LogMeIn, Inc.
Form 4
November 13, 2014

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP OF SECURITIES

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934, Section 17(a) of the Public Utility Holding Company Act of 1935 or Section 30(h) of the Investment Company Act of 1940

OMB APPROVAL

OMB Number:	3235-0287
Expires:	January 31, 2005
Estimated average burden hours per response...	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. *See* Instruction 1(b).

(Print or Type Responses)

1. Name and Address of Reporting Person *
Donahue Michael J

(Last) (First) (Middle)

C/O LOGMEIN, INC., 320 SUMMER STREET

(Street)

BOSTON, MA 02210

(City) (State) (Zip)

2. Issuer Name **and** Ticker or Trading Symbol
LogMeIn, Inc. [LOGM]

3. Date of Earliest Transaction (Month/Day/Year)
11/11/2014

4. If Amendment, Date Original Filed(Month/Day/Year)

5. Relationship of Reporting Person(s) to Issuer

(Check all applicable)

_____ Director _____ 10% Owner
__X__ Officer (give title below) _____ Other (specify below)
SVP and General Counsel

6. Individual or Joint/Group Filing(Check Applicable Line)
_X_ Form filed by One Reporting Person
___ Form filed by More than One Reporting Person

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

1.Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	11/11/2014	11/11/2014	M		9,375	A	$ 40.07	10,375	D	
Common Stock	11/11/2014	11/11/2014	S		9,375 (1)	D	$ 50.0989 (2)	1,000	D	
Common Stock	11/11/2014	11/11/2014	M		8,750	A	$ 39.13	9,750	D	
Common Stock	11/11/2014	11/11/2014	S		8,750 (1)	D	$ 50.0989 (2)	1,000	D	

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.

SEC 1474 (9-02)

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned
(*e.g.*, puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4, and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Underlying Securities (Instr. 3 and 4)		8. D Sec (Ins
				Code	V	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares	
Stock Option (Right to Buy)	$ 40.07	11/11/2014	11/11/2014	M			9,375	(3)	02/17/2021	Common Stock	9,375	
Stock Option (Right to Buy)	$ 39.13	11/11/2014	11/11/2014	M			8,750	(4)	02/17/2022	Common Stock	8,750	

Reporting Owners

Reporting Owner Name / Address	Relationships			
	Director	10% Owner	Officer	Other
Donahue Michael J C/O LOGMEIN, INC. 320 SUMMER STREET BOSTON, MA 02210			SVP and General Counsel	

Signatures

Michael J. Donahue	11/13/2014
**Signature of Reporting Person	Date

Explanation of Responses:

***** If the form is filed by more than one reporting person, *see* Instruction 4(b)(v).

****** Intentional misstatements or omissions of facts constitute Federal Criminal Violations. *See* 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

(1) Sales made pursuant to a 10(b)5-1 plan adopted by the Reporting Person in accordance with Rule 10(b)5-1 of the Securities Exchange Act of 1934, as amended.

(2) The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from $49.75 to $50.55, inclusive. Upon the request of any security holder of the Issuer, or the staff of the Securities and Exchange Commission, full information regarding the number of shares sold at each separate price within the ranges set forth in this Form 4 shall be provided.

(3) 25% of the shares subject to this option will vest on February 17, 2012, and an additional 25% of the shares subject to this option will vest annually thereafter, such that 100% of the shares subject to this option will be fully vested on February 17, 2015.

(4) 25% of the shares subject to this option will vest on February 17, 2013, and an additional 25% of the shares subject to this option will vest annually thereafter, such that 100% of the shares subject to this option will be fully vested on February 17, 2016.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, *see* Instruction 6 for procedure.
Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB number. YMBOL">³7 stools per day or incontinence; need for parenteral support for hydration Physiologic consequences requiring intensive care; hemodynamic collapse

According to data appearing in "Treatment Guidelines for CID" in the April 2004 issue of *Gastroenterology and Endoscopy News*, diarrhea is the most common adverse event reported in chemotherapy patients. We are continuing development of Mytesi for this important and unmet medical need, and two investigator-initiated trials of the product are underway in breast cancer patients suffering from CRD, one funded by Genetech Roche with Herceptin (enrolling patients), and one funded by Puma with neratinib (planning for patient enrollment).

Diarrhea is a common adverse event seen with chemotherapy agents in the therapeutic classes of epidermal growth factor receptor ("EGFR") tyrosine kinase inhibitors ("TKI's") and EGFR monoclonal antibodies (for breast, lung, and other malignancies). The increased need for and use of these agents has made diarrhea one of the most disabling issues for cancer patients. Crofelemer offers the potential for an appropriate mechanism of action against this likely secretory diarrhea and has prompted interest among physicians concerned about this diarrheal symptom, stimulating the aforementioned investigator-initiated trials. Diarrhea is also a common adverse event seen with chemotherapy agents used in colorectal and gastric cancers, and chronic maintenance chemotherapy. There are currently no anti-diarrhea agents approved generally for chemo-therapy induced diarrhea.

Clinical Studies

A study titled *HALT-D: DiarrHeA Prevention and ProphyLaxis with Crofelemer in HER2 Positive Breast Cancer Patients Receiving Trastuzumab, Pertuzumab, and Docetaxel or Paclitaxel with or without Carboplatin* is currently enrolling patients in conjunction with Georgetown University. The primary objective of the study is to characterize the incidence and severity of diarrhea in patients receiving investigational therapy in the setting of prophylactic anti-diarrheal management.

A second study, titled *An open label study to characterize the incidence and severity of diarrhea in patients with early stage HER2+ breast cancer treated with adjuvant trastuzumab and neratinib followed by neratinib monotherapy, and intensive anti-diarrhea prophylaxis*, is currently enrolling patients in conjunction with the University of California at San Francisco. The study is designed to evaluate crofelemer as a salvage anti-diarrheal therapy used with the investigational breast cancer agent neratinib. The primary objective is to characterize the incidence and severity of diarrhea in patients with early stage breast cancer receiving adjuvant trastuzumab and neratinib followed by 1 year of neratinib monotherapy in the setting of prophylactic anti-diarrheal management. The secondary objectives are to evaluate the activity of crofelemer as a rescue anti-diarrheal medication; to assess neratinib adherence, holds, delays, and early discontinuation throughout the course of study therapy. which includes patients receiving neratinib for >1 year; and to assess overall toxicity including constipation and cardiac toxicity with concomitant neratinib and trastuzumab.

Table of Contents

Irritable Bowel Syndrome diarrhea predominant (IBS-D)

Diarrhea is a common symptom of irritable bowel syndrome (IBS), a frustrating, underdiagnosed and undertreated condition. IBS-D is a subtype characterized mainly by loose or watery stools at least 25 percent of the time. According to the U.S. FDA, studies estimate that IBS affects 10 to 15 percent of adults in the United States.

Abdominal pain is the key symptom of IBS, and the pain, which is associated with a change in stool frequency or consistency, can be severe. To improve the diagnosis and outcomes for IBS patients and to update clinicians on the latest research, Dr. William Chey, a gastroenterologist and professor of medicine and nutrition sciences at the University of Michigan, along with an international team of collaborators, compiled *Rome IV*, a updated compendium of diagnostic criteria on functional GI disorders such IBS. *Rome IV* contains a chapter titled Centrally Mediated Disorders of Gastrointestinal Pain.

Although new agents for IBS-D have come on the market, there is an unmet medical need for long-term, safe management of the abdominal pain associated with IBS-D. Mytesi has been demonstrated to be safe for chronic use, and two studies provide statistically significant results of crofelemer use for abdominal pain in women.

The largest group of IBS sufferers are those with the subtype referred to as IBS-M (mixed diarrhea and constipation). IBS-M is also referred to as IBS-A, because the condition often involves frequent alternating between IBS-D and IBS-C (constipation predominant). IBS-M is distressing for patients as well as difficult to diagnose and manage, and is often associated with pain and urgency as well as significant abdominal distension and bloating. No approved drugs currently exist for IBS-M. Leading gastroenterologists have stated that IBS-C drugs may cause diarrhea in an IBS-M patient, and an IBS-D drug may cause significant constipation. We therefore believe an opportunity exists for an IBS-M indication for Mytesi. Resultingly, and due to the demonstrated safety of Mytesi for chronic use and its demonstrated benefit for abdominal pain in women, Napo is considering expanding development efforts to evaluate the IBS-M indication.

Clinical Study

Crofelemer has been tested in safety studies and two significant Phase 2 studies for IBS-D as detailed below. We recognize that patients suffering from IBS-D or IBS-M may require a polypharmacetuical approach to their lifetime management of the disease, and are therefore working to develop a low risk study designed to optimize efforts to develop an approved formulation to address these unmet medical needs.

Completed Studies IBS-D

Phase 2a a randomized double-blind placebo-controlled, dose-ranging (placebo, 125 mg, 250 mg, and 500 mg bid) study over a 12-week treatment period in 246 patients with d-IBS (Rome II criteria), including both males and females, whose average age was 50 years old.

n=245 subjects
61 placebo
62 125 mg crofelemer BID
59 250 mg crofelemer BID
62 500 mg crofelemer BID

IBS symptoms (pain, urgency, stool frequency and consistency, and adequate relief) were self-reported by the patients via an interactive voice response system. Patients needed to exhibit active disease during the two-week baseline period as defined by a mean daily stool frequency greater than or equal to 2/day, pain score greater than or equal to 1 and stool consistency greater than or equal to 3 (5-point Lickert scale for pain and consistency) to be enrolled. Patients received treatment for 12 weeks followed by a two-week treatment free period.

Table of Contents

The protocol-specified primary efficacy measure was daily stool consistency. Statistical analysis of the primary endpoint found no significant differences between placebo and any of the crofelemer dose groups ($p \geq 0.1434$) and no significant dose relationship was seen with regard to change from Baseline to Month 3 in stool consistency scores ($p = 0.1165$) in the ITT population.

