensions.

We are dependent upon third-party contract manufacturers, both for the supply of the active pharmaceutical ingredient in Canalevia and the botanical extract in Neonorm, as well as for the supply of finished products for commercialization.

To date, the CPL, API, botanical extract and some finished products that we have used in our studies and trials were obtained from Napo. We have also contracted with third parties for the formulation of API and botanical extract into finished products for our studies. We have entered into memorandums of understanding with Indena S.p.A. for the manufacture of CPL received from our

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suppliers into the API in Canalevia to support our regulatory filings, as well as the botanical extract in Neonorm and agreed to negotiate a commercial supply agreement. Indena S.p.A. has never manufactured either such ingredient to commercial scale. As a second supplier situation, we have entered into a four-year manufacturing and supply agreement with Glenmark for the supply of the API in Canalevia. Glenmark is the current manufacturer of crofelemer, the active API in Canalevia, for the FDA-approved human anti-secretory product, and the manufacturer on file for the NADA to which we have a right of reference. We have contracted with a third-party manufacturer for formulation development and manufacturing, whereby the manufacturer will provide enteric-coated tablets to us for use in animals. We also may contract with additional third parties for the formulation and supply of finished products, which we will use in our planned studies and commercialization efforts.

We will be dependent upon our contract manufacturers for the supply of the API in Canalevia. We currently have sufficient quantities of the botanical extract used in Neonorm to support initial commercialization of Neonorm. However, we will require additional quantities of the botanical extract if our commercial launch of Neonorm is successful. If we are not successful in reaching agreements with third parties on terms that we consider commercially reasonable for manufacturing and formulation, or if our contract manufacturer and formulator are not able to produce sufficient quantities or quality of API, botanical extract or finished product under their agreements, it could delay our plans and harm our business prospects.

The facilities used by our third-party contractors are subject to inspections, including by the FDA, and other regulators, as applicable. We also depend on our third-party contractors to comply with cGMP. If our third-party contractors do not maintain compliance with these strict regulatory requirements, we and they will not be able to secure or maintain regulatory approval for their facilities, which would have an adverse effect on our operations. In addition, in some cases, we also are dependent on our third-party contractors to produce supplies in conformity to our specifications and maintain quality control and quality assurance practices and not to employ disqualified personnel. If the FDA or a comparable foreign regulatory authority does not approve the facilities of our third-party contractors if so required, or if it withdraws any such approval in the future, we may need to find alternative manufacturing or formulation facilities, which could result in delays in our ability to develop or commercialize our products, if at all. We and our third-party contractors also may be subject to penalties and sanctions from the FDA and other regulatory authorities for any violations of applicable regulatory requirements. The USDA and the European Medicines Agency, or the EMA, employ different regulatory standards than the FDA, so we may require multiple manufacturing processes and facilities for the same product candidate or any approved product. We are also exposed to risk if our third-party contractors do not comply with the negotiated terms of our agreements, or if they suffer damage or destruction to their facilities or equipment.

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

We currently have limited sales, marketing or distribution capabilities, and prior to our launch of Neonorm for preweaned dairy calves, had no experience in the sale, marketing and distribution of animal health products. There are significant risks involved in building and managing a sales organization, including our potential inability to attract, hire, retain and motivate qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively oversee a geographically-dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities and entry into adequate arrangements with distributors or other partners would adversely impact the commercialization of Neonorm, SB-300 and Canalevia, if approved. If we are not successful in commercializing Neonorm, SB-300, Canalevia or any of our other line extension products, either on our own or through one or

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more distributors, or in generating upfront licensing or other fees, we may never generate significant revenue and may continue to incur significant losses, which would harm our financial condition and results of operations.

Changes in distribution channels for animal prescription drugs may make it more difficult or expensive to distribute our prescription drug products.

In the United States, animal owners typically purchase their animal prescription drugs from their local veterinarians who also prescribe such drugs. There is a trend, however, toward increased purchases of animal prescription drugs from Internet-based retailers, "big-box" retail stores and other over-the-counter distribution channels, which follows an emerging shift in recent years away from the traditional veterinarian distribution channel. It is also possible that animal owners may come to rely increasingly on Internet-based animal health information rather than on their veterinarians. We currently expect to market our animal prescription drugs directly to veterinarians, so any reduced reliance on veterinarians by animal owners could harm our business and prospects by making it more difficult or expensive for us to distribute our prescription drug products. Animal owners also may substitute human health products for animal prescription drugs if the human health products are less expensive or more readily available, which could also harm our business.