A supplementary analysis of Rome Foundation-defined stool consistency and abdominal pain showed positive results. Responders were subjects who had stool consistency score of ≥ 4 for < 25% of days in a given week and ≥ 30% improvement in abdominal pain scores a given week (i.e., Rome Foundation-defined stool consistency and abdominal pain responders).

When we look at a supplemental analysis at a reduction in a composite abdominal pain/stool consistency endpoint, the regulatory endpoint in accordance with FDA guidance, we see at the 125 mg dose bid a significant 15% difference with just women patients compared to placebo; and a significant 11% when we include both men and women. The current D-IBS products on the market have a 7-8% reduction (Viberzi and Xifaxan).

In this analysis, Rome Foundation-defined stool consistency and abdominal pain responders were significantly more likely during the entire 3 months in the 125 mg BID group when compared with placebo (24.2% versus 13.1%, $p = 0.0399$) and there was a statistical trend in favor of crofelemer 125 mg BID during Months 1 through 2 (27.4% versus 16.4%, $p = 0.0640$). Similar positive effects of crofelemer 125 mg BID were observed in female subjects ($n = 183$). When the supplementary analysis was applied to the female patients, crofelemer at a dose of 125 mg BID was superior to placebo at Month 3 (26.1% vs 10.9%, p=0-0337).

Results: The 125mg bid of crofelemer exhibited a consistent response during each month among most efficacy endpoints in women with d-IBS reaching statistical significance ($p<0.05$) for pain.

Crofelemer had little effect on the stool consistency score, though there was a trend toward reduced stool frequency.

Treatment benefits were not apparent in men, although relatively few men enrolled in the trial (13-16/group).

As with previous trials of crofelemer, no drug-related serious adverse events were reported. Adverse event rates were similar across all dose groups, although in the two highest doses (250 and 500 mg bid) there were a higher percentage of dropouts. There were no drug-related or dose-related differences in constipation. During the two-week treatment-free follow-up period symptoms approached baseline levels.

Safety: Crofelemer at doses of 125, 250 and 500 mg had a safety profile that was generally similar to placebo among men and women with d-IBS.

Phase 2 A Randomized, double-blind, placebo-controlled study to assess the safety and efficacy of crofelemer for the symptomatic treatment of diarrhea predominant irritable bowel syndrome (d-IBS) in 240 female subjects 18 years or older with active d-IBS according to the Rome II criteria for the diagnosis of d-IBS.

The study consisted of a 2-week screening period and a 12-week blinded treatment period followed by a 4-week treatment-free follow-up period. During the 12-week treatment period 240 subjects were given 125 mg of crofelemer BID or placebo BID and recorded daily assessments of their IBS symptoms in the interactive voice response system.

The primary endpoint was the change from baseline for overall percentage of abdominal pain/discomfort free days (PFDs). On a daily basis, respondents recorded the intensity of their abdominal pain/discomfort for that day using the 5-pint Likert scale: 0=none, 1=mild, 2=moderate, 3=intense, 4=severe. Any day that a score of zero (0) was recorded was considered a PFD.

Table of Contents

Stool consistency and abdominal pain endpoints were analyzed using definitions of symptom improvement from a recent FDA guidance on IBS endpoints (March 2010) and recommendations of the Rome Foundation (letter dated 28 June 2010) concerning the IBS endpoints described in this guidance.

Results: The overall increase in pain-free days (protocol-specified primary endpoint) for subjects in the crofelemer group was not statistically significant when compared with subjects in the placebo group (p = 0.5107)

A supplementary analysis of abdominal pain showed positive results. Responders were subjects who had ≥ 30% improvement in abdominal pain scores a given week (i.e., FDA-defined abdominal pain responders; this definition of abdominal pain responders was presented in the March 2010 guidance on IBS endpoints).

In this analysis, abdominal pain responders were significantly more likely during Months 1 through 2 (58.3% versus 45.0%, p = 0.0303) and during the entire 3 months (54.2% versus 42.5%, p = 0.0371) in the crofelemer group when compared to placebo.

Safety: The overall safety profile for crofelemer 125 mg BID for 12 weeks was comparable to that observed with placebo and was consistent with the IBS population under study.

Rare pediatric disease indications: Congenital Diarrheal Disorders and Short Bowel Syndrome (SBS)

Congenital diarrheal disorders (CDD) are a group of rare, chronic intestinal channel diseases, occurring exclusively in early infancy, that are characterized by severe, lifelong diarrhea and a lifelong need for nutritional intake either parenterally or with a feeding tube. CDDs are related to specific genetic defects inherited as autosomal recessive traits, and the incidence of CDDs is much more prevalent in regions where consanguineous marriage is part of the culture. CDDs are directly associated with serious secondary conditions including dehydration, metabolic acidosis, and failure to thrive, prompting the need for immediate therapy to prevent death and limit lifelong disability.

Orphan Drug: Short Bowel Syndrome (SBS)

SBS is a complex condition characterized by malabsorption of fluids and nutrients due to congenital deficiencies or surgical resection of small bowel segments. Consequently, patients suffer from symptoms such as debilitating diarrhea, malnutrition, dehydration and imbalances of fluids and salts. This could be due to either a genetic disorder or premature birth. In countries such as the United Arab Emirates and Saudi Arabia, SBS occurs with much higher incidence. Napo recently visited with medical centers in this region.

Clinical Study CDD and SBS

We have completed safety studies of crofelemer in children as young as 3 months of age, and a proof-of-concept study is planned for the next year, initially at the Sheif kalifa Hospital in Abu Dhabi, which has many pediatric patients suffering from these diarrheal diseases. We have received orphan-drug status for Mytesi (crofelemer) for the SBS indication and are pursuing orphan-drug status for CDD. The mission of the FDA Office of Orphan Products Development is to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

IBD Supportive care:

Key opinion leaders ("KOLs") identified an unmet need to treat diarrhea in IBD patients, particularly in specific subsets of patients. KOLs felt all IBD patients who undergo ileal pouch-anal anastomosis (IPAA) surgery suffer severe, chronic diarrhea following the procedure. Because this is a

Table of Contents

highly-motivated patient population with a low placebo-responder risk, we believe a relatively small proof-of-concept trial is the appropriate next step from a development standpoint.

KOLs felt crofelemer's novel mechanism of action may also prove to be an effective treatment for diarrhea that results from bile acid malabsorption, which has been shown to occur in approximately 30% of patients with IBD.

Additionally, KOLs felt crofelemer's novel mechanism of action may prove to be an effective treatment for diarrhea experienced by patients receiving IV infusions of Entyvio, a Takeda Pharmaceuticals prescription medicine used in adults with moderate to severe ulcerative colitis or Crohn's disease. Secretory diarrhea occurs when the intestine does not complete absorption of electrolytes and water from luminal contents. This can happen when a nonabsorbable, osmotically active substance is ingested ("osmotic diarrhea") or when electrolyte absorption is impaired ("secretory diarrhea").

Secretory diarrhea can result from bacterial toxins, luminal secretagogues (such as bile acids or laxatives), reduced absorptive surface area caused by disease or resection, circulating secretagogues (such as various hormones, drugs, and poisons), and medical problems that compromise regulation of intestinal function. These studies in acute diarrhea support the normalizing aspect of the mechanism of action, regardless of the cause of the diarrhea, and are supportive of the supportive care indication under development in IBD patients.

Clinical Study

Completed Study Travelers' Diarrhea

Phase 2 a study of crofelemer in 184 persons in a double-blind, placebo-controlled study for the symptomatic treatment of acute diarrhea among travelers to Jamaica and Mexico.

The study was designed to evaluate the effectiveness of crofelemer in the treatment of travelers' diarrhea.

A total of 184 persons from the United States who acquired diarrhea in Jamaica or Mexico were enrolled in a double-blind, placebo-controlled study examining the effectiveness of three doses of crofelemer in reducing illness. Subjects were treated with 125 mg, 250 mg, or 500 mg crofelemer or a matching placebo four times a day for 2 days. Subjects kept daily diaries of symptoms and were seen each day for 3 days. Of the subjects, 169 (92%) were included in the efficacy analysis.

The most common etiological agent identified was enterotoxigenic Escherichia coli, found in 19% of subjects. The mean time interval from taking the first dose of medication until passage of the last unformed stool during 48-hour therapy (TLUS48) was 38.7 hours for the placebo group.

TLUS48 was shortened by crofelemer:

30.6 h for the 125-mg dose group ($p = 0.005$);
30.3 h for the 250-mg group; and
32.6 h for the 500-mg group ($p = 0.01$).

Treatment failures were seen in 29.3% in the placebo group compared with 7.3% ($p = 0.01$), 4.3 ($p = 0.002$), and 9.8 ($p = 0.026$) in the three treatment groups. Crofelemer was well tolerated at all doses.

The study provided statistically significant results of crofelemer use for shortening the duration of travelers' diarrhea. This antisecretory approach works directly against the pathophysiology of travelers' diarrhea and is not likely to potentiate invasive forms of diarrhea or to produce posttreatment constipation.

Table of Contents

Cholera/General Watery Diarrhea

According to the Centers for Disease Control and Prevention of the U.S. Department of Health & Human Services, Cholera is an acute, diarrheal illness caused by infection of the intestine with the bacterium *Vibrio cholerae*. An estimated 3-5 million cases and over 100,000 deaths occur each year around the world. The infection is often mild or without symptoms, but can sometimes be severe. Approximately one in 10 (5-10%) of infected persons will have severe disease characterized by profuse watery diarrhea, vomiting, and leg cramps. In these people, rapid loss of body fluids leads to dehydration and shock. Without treatment, death can occur within hours. At this time, for example, the largest cholera outbreak in recorded history is occurring in Yemen.