Legislation has been or may be proposed in various states that would require veterinarians to provide animal owners with written prescriptions and disclosures that the animal owner has the right to fill the prescriptions through other means. If enacted, such legislation could lead to a reduction in the number of animal owners who purchase their animal pharmaceuticals directly from veterinarians, which also could harm our business.

Consolidation of our customers could negatively affect the pricing of our products.

Veterinarians will be our primary customers for our prescription drug products, as well as, to some extent, our non-prescription products, such as Neonorm. In recent years, there has been a trend towards the consolidation of veterinary clinics and animal hospitals. If this trend continues, these large clinics and hospitals could attempt to leverage their buying power to obtain favorable pricing from us and other animal health product companies. Any downward pressure on the prices of any of our products could harm our operating results and financial condition.

We will need to increase the size of our organization and may not successfully manage such growth.

As of September 1, 2016, we had 23 employees. Our ability to manage our growth effectively will require us to hire, train, retain, manage and motivate additional employees and to implement and improve our operational, financial and management systems. These demands also may require the hiring of additional senior management personnel or the development of additional expertise by our senior management personnel. If we fail to expand and enhance our operational, financial and management systems in conjunction with our potential future growth, it could harm our business and operating results.

Our research and development relies on evaluations in animals, which is controversial and may become subject to bans or additional regulations.

The evaluation of our products and product candidates in target animals is required to develop, formulate and commercialize our products and product candidates. Although our animal testing will be subject to GLPs and GCPs, as applicable, animal testing in the human pharmaceutical industry and in other industries continues to be the subject of controversy and adverse publicity. Some organizations and individuals have sought to ban animal testing or encourage the adoption of additional regulations applicable to animal testing. To the extent that such bans or regulations are imposed, our research and

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development activities, and by extension our operating results and financial condition, could be harmed. In addition, negative publicity about animal practices by us or in our industry could harm our reputation among potential customers.

If approved, our prescription drug product candidates may be marketed in the United States only in the target animals and for the indications for which they are approved, and if we want to expand the approved animals or indications, we will need to obtain additional approvals, which may not be granted.

If our prescription drug product candidates are approved by regulatory authorities, we may market or advertise them only in the specific species and for treatment of the specific indications for which they were approved, which could limit use of the products by veterinarians and animal owners. We intend to develop, promote and commercialize approved products for other animals and new treatment indications in the future, but we cannot be certain whether or at what additional time and expense we will be able to do so. If we do not obtain marketing approvals for other species or for new indications, our ability to expand our business may be harmed.

Under the Animal Medicinal Drug Use Clarification Act of 1994, veterinarians are permitted to prescribe extra-label uses of certain approved animal drugs and approved human drugs for animals under certain conditions. While veterinarians may in the future prescribe and use human-approved products or our products for extra-label uses, we may not promote our products for extra-label uses. If the FDA determines that any of our marketing activities constitute promotion of an extra-label use, we could be subject to regulatory enforcement, including seizure of any misbranded or mislabeled drugs, and civil or criminal penalties, any of which could have an adverse impact on our reputation and expose us to potential liability. We will continue to spend resources ensuring that our promotional claims for our products and product candidates remain compliant with applicable FDA laws and regulations, including materials we post or link to on our website. For example, in 2012, our Chief Executive Officer received an "untitled letter" from the FDA while at Napo regarding preapproval promotion statements constituting misbranding of crofelemer, which was then an investigational drug. These statements were included in archived press releases included on Napo's website. Napo was required to expend time and resources to revise its website to remove the links in order to address the concerns raised in the FDA's letter.

If our prescription drug product candidates are approved by regulatory authorities, the misuse or extra-label use of such products may harm our reputation or result in financial or other damages.

If our prescription drug product candidates are approved by regulatory authorities, there may be increased risk of product liability if veterinarians, animal owners or others attempt to use such products extra-label, including the use of our products in species (including humans) for which they have not been approved. Furthermore, the use of an approved drug for indications other than those indications for which such products have been approved may not be effective, which could harm our reputation and lead to an increased risk of litigation. If we are deemed by a governmental or regulatory agency to have engaged in the promotion of any approved product for extra-label use, such agency could request that we modify our training or promotional materials and practices and we could be subject to significant fines and penalties, and the imposition of these sanctions could also affect our reputation and position within the industry. Any of these events could harm our reputation and our operating results.

We may not maintain the benefits associated with MUMS designation, including market exclusivity.

Although we have received MUMS designation for Canalevia for the treatment of CID in dogs, we may not maintain the benefits associated with MUMS designation. MUMS designation is a status similar to "orphan drug" status for human drugs. When we are granted MUMS designation, we are eligible for incentives to support the approval or conditional approval of the designated use. This

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designation does not allow us to commercialize a product until such time as we obtain approval or conditional approval of the product.

Because Canalevia has received MUMS designation for the identified particular intended use, we are eligible to obtain seven years of exclusive marketing rights upon approval (or conditional approval) of Canalevia for that intended use and become eligible for grants to defray the cost of our clinical work. Each designation that is granted must be unique, *i.e.*, only one designation can be granted for a particular API in a particular dosage form for a particular intended use. The intended use includes both the target species and the disease or condition to be treated.

At some point, we could lose MUMS designation. The basis for a lost designation can include but is not limited to, our failure to engage with due diligence in moving forward with a non-conditional approval, or a competing product has received conditional approval or approval prior to our product candidate for the same indication or species. In addition, MUMS designation may be withdrawn for a variety of reasons such as where the FDA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the prescription drug product to meet the needs of animals with the rare disease or condition. If this designation is lost, it could have a negative impact on the product and our company, which includes but is not limited to, market exclusivity related to MUMS designation, or eligibility for grants as a result of MUMS designation.

The market for our products, and the animal health market as a whole, is uncertain and may be smaller than we anticipate, which could lead to lower revenue and harm our operating results.

It is very difficult to estimate the commercial potential of any of our products because of the emerging nature of our industry as a whole. The animal health market continues to evolve and it is difficult to predict the market potential for our products. The market will depend on important factors such as safety and efficacy compared to other available treatments, changing standards of care, preferences of veterinarians, the willingness of companion and production animal owners to pay for such products, and the availability of competitive alternatives that may emerge either during the product development process or after commercial introduction. If the market potential for our products is less than we anticipate due to one or more of these factors, it could negatively impact our business, financial condition and results of operations. Further, the willingness of companion and production animal owners to pay for our products may be less than we anticipate, and may be negatively affected by overall economic conditions. The current penetration of animal insurance in the United States is low, animal owners are likely to have to pay out-of-pocket, and such owners may not be willing or able to pay for our products.

Our largest stockholder, Napo, controls a significant percentage of our common stock, and its interests may conflict with those of our other stockholders.

As of September 1, 2016, Napo owned in the aggregate 22.8% of our common stock. This concentration of ownership gives Napo significant influence over the way we are managed and the direction of our business. In addition, because we and Napo are party to a license agreement, Napo's interests as the licensor of our technology may be different from ours or those of our other stockholders. As a result, the interests of Napo with respect to matters potentially or actually involving or affecting us, such as future acquisitions, licenses, financings and other corporate opportunities and attempts to acquire us, may conflict with the interests of our other stockholders. Further, Napo has pledged its interests in our common stock as security for certain of its monetary obligations. Accordingly, Napo's ability to take action with respect to these shares may be limited by its agreements with its secured lenders, which may conflict with your interests or those of our other stockholders. If these secured lenders were to foreclose on such shares, these lenders would have significant influence over the way we are managed and the direction of our business. In addition, our Chief Executive Officer is also the interim chief executive officer of Napo and her duties as interim chief executive

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officer of Napo may conflict with her duties as our Chief Executive Officer, and the resolution of these conflicts may not always be in our or your best interest. Further, Jaguar and Napo are engaged in preliminary exploratory discussions to review a potential merger and/or other ways to cooperate with their respective business endeavors; however, there is no assurance that any agreement will be reached to merge or further cooperate with their respective business endeavors.