We are investigating SB-300 for the indication of cholera/general watery diarrhea. SB-300 is a distinct and proprietary Napo pharmaceutical formulation of a standardized botanical extract, also sustainably derived from the *Croton lechleri* tree. We believe SB-300 represents a long-term pipeline opportunity as a second-generation anti-secretory agent, on a global basis, for multiple gastro-intestinal diseases. Additionally, we believe SB-300, which has the same mechanism of action as crofelemer and is less costly to produce, may support efforts to receive a priority review voucher from the U.S. FDA for a cholera indication. Priority review vouchers are granted by the FDA to drug developers as an incentive to develop treatments for neglected diseases and rare pediatric diseases. If approved for this indication, SB-300 could serve as long-term pipeline anti-secretory agent for cholera/general watery diarrhea in geographies where cost of goods is a critical factor, for example, in resource-constrained regions and countries in which a requirement exists for drug prices to decrease annually.

Clinical Study

We have initiated CMC and have multiple animal and a human studies in secretory diarrheas with SB-300. We have also completed a successful trial design for cholera with an anti-secretory mechanism of action, published studies with crofelemer in patients with cholera and other acute severe watery diarrhea disease.

Completed Studies Cholera and Severe Acute Dehydrating Watery Diarrhea

Phase 2 study of crofelemer in the treatment acute, severely dehydrating watery diarrhea with confirmed cholera with the use of an antibiotic (azithromycin) and oral rehydration therapy in 100 adult patients between 18 and 55 in Bangladesh.

A total of 100 adult patients, from Bangladesh, between the ages of 18 and 55, with acute, severely dehydrating watery diarrhea with confirmed cholera were treated with crofelemer on a background of an antibiotic (azithromycin) and oral rehydration therapy. After a four hour period of rapid rehydration therapy, patients were randomized 1:2:2 to placebo or 125 mg or 250 mg oral dose of crofelemer. Crofelemer or placebo doses were administered about one hour after the oral administration of azithromycin (1 gm dose). The primary objective was to evaluate the safety and effects of crofelemer on reducing the watery stool output normalized to body weight (mL/kg) in the first 24 hours on the background of azithromycin and rehydration therapy. Crofelemer was well tolerated and there were no drug related adverse events in this study. Both doses of crofelemer produced approximately 25-30% reduction in median watery stool volumes in the 0-6 and 0-12 hour period following initiation of therapy. Crofelemer showed a strong trend in the reduction of watery stool output in the 0-6 hour and 0-12 hour intervals (p=0.07). Upon exclusion of three outlier patients, the crofelemer dose of 125 mg produced a statistically significant reduction in the normalized stool output (p=0.028) and the dose of 250 mg crofelemer showed a strong trend for reduction of watery stool output (p=0.07).

In another study, the effects of crofelemer were evaluated in patients with acute dehydrating watery diarrhea caused by various bacterial pathogens, such as enterotoxic strains of Escherichia coli (ETEC) and Vibrio cholerae infection. Crofelemer was evaluated in adult Indian patients with acute

Table of Contents

watery diarrhea of less than 24 hour duration with suspected bacterial infections, without the use of antibiotics. In this study, patients received oral doses of placebo or crofelemer at a dose of 250 mg every 6 hours for 2 days on the background of oral rehydration therapy only. The use of antibiotics was prohibited in this study. A total of 98 patients were randomized into this study (47 in placebo group and 51 in the crofelemer group). Primary endpoints for this study were changes in stool weight, frequency, consistency, duration of diarrhea. Secondary endpoints included the assessment of clinical symptoms scored as total of 7-item GI index. Clinical success was defined as no diarrhea within 48 hrs from study start date and treatment failure was defined as no improvement/worsening of symptoms after 24 hrs, fever, bloody stools or dehydration.

Results: 98 patients (51 crofelemer, 47 placebo) were enrolled in the study. 16 patients (4 in the crofelemer group and 12 in the placebo group) used antibiotics and were considered as treatment failures and were excluded from the "per protocol efficacy analysis". Groups were similar in age, weight, vital signs, stool frequency, consistency, dehydration and GI index.

The crofelemer group had improvement over baseline and compared to placebo at day 3. More specifically, crofelemer showed superior effects in reducing stool weight (61% vs 11%), stool frequency (65% vs 21%), reversion to soft stool (92% vs 49%) and improved the 7-item GI index (70% C vs 33% P), (all $p<0.05$).

Crofelemer was well tolerated with no related serious adverse events or concerning changes in lab values. Progression to dehydration and report of fecal incontinence was more common in placebo group ($p<0.05$).

Conclusions: Clinical success (cessation of diarrhea within 48 hrs of 1st dose) was achieved in 79% of crofelemer patients compared to 28% placebo patients ($p<0.05$).

Other Human Product Potential Future indications

Institutional Diarrhea

Patients in medical institutions such as hospitals often experience diarrhea following infection with *Clostridium difficile*, an anaerobic bacillus shed in feces. According to the Centers for Disease Control and Prevention of the U.S. Department of Health & Human Services, any surface, device, or material (e.g., commodes, bathing tubs, and electronic rectal thermometers) that becomes contaminated with feces may serve as a reservoir for the *C. difficile* spores, which are transferred to patients mainly via the hands of healthcare personnel who have touched a contaminated surface or item. We believe development of an approved formulation of crofelemer for use in *C. difficile* has the potential to help patients infected with *C. difficile* leave the hospital sooner, help keep patients infected with *C. difficile* out of the hospital, and aid in controlling *C. difficile* contagion in institutional settings, which would also represent a significant economic benefit.

Animal Products in Development

Portfolio planning for the animal health space is of utmost importance to us, given the wide array of potential species-specific products and because we do not want animal-related research and development activities to divert significant financial resources while we are focusing on growing Mytesi sales and seeking to move our company towards profitability. Additional formulations and additional animal product expenditures will be considered from time to time as part of portfolio planning and prioritization in the context of the combined company.

Canalevia is our lead prescription drug product candidate, intended for the treatment of various forms of diarrhea in dogs. Equilevia is our personalized product candidate for total gut health in high performance equine athletes. Canalevia and Equilevia contain ingredients isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Neonorm Calf and Neonorm Foal are our lead

Table of Contents

non-prescription products. Neonorm is a standardized botanical extract derived from the *Croton lechleri* tree, which is also provided as a botanical extract for piglets and dairy calves in China under an exclusive distribution agreement. 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 Equilevia and Neonorm as a non-prescription products due to differences between the companion, horse and production animal markets. Owners of companion animals generally visit veterinarians, who prescribe a product to treat a disease or condition. We believe the ability to make a disease treatment claim is important in this market, and such a claim is only possible with FDA approval as a prescription product. In contrast, dairy farmers and other production animal owners generally make purchasing decisions based on a product's ability to demonstrate an economic benefit from health endpoints, such as weight gain. Owners and trainers of high end equine athletes review clinical data and are seeking products tailored to their specialized training and husbandry practices to optimize the health and performance.

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 also have a pipeline of prescription drug product candidates for diabetes and metabolic syndrome for dogs, cats and horses, as well as a topical herpes product for cats. As with our lead prescription drug product candidate, these products candidates 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.

The equine athlete business continues to be a major focus area for the animal health side of our business. The demand, particularly in the Middle East, for a "total gut health" product for high performance equine athletes appears to be quite strong, and we believe this is indicative of an unmet medical need. Based on this demand, and with support from studies we conducted in horses with gastric ulcers a prevalent problem in competing horses and also horses with diarrhea, we have transitioned development of Equilevia to a create a non-prescription, personalized, premium proprietary product for total gut health in equine athletes. Gut health is of critical importance in horses, as conditions such as colic can lead to the death of an otherwise healthy horse in a matter of hours. Although we are still assessing the size of the opportunity represented by this self-funded program, we expect to begin generating revenue from the sale of Equilevia in the fourth quarter of 2017.

To date, our non-prescription animal health products have generated approximately $206,805 in net revenue in 2017.

As we announced on January 31, 2017, we signed an agreement with Elanco US Inc., a subsidiary of Eli Lilly and Company, to license, develop, co-promote and commercialize Canalevia for treatment of acute diarrhea in dogs. The agreement grants Elanco exclusive global rights to Canalevia for use in companion animals. We and Elanco will collaborate on the global development of the product and on its commercialization in the US. We have received Minor Use in a Minor Species (MUMS) designation for Canalevia for CID in dogs. The FDA has indicated that the use of Canalevia for the treatment of EID in dogs qualifies as a "minor use", which means that Canalevia is eligible for conditional approval for the indication of EID in dogs. Under the terms of the agreement with Elanco, we have retained the

Table of Contents

commercial responsibility for the CID and EID indications of Canalevia in dogs. We expect to conduct the commercial launch of Canalevia for CID and EID in dogs in the first half of 2018. This is expected to be the first prescription product approval for Jaguar's animal health product development program. On November 1, 2017, we received a letter from Elanco serving as formal notice of Elanco's decision to terminate the Elanco Agreement by giving us 90 days written notice. Pursuant to the terms of the Elanco Agreement, termination of the Agreement will become effective on January 30, 2018, which is 90 days after the date of the letter. On the effective date of termination of the Elanco Agreement, all licenses granted by us to Elanco under the Elanco Agreement will be revoked and the rights granted thereunder revert back to us.

Canalevia is a canine-specific formulation of crofelemer, and as such the CMC development of this product has benefited from the regulatory approval of Mytesi and the supply chain and quality system that supports the commercial distribution of Mytesi.

Neonorm is a standardized botanical extract derived from the *Croton lechleri* tree. We launched Neonorm Calf in the United States at the end of 2014. The reception among users of Neonorm Calf and Neonorm Foal has been quite positive. The clinically-proven performance of Neonorm Foal, in combination with our heightened understanding of market needs within the global equine space, is driving our increased focus on developing a full suite of equine products to support and improve gastrointestinal health in foals and adult horses. Gastrointestinal conditions such as acute diarrhea, ulcers and diarrhea associated with acute colitis can be extremely debilitating for horses, and present a significant economic and emotional burden for veterinarians and owners around the world. Equilevia (formerly referred to as SB-300) is our personalized product for total gut health in equine athletes.

As we announced in December 2016, we have signed a distribution agreement with Henry Schein, Inc., the world's largest provider of health care products and services to office-based dental, animal health and medical practitioners, for exclusive distribution of Neonorm Foal product to all segments of the U.S. equine market. Henry Schein's animal health business, Dublin, Ohio-based Henry Schein Animal Health, employs approximately 900 team members and had 2015 net sales of $2.9 billion. The agreement became effective on December 9, 2016, and, subject to provisions specified in the agreement, shall continue in force for an initial period of one year. Thereafter, unless either party notifies the other of its intent not to renew the term of the agreement at least 30 days prior to the end of the then current term, the term shall be automatically renewed upon expiration for successive renewal terms of one year.

In July 2016 we released data from two China-based studies sponsored by Fresno, California-based Integrated Animal Nutrition and Health Inc. showing remarkable resolution of diarrhea and cure of piglets afflicted with diarrhea following treatment with a *Croton lechleri* botanical extract administered in water. As we announced in September 2016, we signed an exclusive supply and distribution agreement for this botanical extract with Integrated Animal Nutrition and Health Inc. for dairy cattle and pigs in the Chinese marketplace. According to Index Muni, swine production is projected to reach 672.5 million head in 2017 in China, where pork is still the main protein source for many consumers. According to New Zealand-based NZX Agri, in 2017 there will be 7 million cows "in milk" (lactating cows) in China. With the world's largest population, China 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. Integrated Animal Nutrition and Health, Inc. has minimum purchase requirements of the botanical extract to maintain their exclusivity.

As we announced on February 2, 2017, we have begun entry into the organic market with Neonorm Calf, following listing of Neonorm Calf with an organization that evaluates livestock products in accordance with the U.S. Department of Agriculture (USDA) National Organic Standards on behalf

Table of Contents

of specified producers in New York state. Additionally, we are applying to have Neonorm Calf listed by the Organic Materials Review Institute (OMRI). OMRI is an international nonprofit organization that determines which input products are allowed for use in organic production and processing. OMRI Listed® products are allowed for use in certified organic operations under the USDA National Organic Program. According to the Organic Trade Association's (OTA) 2016 Organic Industry Survey, the U.S. organic industry posted new records in 2015, with total organic product sales hitting a new benchmark of $43.3 billion, up 11% from the previous year's record level and outpacing the overall food market's growth rate of 3%. According to OTA, dairy, the second biggest organic food category, accounted for $6.0 billion in sales, an increase of over 10%, and dairy accounts for 15% of total organic food sales.

Organic livestock production plays a vital role in support of a sustainable and safe farm and food system, both in the U.S. and internationally. According to a report published by Allied Market Research, the global market for organic dairy food and drinks organic milk, yogurt, cheese, and others is expected to grow at a compound annual growth rate of 14.25% from 2016 to reach $36.7 billion by 2022 from $14.5 billion in 2015. We believe Neonorm Calf will qualify as allowable for use on certified organic dairies throughout the U.S., and we are currently working to obtain additional required listings.

Through the Merger, we have access to Napo's intellectual property rights and technology, including rights to Napo's 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.

Animal Product Pipeline

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

Jaguar Animal 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	Commercial launch in first half of 2018
			Received MUMS designation	
	Dogs	EID		
			Completed safety study with commercial formulation in June 2015	Commercial launch in first half of 2018
			Received MUMS designation	

Table of Contents

Product Candidates	Species	Indication	Recent Developments	Anticipated Near-Term Milestones
	Dogs	General diarrhea		
			Concurred protocol	Program specifics funded by Elanco, including initiating development of second generation flavored chew formulation
			Initiated pivotal field trial to evaluate safety and effectiveness	
			Entered into License, Development, Co-Promotion and Commercialization Agreement with Elanco in January 2017	
Species-specific formulations of crofelemer	Cats	General diarrhea		
			INAD opened in 2014	Program specifics funded by Elanco
			Entered into License, Development, Co-Promotion and Commercialization Agreement with Elanco in January 2017	
Virend (topical)	Cats	Herpes virus		
			INAD opened in 2014	Subject to future portfolio planning and prioritization
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	

Table of Contents

Jaguar Animal Non-Prescription Products

Products	Species	Use	Recent Developments	Anticipated Near-Term Milestones
Equilevia	Horses	Total gut health		
			Proof-of-concept safety and effectiveness results in January 2016 for gastrointestinal ulcers	Finalize formulation and conduct commercial launch in Q4 2017
Neonorm Calf	Dairy & beef calves	Helps proactively retain fluids in calves aiding the animals in avoiding debilitating, dangerous levels of dehydration	Positive racing results	Launch second generation formulation for administration in liquid, prophylaxis in Q2 2018
			Field study supports beneficial effect on prewean weight gain	Commercial launch and business development activities in selected international geographies in the first half of 2018
			Positive prophylactic results	
			Distribution deal China	
Species-specific formulations of Neonorm	Horse foals	Anti-diarrheal for newborn horses		
			Completed proof-of-concept study in November 2015	Evaluation of Neonorm Horse product
			Soft-launched product in December 2015	
			Commercial launch with exclusive Henry Schein distribution deal at AAEP, 2016	
	Piglets	Normalize fecal formation in piglets		
			Positive preliminary topline results of two studies by Integrated	Expansion of distribution in China

		Animal Nutrition and Health Inc. to evaluate the safety and effectiveness of Neonorm in piglets	
Other farm/production animals	Supports gut health normalizing fecal formation	Selected clinical research	Initiate proof-of-concept studies and partnering discussions, multiple species; multiple geographies, subject to future portfolio planning and prioritization

Table of Contents

Market Background

Canalevia Chemotherapy-Induced Diarrhea (CID) and Exercise Induced Diarrhea (EID) in Dogs

Overview

Canalevia is a three-day, twice-daily formulation of crofelemer that we are developing for the treatment of CID in dogs. Canalevia is enteric-coated for targeted release of crofelemer, the active pharmaceutical ingredient, or API, in Canalevia, in the intestine. We have received MUMS designation for Canalevia for the treatment of CID in dogs, which provides an opportunity to shorten the timeframe to commercialization. We have received Minor Use in a Minor Species (MUMS) designation for Canalevia for CID in dogs. The FDA has indicated that the use of Canalevia for the treatment of EID in dogs qualifies as a "minor use", which means that Canalevia is eligible for conditional approval for the indication of EID in dogs. In June 2015 we completed a multi-site pilot safety study involving the anticipated commercial formulation of Canalevia for CID and EID. We will have completed submission of all required major technical sections for the NADA for CID to the FDA for phased review by the end of December. We expect to receive FDA acknowledgment of the completion of all required technical sections in support of conditional approval of Canalevia in 1H, 2018 for CID and EID in dogs. Under MUMS designation, we would be required to initiate a pivotal study in the five years following conditional approval to generate the data required for full approval.

Market Opportunity

We believe there is an important unmet medical need for the treatment of CID and EID in dogs.

CID: There is currently no FDA-approved anti-secretory product that we are aware of to treat CID in dogs. We estimate that there are over 230,000 dogs receiving chemotherapy treatment for cancer each year in the United States, with over 25% suffering from CID. Severe diarrhea is a frequent side effect of the most commonly administered chemotherapy drugs. Similar to the effects in humans, we believe that if left untreated, CID in dogs can result in:

- fluid and electrolyte losses, which can cause dehydration, electrolyte imbalance and renal insufficiency;
- nutritional deficiencies from alteration of gastrointestinal transit and digestion; and
- increased risk of infectious complication.

Efficacy of the underlying cancer treatment may also be jeopardized if CID severity requires reductions in the absorption, frequency and/or dosage of chemotherapy. From the dog owner's perspective, there are significant practical implications of CID in dogs that may affect living arrangements, as well as the cost, time and attention required to clean and care for the dog and its surroundings on a daily basis. Veterinarians sometimes prescribe human drugs in an effort to treat CID in dogs, but do not have the benefit of clinical support with respect to efficacy or dosing. In addition, administering a potentially unpalatable human formulation is often difficult and may lead to further uncertainty of the amount actually ingested by the dog.

EID is a distinct physiological manifestation that has been recorded in dogs, humans and horses. EID may occur before, during or after sustained physical exertion. EID is a common problem among working dogs, such as sled dogs and military dogs, when subjected to periods of intense, long-duration exercise off-leash. Several mammalian species that physically train and run in competitive events can push themselves to extreme physical demands. At this highest level of physical exertion, secretory diarrhea is a common result, and the diarrhea can be debilitating enough to require medical attention and removal from competition or training. Diarrhea can have serious consequences for the canine athlete due to their high capacity for metabolic heat generation and reliance on evaporative cooling to dissipate that heat.

Table of Contents

Our Solution

We believes that Canalevia is an ideal treatment for both CID and EID in dogs because of its demonstrated novel anti-secretory mechanism of action. Canalevia acts locally in the gut and is minimally absorbed systemically. It does not alter gastrointestinal motility, has no significant effects on normally functioning intestinal ion channels and electrolyte or fluid transport, and has no side effects different from placebo. With regard to CID, these features are further augmented by Canalevia's lack of effects on the absorption and/or metabolism of co-administered chemotherapy drugs, orally or by other routes of administration. Canalevia acts by normalizing the flow of excess ions and water in the intestinal lumen. The flow of excess ions and water into the intestinal lumen is the last step common to the manifestation of acute diarrhea. As a result, we believes Canalevia may be effective in the treatment of acute diarrhea, regardless of cause, including CID and EID.

Canalevia General Watery Diarrhea in Dogs

Market Opportunity

Diarrhea is one of the most common reasons for veterinary office visits for dogs and the second most common reason for visits to the veterinary emergency room, yet there are currently no FDA-approved anti-secretory agents we are aware of to treat the indication.