Napo's principal business currently consists of, among other activities, the management of its intellectual property portfolio, including rights under license agreements with respect to such intellectual property. Napo has limited assets, and its primary sources of revenues in recent years have been license fees, warrant exercises, equity and debt investments and, since late 2013, the receipt of royalties pursuant to its license agreements, which have been limited to date. If Napo fails to generate sufficient revenues to cover its operating costs, it could revise its business strategy in ways that could affect its relationship with our company. For example, it could decide to divest its assets, including its stock in our company. Napo's interests in managing its business, including its ownership in our company, may conflict with your interests.

We may engage in future acquisitions that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may evaluate various strategic transactions, including licensing or acquiring complementary products, technologies or businesses. Any potential acquisitions may entail numerous risks, including increased operating expenses and cash requirements, assimilation of operations and products, retention of key employees, diversion of our management's attention and uncertainties in our ability to maintain key business relationships of the acquired entities. In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Certain of the countries in which we plan to commercialize our products in the future are developing countries, some of which have potentially unstable political and economic climates.

We may commercialize our products in jurisdictions that are developing and emerging countries. This may expose us to the impact of political or economic upheaval, and we could be subject to unforeseen administrative or fiscal burdens. At present, we are not insured against the political and economic risks of operating in these countries. Any significant changes to the political or economic climate in any of the developing countries in which we operate or plan to sell products either now or in the future may have a substantial adverse effect on our business, financial condition, trading performance and prospects.

Fluctuations in the exchange rate of foreign currencies could result in currency transactions losses.

As we expand our operations, we expect to be exposed to risks associated with foreign currency exchange rates. We anticipate that we will commercialize Neonorm for preweaned dairy calves and its line extensions, as well as possibly Canalevia and its line extensions in jurisdictions outside the United States. As a result, we will also be further affected by fluctuations in exchange rates in the future to the extent that sales are denominated in currencies other than U.S. dollars. We do not currently employ any hedging or other strategies to minimize this risk, although we may seek to do so in the future.

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Risks Related to Intellectual Property

We are dependent upon our license agreement with Napo and if the agreement is terminated for any reason our business will be harmed.

In January 2014, we entered into a license agreement with Napo, or the Napo License Agreement, which we amended and restated in August 2014 and further amended in January 2015. Pursuant to the Napo License Agreement, we acquired an exclusive worldwide license to Napo's intellectual property rights and technology, including rights to its library of over 2,300 medicinal plants, for all veterinary treatment uses and indications for all species of animals except humans. Under the terms of the Napo License Agreement, we are responsible for, and shall ensure, the development and commercialization of products that contain or are derived from the licensed Napo technology worldwide in the field of veterinary treatment uses and indications for all species of animals. In consideration for the license, we are obligated to pay a one-time non-refundable license fee and royalties. Napo has the right to terminate the Napo License Agreement upon our uncured material breach of the agreement or if we declare bankruptcy. If the Napo License Agreement is terminated for any reason, our business will be harmed.

Napo has also entered into secured financing agreements with certain secured lenders, for whom Nantucket Investments Limited is acting as collateral agent. The security includes certain assets, including the intellectual property and technology licensed to us pursuant to the Napo License Agreement and Napo's shares of our common stock. Although Napo and Nantucket Investments Limited, on behalf of the secured lenders, have entered into a non-disturbance agreement with respect to the Napo License Agreement, in the event of a bankruptcy of Napo or foreclosure action with respect to Napo's assets, there can be no guarantee that the bankruptcy trustee or any other party to such action will not attempt to interfere with or terminate the Napo License Agreement or otherwise require its terms to be changed, which could harm our business. Under the terms of the Napo License Agreement, certain events, such as an acquisition of Napo or a sale by Napo of all of the intellectual property and technology licensed to us pursuant to the Napo License Agreement, should result in a fully-paid up license to us of all of such intellectual property and technology. If for any reason, Napo ceases to be the owner of the intellectual property and technology licensed to us pursuant to the Napo License Agreement in such a manner that did not result in a fully-paid up license provided for therein, the owner of such intellectual property and technology could attempt to interfere with or terminate the Napo License Agreement or otherwise attempt to renegotiate the arrangement, which would harm our business.