Veterinarians typically treat general watery diarrhea in dogs with antibiotics, probiotics, dietary restrictions and products approved and formulated for humans, such as Imodium and other anti-motility agents, as well as binding agents that absorb water such as Kaopectate and Pepto-Bismol. None of these treatment options address the water loss associated with acute diarrhea. Further, because none of the human products are FDA approved for animal use, veterinarians do not have the benefit of clinical support with respect to efficacy or dosing. Moreover, administering a potentially unpalatable human formulation is often difficult and may lead to further uncertainty of the amount actually ingested by the dog.

We believe that Canalevia is an ideal treatment for general watery diarrhea in dogs because of its demonstrated novel anti-secretory mechanism of action. If approved for use in general watery diarrhea in dogs, we believe Canalevia will be the only FDA-approved anti-secretory agent to treat diarrhea in dogs.

Equilevia

The equine athlete business continues to be a major focus area for the animal health side of our business. The demand, particularly in the Middle East, for a "total gut health" product for high performance equine athletes appears to be quite strong, and we believe this is indicative of an unmet medical need. Based on this demand, and with support from studies we conducted in horses with gastric ulcers a prevalent problem in competing horses and also horses with diarrhea, we have transitioned development of Equilevia to a create a non-prescription, personalized, premium proprietary product for total gut health in equine athletes. Gut health is of critical importance in horses, as conditions such as colic can lead to the death of an otherwise healthy horse in a matter of hours. Although we are still assessing the size of the opportunity represented by this self-funded program, we expect to begin generating revenue from the sale of Equilevia in the fourth quarter of 2017.

Ulcers are lesions of the lining of the digestive tract and are very common in horses used for many competitive activities. *Croton lechleri*-derived products have been shown to act locally in the gut and have traditional use and rodent model benefit for ulcers, and we have generated clinical data for Equilevia in race horses with ulcers.

Table of Contents

Equine gastric ulcer syndrome ("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.

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 our investigational new animal drug, Equilevia, for the treatment of EGUS in horses.

In this prospective, blinded, randomized, negative controlled study, Standardbred or Thoroughbred racehorses were randomized to one of three groups (10 horses per group) and treated for 28 days: horses in the placebo group received water-filled syringes every 6 hours; those in the TRT5 group received 5 grams of Equilevia divided into 2 doses per day; and those in the TRT40 group received 40 grams of Equilevia divided into 4 doses per day. Strict enrollment criteria required patients to have both squamous (non-glandular) and glandular gastric ulcerations. All horses were examined by gastroscopy (stomach endoscope) by blinded equine investigators on Day 0 (prior to treatment; baseline), and on Day 14 (mid-study), Day 28 (last day of treatment) and Day 35 (7 days after last treatment). Treatment-related adverse events were not observed.

With respect to glandular ulcerations, a statistically significantly greater number of horses in both the TRT40 (89%) and the TRT5 (78%) group had an improvement or a resolution of glandular ulcerations, compared with the placebo (25%) group as soon as Day 14. By Day 35, all of the Equilevia treated horses had experienced improvement or resolution, whereas 25% of horses in the placebo group still had not improved or resolved during the study.

With respect to squamous ulcerations, a non-statistically significant dose-dependent effect was observed with 40% and 33% of horses achieving an improvement or a resolution by Day 14 in the TRT40 and TRT5 groups, respectively, compared with 11% of placebo horses. By Day 35, numerically more horses in the TRT40 (60%) and TRT5 (55%) groups had achieved an improvement or a resolution compared with 33% of placebo horses.

In February 2016 we announced that further analysis of the study results indicated that Equilevia did not alter gastric pH during the trial, or for 7 days after therapy. Gastric pH during therapy was observed to be similar to baseline gastric pH at all measured study time points. Whereas other ulcer treatments (e.g. proton pump inhibitors like omeprazole) rely on a mechanism of action that blocks gastric acid secretion for the treatment and prevention of EGUS, our preliminary data indicate that Equilevia may have advantages. Treatments for EGUS that do not alter gastric pH are important because maintaining low gastric pH is essential for digestion, for gut immunity and first line defense against pathogens, for the absorption of vitamins and minerals, and for potentially other downstream effects.

In April 2016, we announced that standard drug testing in race horses having received Equilevia did not detect any substances commonly disallowed by horse racing authorities. The results of this initial study show that Equilevia may offer horse owners an additional advantage in the competition horse world, where requirements exist for animals to compete free from the effect of any drugs. Future work is being planned to confirm these results. The study also provided visual evidence suggesting that feed does not interfere with the product candidate's local availability in the gut.

Table of Contents

Equilevia may offer horse owners an additional advantage over omeprazole in the competition horse world, where the requirement exists for equine athletes to compete free from the effect of any drugs. International screening limits for horse racing state that omeprazole has a 72-hour detection time. Detection time is defined as the first observed time point at which urine and/or plasma samples collected from a horse are negative for the presence of a specified drug. Because Equilevia acts locally in the gut and is minimally absorbed, it is unlikely that use of this drug product candidate will present any issues related to detection time. We intend to demonstrate that Equilevia is not systemically absorbed in horses, thereby providing a treatment regimen that can continue without mandatory withdrawal prior to competition. Moreover, we also aim to demonstrate that Equilevia can be administered in the presence of feed, another constraint of omeprazole administration.

The U.S. patent for use of omeprazole to treat equine ulcers expired in 2015 thereby subjecting manufacturers of omeprazole to greater competition.

Until recently, treatment recommendations for equine ulcers have not differentiated between squamous and glandular disease. However, a series of recent third-party studies indicate considerably lower healing rates for glandular ulcers with standard of care (e.g. omeprazole). Subclinically, these lesions can compromise athletic performance.

We completed a dose determination study of the target commercial paste formulation of Equilevia in the fourth quarter of 2016. The equine veterinarians who performed the study were blinded to the treatment assignment, and we were also blinded to the data at that time. A full analysis of the study data with scoring of squamous and glandular ulcers has undergone independent, blinded review by Dr. Frank Andrews, DVM, MS, Dipl. ACVIM, Professor and Director of the Equine Health Studies Program at Louisiana State University College of Veterinary Medicine, an equine internist specializing in gastric ulcer disease.

As we announced on March 28, 2017, the third-party review Dr. Andrews conducted of the study data involved viewing gastroscopy videos for all participating horses and evaluating each horse against three separate EGUS grading scales: the McAllister scoring system (which assesses the number and severity of ulcers), the EGUS Council scoring system (which is relevant only for squamous ulcers), and a new visual analog scoring system, relevant for both squamous and glandular ulcers, developed by Dr. Andrews. This study showed consistency in the evaluation of gastric ulcers by the newly developed visual analog scoring system compared to the published McAllister and EGUS Council grading scales, and the visual analog scoring system could be an important tool in providing greater precision in gastric ulcers of differing tissue type, such as glandular lesions.

Our goal is to see Equilevia serve as an important tool for total gut health in high performance equine athletes.

Crofelemer Cats

According to the American Veterinary Medical Association, there were approximately 74.0 million cats in the United States in 2012. We estimate that veterinarians see approximately 2.9 million annual cases of acute diarrhea in cats. Veterinarians typically treat acute diarrhea in cats with the same treatments used for dogs, namely antibiotics, probiotics, dietary restrictions and products approved and formulated for humans, such as Imodium and other anti-motility agents, as well as binding agents that absorb water such as Kaopectate and Pepto-Bismol.

We are currently developing a species-specific formulation of crofelemer, Felevia, for cats. We intend to initiate safety and proof-of-concept studies in cats in 2017.

Table of Contents

Neonorm Calf Helps proactively retain fluids in dairy and beef calves aiding the animals in avoiding debilitating, dangerous levels of dehydration

Overview

This formulation of Neonorm is an enteric-coated tablet designed to be orally administered to preweaned dairy and beef calves twice daily for three days.

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.

In 2014 we launched Neonorm for preweaned calves in the United States under the brand name Neonorm Calf. We do not believe that Neonorm Calf fits within the FDA's definition of an animal drug, food or feed additive. Thus, we do not believe that it is regulated by the FDA at this time. The FDA previously regulated a human-specific formulation as a dietary supplement, rather than as a drug. To support the commercial launch, we completed field studies of Neonorm Calf involving approximately 400 preweaned dairy calves in total with Cornell University and in collaboration with its distributor, Animart.

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.

We are developing a second generation Neonorm Calf product formulation to be administered in liquid for total head prophylactic management of diarrhea, or scours. In January 2016 we announced the initiation of a placebo-controlled study in conjunction with researchers from Cornell to evaluate the efficacy of the prophylactic use of a second-generation formulation of Neonorm Calf administered in liquid on naturally occurring diarrhea and dehydration in preweaned dairy calves and investigate the possible prebiotic benefit of the product. This double-blinded, randomized study involved 40 Holstein bull calves affected with naturally occurring diarrhea. The study results, announced in June and September of 2016, show that calves under prophylactic administration of Neonorm Calf had significantly lower water content in fecal samples at multiple measurement points, lower incidence of diarrhea, and had fewer fluid therapy interventions. A paper on this study, titled "Prophylactic use of a standardized botanical extract for the prevention of naturally occurring diarrhea in newborn Holstein calves", was published in the official journal of the American Dairy Science Association, *Journal of Dairy Science* a leading peer-reviewed general dairy research journal.

Scours Market Opportunity

Scours refers to watery diarrhea in production animals, including dairy calves, which results from infectious agents that cause the secretion of ions and water into the intestinal lumen. Animals with scours may experience severe dehydration and electrolyte imbalance, which can lead to renal insufficiency, nutritional deficiencies, lower production in dairy cattle and even death. Current therapy

Table of Contents

includes fluid and electrolyte replacement, continuous milk feeding, antibiotics (for calves with systemic involvement (*e.g.*, fever) with an increased risk of bacteremia), non-steroidal anti-inflammatory drug therapy and vaccines.

According to the USDA, there are approximately 9.2 million lactating dairy cows in the United States. We estimate from USDA sources that there were over 11.0 million dairy calves born in 2013. Dairy cows are continuously bred, both to maintain lactation and to produce dairy calves to maintain the herd. Dairy calves are separated from their mothers shortly after birth and raised on commercial milk replacers until weaned at about 60 days of age. Almost one in four, or 23.9%, of dairy heifer calves had diarrhea or other digestive problems according to the USDA *Dairy 2007* study. Scours, diarrhea or other digestive problems are responsible for more than half of all preweaned calf deaths, and result in supportive care and treatment costs, impaired weight gain and long-term reduction in milk production. Of dairy farm operations surveyed in the *Dairy 2007* study, 62.1% used antibiotics for diarrhea or other digestive problems, including preweaned heifer calves not reporting diseases or disorders. Of preweaned calves that were affected by diarrhea or other digestive problems, almost three-fourths, or 74.5%, were treated with an antibiotic.

Our Solution

We believe Neonorm Calf is an ideal solution to aid fluid retention in dairy and beef calves suffering from scours. Neonorm Calf has been formulated and clinically tested to support fluid retention by specifically addressing the normalization of stool formation and ion and water flow in the intestinal lumen of newborn dairy calves with scours. There are an estimated 22.0 million beef calves in the United States, and published sources indicate that approximately 2.4% of beef calves younger than three weeks old suffer from diarrhea. Like Canalevia, Neonorm Calf acts locally in the gut and is minimally absorbed systemically. It does not alter gastrointestinal motility, has no significant effects on normally functioning intestinal ion channels and electrolyte or fluid transport, and has no side effects different from placebo. As a result, stool formation is normalized in a short period of time, weight loss is mitigated, supportive care costs and rehydration therapies such as ORS are reduced, and the risk of mortality is minimized.

Clinical Data

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.

We recently completed a placebo-controlled study in conjunction with researchers from Cornell to evaluate the herd-wide efficacy of the prophylactic use of a second-generation formulation of Neonorm Calf administered in liquid on naturally occurring diarrhea in preweaned dairy calves and investigate the possible prebiotic benefit of the product. This double-blinded, randomized study involved 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. The possible beneficial prebiotic mechanism of Neonorm Calf would supplement and is potentially synergistic with the anti-secretory and weight gain benefits of the product.

Table of Contents

Fecal scoring, which was conducted daily during the study period, indicated a significantly lower incidence of diarrhea among Neonorm-treated calves on most treatment days than among calves in the placebo group. The study also assessed the incidence of diarrhea from days 1 to 25 of life. Calves in the Neonorm-treated group experienced a highly significant reduction in the incidence of diarrhea during this period compared to those in the placebo group.

Dehydration was assessed twice daily for all calves in the study. Results showed that severe dehydration requiring the administration of intravenous ("IV") fluid therapy was reduced by approximately 50% in the Neonorm-treated calves. Moreover, overall rescue therapy, requiring either oral or IV fluid administration, for both severe and moderate dehydration, was significantly reduced in the Neonorm-treated animals.

As we announced on February 2, 2017, we have begun entry into the organic market with Neonorm Calf, following listing of Neonorm Calf with an organization that evaluates livestock products in accordance with the U.S. Department of Agriculture (USDA) National Organic Standards on behalf of specified producers in New York state. Additionally, we are applying to have Neonorm Calf listed by the Organic Materials Review Institute (OMRI). OMRI is an international nonprofit organization that determines which input products are allowed for use in organic production and processing. OMRI Listed® products are allowed for use in certified organic operations under the USDA National Organic Program. According to the Organic Trade Association's (OTA) 2016 Organic Industry Survey, the U.S. organic industry posted new records in 2015, with total organic product sales hitting a new benchmark of $43.3 billion, up 11% from the previous year's record level and outpacing the overall food market's growth rate of 3%. According to OTA, dairy, the second biggest organic food category, accounted for $6.0 billion in sales, an increase of over 10%, and dairy accounts for 15% of total organic food sales.

Organic livestock production plays a vital role in support of a sustainable and safe farm and food system, both in the U.S. and internationally. According to a report published by Allied Market Research, the global market for organic dairy food and drinks organic milk, yogurt, cheese, and others is expected to grow at a compound annual growth rate of 14.25% from 2016 to reach $36.7 billion by 2022 from $14.5 billion in 2015. We believe Neonorm Calf will qualify as allowable for use on certified organic dairies throughout the U.S., and we are currently working to obtain additional required listings.

Neonorm Line Extensions

We believe that due to Neonorm Calf's mechanism of action and its data in preweaned dairy calves, we will be able to develop and commercialize species-specific formulations of Neonorm for multiple other animal species, such as horses, goats and sheep. We believe that there is an opportunity to target large-scale commercial livestock operations, first in the United States, and later, internationally. In less developed nations, where not only dairy and beef cattle but also buffalo, goat and sheep provide livelihoods for local populations, reducing losses related to diarrhea can provide significant monetary, social and health benefits. Today, these groups are already accessed by distributors with whom we intend to work to extend the reach of Neonorm Calf and line extension products.

In November 2015 we completed an initial proof-of-concept study (NEO101) of Neonorm Foal, our lead non-drug product to promote normal fecal formation and reduce fluid loss in foals, 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, which both took place in Argentina, demonstrated a significantly higher percentage of foals

Table of Contents

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 in early 2016 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.

In December 2015 we conducted the soft launch of Neonorm Foal. We are planning studies of an equine formulation of Neonorm for adult horses with episodic diarrhea. Published studies estimate that there were 9.2 million horses in the United States in 2005. Diarrhea is among the most common clinical complaints in foals. Often, diarrhea occurs in the first 30 days of the foal's life, both from infections and non-infectious causes, such as lactose intolerance and overfeeding. Some cases are severe and life threatening. A majority of foals will exhibit diarrhea at some point within the first two months of life. In adult horses, episodic diarrhea is mostly associated with diseases of the large intestine and damage to the colon or disturbance of colonic function. Typically, diarrhea in horses is treated with fluid replenishment and electrolytes, deworming agents and antibiotics, and intestinal protectants and absorbents, as well as anti-motility agents. To our knowledge there are currently no anti-secretory products approved by the FDA for veterinary use.

Other Animal Product Candidates and Development

We have planned multiple clinical studies over the next 12 to 18 months to expand Canalevia and Neonorm to additional species. We believe that we will be successful because:

- We have existing safety and efficacy data for our products and product candidates in dogs, dairy calves and/or humans;
- each of these products works through the normalization of ion and water flow into the intestinal lumen; and
- this physiological pathway is generally present in mammals.

Additionally, we plan to initiate a safety and proof of concept study for Virend in 2017. Both Virend and NP-500 have been through Phase 2 human clinical testing by third parties and studies with combinations of rifaximin and *Croton lechleri* derived products. NP-500 is isolated and purified from a plant indigenous to the southwestern United States, and in traditional medicine, the plant was brewed as a tea and used for the treatment of diabetes and other various illnesses. We are currently developing

Table of Contents

species-specific formulations of NP-500 to treat obesity-related metabolic dysfunction in dogs, Type II diabetes in cats and metabolic syndrome in horses, and have filed three INADs for these indications.

According to a 2013 national survey of veterinarians, approximately 17% of dogs in the United States are obese. Studies show that obesity is more common in elderly dogs, as well as in neutered dogs. Obesity-related metabolic dysfunction manifests in altered lipid profiles, insulin resistance and mild hypertension, which could decrease a dog's lifespan. There are currently no FDA-approved products for the treatment of metabolic syndrome or insulin resistance in dogs. In cats, the prevalence of obesity-related diabetes or Type II diabetes is high and increasing. In horses, insulin resistance is associated with an equine metabolic syndrome characterized by obesity, regional adiposity and hypertriglyceridemia. It is also known to be a risk factor for laminitis. Various studies report the prevalence of insulin resistance as 10% and 28% in horses and ponies, respectively. There are also currently no FDA-approved products for the treatment of metabolic syndrome in horses.

We anticipate that our development activities will benefit from centralized activities, including shared use of the manufacturing and regulatory documentation for chemistry, manufacturing and controls, or CMC. We also anticipate being able to enter into combined clinical research agreements and activities with companion animal clinical trial sites for dogs and cats.

Sales and Distribution

As we announced on December 12, 2016, we have signed a distribution agreement with Henry Schein, Inc., the world's largest provider of health care products and services to office-based dental, animal health and medical practitioners, for exclusive distribution of our Neonorm Foal product to all segments of the U.S. equine market. Henry Schein's animal health business, Dublin, Ohio-based Henry Schein Animal Health, employs approximately 900 team members and had 2015 net sales of $2.9 billion. With 12 strategically positioned, state-of-the-art distribution facilities and 10 inside sales centers nationwide, we believe Henry Schein Animal Health is positioned to bring a broad selection of veterinary products and strategic business solutions to more than 26,000 veterinary professionals nationwide. The agreement became effective on December 9, 2016, and, subject to provisions specified in the agreement, shall continue in force for an initial period of one year. Thereafter, unless either party notifies the other of its intent not to renew the term of the agreement at least 30 days prior to the end of the then current term, the term shall be automatically renewed upon expiration for successive renewal terms of one year.