If Napo experiences financial difficulties, becomes unable to pay its liabilities when due, or declares bankruptcy, its creditors could attempt to assert claims against Napo relating to the formation of our company and the grant of an exclusive license to us.

Napo formed our company in June 2013, and in January 2014, we entered into the Napo License Agreement. Napo currently has no commercial operations and its potential sources of revenue are limited to the third parties who have licensed or may license Napo's intellectual property and technology, or collaborate with Napo in the future. Napo has been involved in litigation with Salix and has expended significant resources in the litigation. At the time of the formation of our company and the date of the Napo License Agreement, Napo's liabilities exceeded its assets on a balance sheet prepared in conformity with U.S. generally accepted accounting principles. Napo has been able to pay its liabilities when due but if Napo experiences financial difficulties, becomes unable to pay its liabilities when due, or declares bankruptcy, a creditor, trustee in bankruptcy, or other representative of a Napo bankruptcy estate could attempt to assert claims against us relating to our formation and Napo's grant of an exclusive license to us. One theory such a party could use to challenge our formation and the license grant is that of fraudulent conveyance. This theory is used by creditors to challenge the transfer of assets made with actual intent to hinder, delay, or defraud creditors, or where a financially distressed

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entity transfers assets without receiving reasonably equivalent value in exchange, provided such litigation is brought within the applicable statute of limitations. Although we do not believe that our formation or Napo's grant of the license was a fraudulent conveyance, litigation based on such theory, if successful, could result in a court order setting aside the license for the benefit of the creditor pursuing the litigation or all creditors of Napo should it occur in the context of a Napo bankruptcy. Even if unsuccessful, any such action would divert management's attention, potentially be costly to defend and could harm our business.

We currently do not own any issued patents, most of our intellectual property is licensed from Napo and we cannot be certain that our patent strategy will be effective to enhance marketing exclusivity.

The patent prosecution process is expensive and time-consuming, and we may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of inventions made in the course of development and commercialization activities in time to obtain patent protection on them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In particular, we are dependent upon Napo and its licensees to file, prosecute and maintain the intellectual property we license pursuant to the Napo License Agreement. The patents and patent applications we licensed from Napo, or the Napo Patents, which cover both human and veterinary uses, were previously licensed by Napo to Salix for certain fields of human use. On March 4, 2016, Napo and Salix settled litigation and all rights to crofelemer and Fulyzaq were returned to Napo and the collaboration agreement between Salix and Napo, or the Salix Collaboration Agreement, was terminated. Napo has the responsibility to file, prosecute and maintain the Napo Patents. As a result, under the Napo License Agreement, we only have the right to maintain any issued patents within the Napo Patents that are not maintained in accordance with the responsibilities of Napo. There are three issued Napo Patents in the United States that cover, collectively, enteric protected formulations of proanthocyanidin polymers isolated from *Croton spp.* and methods of treating watery diarrhea using the enteric protected formulations for both human and veterinary uses.

Napo has also licensed its *Croton lechleri* related intellectual property to Glenmark and Luye Pharma Group Limited to develop and commercialize crofelemer for human indications in various geographies. Fulyzaq is dependent upon intellectual property protection from the Napo Patents. Napo currently markets Fulyzaq in the United States for human use and the three issued Napo Patents that cover enteric protected formulations of proanthocyanidin polymers isolated from *Croton spp*. and methods of treating watery diarrhea using the enteric protected formulations are listed in the FDA's Orange Book for Fulyzaq. We rely on these issued Napo Patents as intellectual property protection for our prescription drug product candidates and non-prescription products. Pending patent applications within Napo Patents either may not be relevant to veterinary indications and/or may not issue as patents. If any patent application within the Napo Patents is not filed or prosecuted for any reason, including as a result of a lack of financial resources, and we are not able to file and prosecute such patent application within the Napo Patents, our business may be harmed. In addition, as between Napo and us, Napo has the first right to enforce the Napo Patents against potential infringers. If we are not the party who enforces the Napo Patents, we will receive no proceeds from such enforcement action. In each case, such proceeds are subject to reimbursement of costs and expenses incurred by the other party in connection with such action. If our current or future licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated.