In September 2014, we launched Neonorm for preweaned dairy calves under the brand name Neonorm Calf in the Upper Midwest region, and expanded the launch nationwide in early 2015. In December 2015 we conducted the soft launch of Neonorm Foal, our non-prescription anti-diarrheal product for newborn horses. We expect to launch Canalevia in 2017 for CID, and for acute diarrhea in early 2018. We intend to continue the development of our focused commercial effort for both the production and companion animal markets. We will focus our commercial efforts on educational activities and outreach to key opinion leaders and decision makers at key regional and global accounts for production animals and high prescriber veterinarians for companion animals. In August 2014, we entered our first regional distribution agreement for the Upper Midwest region, and in September 2014, entered an agreement with a national master distributor, who also distributes prescription products for the companion animal market. In February 2015, we entered a five-year distribution agreement with Biogenesis Bagó for sale and distribution of Neonorm Calf in South America. Biogenesis Bagó is the largest 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. In 2014 Biogenesis Bagó was named "Best Animal Health Company in Latin/South America" by a publication called Animal Pharm. Our distribution agreement provides Biogenesis Bagó with exclusive distribution rights for Neonorm Calf in Argentina, Brazil, Paraguay, Uruguay, and Bolivia. Under the terms of the distribution agreement, we can terminate the agreement

Table of Contents

if Biogenesis Bagó fails to meet annual sales goals for each year of the five-year agreement, and we may revoke exclusivity if Biogenesis Bagó fails to meet guaranteed minimum sales. We also agreed to additional incentive payments if stretch goals are exceeded.

We plan to partner with other leading distributors to deliver our products to customers both in the United States and internationally, and may also explore entering partnerships that include payment of upfront licensing fees for our products and product candidates for markets outside the United States where appropriate. We expects that our current and future 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, as well as when we further expand internationally including to resource-constrained countries where food safety issues are emerging global challenges.

Manufacturing

The plant material used to manufacture is crude plant latex ("CPL") extracted and purified from *Croton lechleri*, a widespread and naturally regenerating tree in the rainforest that is managed as part of sustainable harvesting programs. The tree is found in several South American countries and has been the focus of long-term sustainable harvesting research and development work. Napo's collaborating suppliers obtain CPL and arrange for the shipment of CPL to Napo's third party contract manufacturer.

Napo's third-party contract manufacturer, Glenmark Pharmaceuticals Ltd., a research-driven, global, integrated pharmaceutical company, processes CPL into crofelemer utilizing a proprietary manufacturing process. The processing occurs at two FDA-approved Glenmark facilities. Additionally, Napo plans to establish a third processing site, which will be operated by Indena S.p.A., a Milan, Italy-based contract manufacturer dedicated to the identification, development and production of high-quality active principles derived from plants, for use in the pharmaceutical, health food and personal care industries. Indena has completed the required technology transfer and has equipment in place for pilot manufacturing.

Competition

Human Health

There are several significantly larger pharmaceutical companies competing with us in the gastrointestinal segment. These companies include Valeant Pharmaceuticals International, Merck & Co., Inc., and Allergan plc as well as smaller pharmaceutical companies.

Diarrhea in adult patients living with HIV/AIDs. We are not aware of any other FDA-approved drugs for the symptomatic relief of diarrhea in HIV/AIDs patients. HIV/AIDs patients also use loperimide and over the counter anti-diarrheal remedies such as Mylanta or Kaopectate to treat their diarrhea, but these medicines affect motility and can result in rebound diarrhea.

Diarrhea predominant irritable bowel syndrome. Two drugs were approved in 2015 for the treatment of diarrhea predominant irritable bowel syndrome, Allergan plc's Virbezi and Xifaxan which is marketed by Valeant Pharmaceuticals International. Also, Lotronex was approved by the FDA in 2000 but was withdrawn from the market and later reintroduced in 2002 under a Risk Management Program. With the exception of Lotronex, the sponsors of Verbezi and Xifaxan employ extensive media and print promotion for the commercialization of these products. We are seeking a partner to further the clinical development and commercialization of crofelemer for d-IBS. There are currently numerous trials on going for d-IBS.

Table of Contents

Pediatric diarrhea. Acute diarrhea in children is commonly treated by a change in diet, oral rehydration therapy and/or antibiotics, assuming the cause of the diarrhea is bacterial in nature. Children aged 12 and younger are advised not to use anti-motility drugs (loperamide for example) unless directed to do so by a physician. There are recent clinical trials for probiotics and zinc sulfate. Other recent anti-diarrheal studies in children include a safety and tolerability study of Fidaxomicin for C difficile associated diarrhea.

Cancer related diarrhea. We are not aware of any FDA-approved drugs specifically indicated for chemotherapy induced diarrhea. A recent Phase IIb trial of elsiglutide for the treatment of chemotherapy induced diarrhea in colorectal cancer patients did not meet statistical significance. Opioids and over the counter drugs are commonly used to treat chemotherapy induced diarrhea, but these drugs affect motility. Certain tyrosine-kinase inhibitor chemotherapy agents have diarrhea as a significant side effect.

Congenital Diarrheal Disorders and Short Bowel Syndrome. We are not aware of any FDA-approved drugs specifically indicated for Congenital Diarrheal Disorders and Short Bowel Syndrome.

Cholera. We are not aware of any FDA-approved drugs specifically indicated as an anti-secretory agent for use to address the devastating dehyrdation in cholera patients.

Irritable Bowel Syndrome (IBS). If we receive regulatory approval for Mytesi for IBS, we expect to compete with major pharmaceutical and biotechnology companies that operate in the gastrointestinal space, such as Sucampo AG, Takeda Pharmaceuticals, Allergan, Inc., Ironwood Pharmaceuticals, Inc., Synergy Pharmaceuticals Inc., Sebela Pharmaceuticals, Inc. and Salix Pharmaceuticals. Because Mytesi is approved with chronic safety and several of the other agents have safety concerns, there is likely to be an opportunity for a polypharmacetuical approach to long-term management of these patients, removing a direct competitive scenario from Mytesi's potential entry to the marketplace and disease indication.

To our knowledge, there are currently no FDA-approved anti-secretory products, in particular which act locally in the gut with the chronic safety profile of crofelemer, in development or on the market. Crofelemer represents a new tool in gastro-intestinal disease management.

Animal Health

The animal health industry is dominated by large independent companies such as Zoetis Inc., a standalone animal health company that was spun out from Pfizer, Inc. in 2013, as well as subsidiaries of large pharmaceutical companies, including Novartis Animal Health Inc., a subsidiary of Novartis International AG., Merck Animal Health, the animal health division of Merck & Co., Inc., Merial Inc., the animal health division of Sanofi S.A., Elanco Animal Health, the animal health division of Eli Lilly and Company, Bayer Animal Health GmbH, a subsidiary of Bayer AG, and Boehringer Ingelheim Animal Health, the animal health division of Boehringer Ingelheim GmbH. There are also animal health companies based in Europe, including Vétoquinol S.A., Virbac S.A., Dechra Pharmaceuticals PLC and Ceva Animal Health S.A.

Additionally, smaller animal health companies, such as Aratana Therapeutics, Inc., Kindred Biosciences, Inc., Phibro Animal Health Corporation, Nexvet Biopharma and Parnell Pharmaceuticals Holdings Ltd, recently completed initial public offerings of their stock in the United States and may choose to develop competitive products. We believe that the large human pharmaceutical companies may also decide to spin out their animal health subsidiaries into standalone companies.

Table of Contents

We anticipates that Canalevia, if approved for the indication of general watery diarrhea in dogs, will face competition from various products, including products approved for use in humans that are used extra-label in animals. We are aware that veterinarians typically treat diarrhea in dogs with antibiotics, probiotics, dietary restrictions and products approved and formulated for humans, such as Imodium and other anti-motility agents, as well as binding agents that absorb water, such as Kaopectate and Pepto-Bismol. None of these treatment options address the water loss associated with acute diarrhea. We are not aware of any veterinarians prescribing Mytesi (formerly known as Fulyzaq) extra-label for use in dogs, and the indication of Mytesi is for a disease that does not occur in dogs. Further, because none of the human products are FDA approved for animal use, veterinarians, although allowed to dispense human products for animal use, do not have the benefit of clinical support with respect to efficacy or dosing. Moreover, administering a potentially unpalatable human formulation is often difficult and may lead to further uncertainty of the amount actually ingested by the dog. However, this practice may continue and Canalevia may face competition from these products. Canalevia could also potentially face competition from Mytesi were veterinarians to prescribe it extra-label. 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.

Distribution and Marketing Agreements

Napo has agreements in place with BexR, a distributor in Texas and SmartPharma, a marketing and commercialization advisory firm for the distribution, marketing and sale of Mytesi®, its FDA approved drug product for the systematic relief of non-infectious diarrhea in adult patients living with HIV/AIDs on antiretroviral therapy. The agreements compensate these parties with a percentage of net sales, as defined. Payments by Napo to BexR will be a specified percentage of net sales, ranging in the low double digits but in no instance exceeding 20% of net sales, depending on the period in which the sales occur and the amount of such sales. Payments by Napo to SmartPharma will be a specified percentage of net sales, ranging in the low double digits but in no instance exceeding 20% of net sales, depending on the amount of such sales. In addition, under certain circumstances, Napo will be required to pay SmartPharma a termination fee equal to a certain percentage of net sales generated within a specified period after the termination date.

Business Strategy

Our goal is to become a leading pharmaceuticals company with first-in-class, sustainably derived products that address significant unmet gastrointestinal medical needs globally. To accomplish this goal, we plan to:

Expand Mytesi by leveraging our significant gastrointestinal knowledge, experience and intellectual property portfolio.

Mytesi is a novel, first-in-class anti-secretory agent which has a basic normalizing effect locally on the gut, and this mechanism of action has the potential to benefit multiple disorders. Our Mytesi (crofelemer) product is approved by the U.S. FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. We believe we control commercial rights for Mytesi for all indications, territories and patient populations globally, and we are pursuing a follow-on indication for Mytesi in CRD, an important supportive care indication for patients undergoing primary or adjuvant chemotherapy for cancer treatment. Mytesi is also in development for rare disease indications for infants and children with congenital diarrheal disorders and short bowel syndrome; for IBS (Mytesi has demonstrated benefit to IBS-D patients in published Phase 2 studies); for supportive

Table of Contents

care for IBD; and as a second-generation anti-secretory agent for use in cholera patients. Mytesi has received orphan-drug designation for SBS.