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We currently do not own any issued patents. We have filed and have currently pending three applications under the Patent Cooperation Treaty, or PCT, one U.S. non-provisional patent application and eight provisional patent applications in the veterinary field, of which we control the filing, prosecution and maintenance; however, patents based on any patent applications we may submit may never be issued. We have an exclusive worldwide license from Napo to various issued patents and pending patent applications in the field of animal health. The strength of patents in the field of animal health involves complex legal and scientific questions and can be uncertain. Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents, if issued, and the patents we have licensed may not adequately protect our intellectual property or prevent others from designing around their claims. If we cannot obtain issued patents or the patents we have licensed are not maintained or their scope is significantly narrowed, our business and prospects would be harmed.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of any patent applications and the enforcement or defense of any patents that issue. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO has developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, became effective on March 16, 2013. Among some of the other changes to the patent laws are changes that limit where a patentee may file a patent infringement suit and that provide opportunities for third parties to challenge any issued patent in the USPTO. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that issue, all of which could harm our business and financial condition.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering prescription drug product candidates and non-prescription products, our competitors might be able to enter the market, which would harm our business.

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Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, which would be costly, time-consuming and, if successfully asserted against us, delay or prevent the development and commercialization of our current or future products and product candidates.

Our research, development and commercialization activities may infringe or otherwise violate or be claimed to infringe or otherwise violate patents owned or controlled by other parties. There may be patents already issued of which we are unaware that might be infringed by one of our current or future prescription drug product candidates or non-prescription products. Moreover, it is also possible that patents may exist that we are aware of, but that we do not believe are relevant to our current or future prescription drug product candidates or non-prescription products, which could nevertheless be found to block our freedom to market these products. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that may be infringed by our current or future prescription drug product candidates or non-prescription products. We cannot be certain that our current or future prescription drug product candidates or non-prescription products will not infringe these or other existing or future third-party patents. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

To the extent we become subject to future third-party claims against us or our collaborators, we could incur substantial expenses and, if any such claims are successful, we could be liable to pay substantial damages, including treble damages and attorney's fees if we or our collaborators are found to be willfully infringing a third party's patents. If a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the prescription drug or non-prescription product that is the subject of the suit. Even if we are successful in defending such claims, infringement and other intellectual property claims can be expensive and time-consuming to litigate and divert management's attention from our business and operations. As a result of or in order to avoid potential patent infringement claims, we or our collaborators may be compelled to seek a license from a third party for which we would be required to pay license fees or royalties, or both. Moreover, these licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain such a license, the rights may be nonexclusive, which could allow our competitors access to the same intellectual property. Any of these events could harm our business and prospects.

There has been substantial litigation regarding patents and other intellectual property rights in the field of therapeutics, as well as patent challenge proceedings, including interference, derivation and administrative law proceedings before the USPTO, and oppositions and other comparable proceedings in foreign jurisdictions. Under U.S. patent reform laws, new procedures, including *inter partes* review and post-grant review, were implemented as of September 16, 2012, with post-grant review available for patents issued on applications filed on or after March 16, 2013, and the implementation of such reform laws presents uncertainty regarding the outcome of any challenges to our future patents, if any, and to patents we have in licensed. In addition to possible infringement claims against us, we may be subject to third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, or other patent office proceedings or litigation in the United States or elsewhere, challenging our patent rights or the patent rights of others. For applications filed before March 16, 2013 or patents issuing from such applications, if third parties have prepared and filed patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine the priority of invention. Because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either file patent applications on or invent any of the inventions claimed in our patent applications. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide

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evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. We may also become involved in opposition or similar proceedings in patent offices in other jurisdictions regarding our intellectual property rights with respect to our prescription drug or non-prescription products and technology. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our future patent rights, if any, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Our proprietary position depends upon patents that are formulation or method-of-use patents, which do not prevent a competitor from using the same drug candidate for another use.

Composition-of-matter patents on the API in prescription drug products are generally considered to be the strongest form of intellectual property protection because such patents provide protection without regard to any particular method of use or manufacture or formulation of the API used. The composition-of-matter patents for crofelemer, the API in Canalevia, have expired, and we have licensed from Napo patents and applications covering formulations and methods of use for crofelemer and the botanical extract in Neonorm.

Method-of-use patents protect the use