Our management team 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, GMP manufacturing, and regulatory strategy. Key members of this team successfully developed Mytesi.

Establish and expand commercial capabilities in Mytesi sales and marketing efforts.

We plan to significantly expand Mytesi sales and marketing efforts during the third quarter of 2017. As announced on August 7, 2017, we appointed Pete Riojas, a 29-year pharmaceutical industry veteran, to lead Mytesi sales nationally. We also significantly expanded our internal national salesforce for Mytesi through the hire in key U.S. markets of nine sales representatives experienced in the sale of drugs to HIV physicians and gastroenterologists. Our new sales representatives are based in and will cover New York, Miami, Atlanta, Los Angeles, Houston, San Francisco, New Orleans, Philadelphia/Washington D.C., Chicago, St. Louis and the surrounding regions. All of these regions are key markets for HIV-related drug sales. Six of our new territory managers have been calling on HIV physicians for over 15 years, and others possess extensive experience in drug sales to both gastroenterologists and HIV healthcare providers.

Strategically sequence the development of follow-on indications of Mytesi and seek geographically-focused licensing opportunities.

Although it is possible that we may enter into corporate partnering relationships related to Mytesi, our intention would be to retain all commercialization and promotional rights in the U.S., so that we do not become primarily a royalty-collecting organization, and we are opposed to entering into any Mytesi partnering relationship that would require splitting indications. We are seeking to put limited geographically-focused partnerships in place in the near term, while also considering possibilities for a worldwide partnership with a leading global entity in the field of gastrointestinal care and cancer in the long term.

Strategically plan our portfolio in the animal health space.

Portfolio planning for the animal health space is of the utmost importance to us, given the wide array of potential species-specific products and because we do not want animal-related research and development activities to divert significant financial resources while we are focusing on growing Mytesi sales and seeking to move our company towards profitability. Additional formulations and additional animal product expenditures will be considered from time to time as part of portfolio planning and prioritization in the context of the combined company. Canalevia is our lead veterinary prescription drug product candidate, intended for treatment of various forms of diarrhea in dogs. Our next expected veterinary product commercial launch will be for Equilevia, a personalized premium proprietary total gut health product for equine athletes, which will be non-prescription.

Reduce risks relating to product development.

Risk reduction is a key focus of our product development planning. Mytesi is approved for chronic indication, providing us the ability to leverage this corresponding safety data when seeking approval for planned follow-on indications. Crofelemer manufacturing is being conducted at a new, multimillion-dollar commercial manufacturing facility that has been FDA-inspected and approved. In an effort to reduce risk further, we have implemented the following approach: First, we meet with key opinion leaders, typically at medical conferences as we have already done in 2017 at Digestive Disease Week for IBS and IBD, the American Society of Clinical Oncology annual meeting, and the Multinational

Table of Contents

Association of Supportive Care and Congress. Next, we confirm unmet medical needs with these key opinion leaders, and discuss the practicality of patient enrollment and trial implementation. We then generate protocols to discuss with the FDA, seeking, when possible, special protocol assessments. Our goal is to have derisked the program as much as we believe we possibly can by the time we start devoting funds to a clinical trial. We believe this approach will lead to better long-term outcomes for our products in development.

Manufacturing

The plant material used to manufacture Canalevia, Neonorm and related products is crude plant latex, or CPL, extracted and purified from *Croton lechleri*, a widespread and naturally regenerating tree in the rainforest that is managed as part of sustainable harvesting programs. The tree is found in several South American countries and has been the focus of long-term sustainable harvesting research and development work. Our collaborating suppliers obtain CPL and arrange for the shipment of CPL to our third-party contract manufacturer. CPL will also be shipped to us for manufacturing after we establish our own API manufacturing capability.

Our third-party contract manufacturer will process CPL into both crofelemer, the API in Canalevia, and the botanical extract used in both Neonorm Calf and Neonorm Foal. Canalevia will be manufactured by the same process used to manufacture the API that was used in the animal safety studies and the human studies in support of the approval of Mytesi (formerly known as Fulyzaq). Napo has also licensed this intellectual property to third parties in connection with its licenses related to the development and commercialization of crofelemer for human use. While we believe these third parties have developed their own proprietary manufacturing specifications pursuant to their license agreements, such third-party intellectual property is unknown to us, and is not part of the intellectual property that we intend to use for the manufacture of API in its licensed field of use. Similarly, the manufacture of Neonorm depends only on technology licensed from Napo. The license grant specifically excludes intellectual property rights developed pursuant to a prior collaboration agreement between Napo and Glenmark, the manufacturer of the API in Mytesi (formerly known as Fulyzaq). In May 2014 and June 2014, and as amended in February 2015, we entered into binding memorandums of understanding with Indena S.p.A. to negotiate a definitive commercial supply agreement for the manufacture of the API in Canalevia and the botanical extract in Neonorm. We have furnished equipment to Indena S.p.A. for use in a facility that will be dedicated to the manufacture of crofelemer and the botanical extract.

In December 2015, Indena delivered 360 kilos of the standardized botanical extract to us. We currently own enough of the Neonorm standardized botanical extract to formulate a combination of approximately one million treatments of Neonorm Calf or Neonorm Foal.

Pursuant to the memorandums of understanding as amended, we agreed to pay Indena S.p.A. the following fees in connection with the establishment of its manufacturing arrangement:

- a start-up fee equal to €500,000, payable in two equal installments, both of which were paid in May 2015;
- fees associated with the technology transfer and manufacturing process adaptation equal to €620,000 for API which was paid in May and July 2015;
- fees for the design and set up of a dedicated suite qualified for pharmaceutical and veterinary products equal to €170,000 which was paid in May 2015;
- deliverables fees equal to €500,000, €250,000 of which was paid in December 2015, and €250,000 of which was payable by the end of March 2016, with the understanding that these fees will be credited against payments agreed to under the future commercial supply agreement; and

Table of Contents

a €300,000 bonus fee payable in two equal installments, the first of which was paid in March 2015, with the remainder paid by the end of March 2016.

We have made all contractual payments to Indena as of March 31, 2016. In March 2015, Indena S.p.A. agreed to delay payment of the fees payable by the end of March 2015 until the earlier of April 30, 2015 or the completion of our initial public offering. In July 2015 and December 2015 Indena S.p.A agreed to delay payment of certain fees payable until March 2016. In June 2014, as contemplated by the memorandums of understanding, we also issued Indena S.p.A. a warrant to acquire 16,666 shares our common stock at an exercise price per share equal to 90% of the initial public offering price, which expires in June 2019.

In September, 2015 we entered a distribution agreement with Glenmark. With the execution of the agreement, we intend to use Glenmark as our primary manufacturer of crofelemer for animal health use. Our agreement with Glenmark supplements our previously announced manufacturing agreement with Indena S.p.A for the standardized botanical extract in Neonorm Calf and Neonorm Foal. We intend to eventually use Indena as an alternative supplier for crofelemer.

In October 2015, we announced that we signed a crofelemer formulation development and manufacturing contract with Patheon Pharmaceuticals Inc. ("Patheon"), a leading global provider of drug development and delivery solutions to the global pharmaceutical and biopharma industries. Under the terms of the contract, Patheon will provide enteric-coated crofelemer tablets for us for use in animals. The tablets were used in our pivotal efficacy trial for Canalevia, which began in the fourth quarter of 2015.

Patheon is the manufacturer of Mytesi (formerly known as Fulyzaq), a human-specific, enteric-coated formulation of crofelemer that 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 working at Napo where the drug was initially developed.

We also plan to enter agreements with third parties for the formulation of the API and botanical extracts into finished products to be used for planned studies and commercialization.

We plan to ensure that the facilities of our third-party contract manufacturers that will manufacture our API and botanical extract, as well as formulate our finished products, comply with cGMP and other relevant manufacturing requirements.

Proprietary Library of Medicinal Plants

We possess a proprietary library of more than 2,300 medicinal plants.

Intellectual Property

Trademarks

We plan to market all of our products under a trademark or trademarks we select and we will own all rights, title and interest, including all goodwill, associated with such trademarks. Mytesi is a registered trademark owned by Napo.

License Agreements

License Agreement with Glenmark Pharmaceuticals Limited

In 2005 Napo entered into a collaboration agreement with Glenmark Pharmaceuticals Limited (the "Glenmark Collaboration Agreement") for the development of crofelemer for the indications of for HIV/ AIDS diarrhea, pediatric diarrhea and adult acute infectious diarrhea in approximately 140 countries outside of the United States, Japan, most EU countries and Japan. The Glenmark

Table of Contents

Collaboration Agreement provides for royalties to be paid to Napo based upon net sales of crofelemer derived products in the licensed territories. Annual royalty payments will be a specified percentage of net sales, ranging from the high single digits to the low double digits but in no case exceeding 15% of net sales, depending on the annual amount of net sales.

Glenmark has obtained marketing approval for the crofelemer derived product for control and symptomatic relief of diarrhea in patients living with HIV/AIDs in two countries in Africa and two in South America. Two of these four countries have also approved the crofelemer derived product for control and symptomatic relief of diarrhea in patients with acute infectious diarrhea. Napo has not received any royalty income from these approvals nor is it aware of any sales made by Glenmark in its licensed territories.

Termination, Asset Transfer and Transition Agreement

On September 19, 2017 (the "Transfer Date"), Napo entered into the Termination, Asset Transfer and Transition Agreement (the "Glenmark Transition Agreement") with Glenmark. The Glenmark Transition Agreement supersedes the Glenmark Collaboration Agreement and returns to Napo certain rights which Napo licensed to Glenmark pursuant to the Glenmark Collaboration Agreement related to the development and commercialization of crofelemer for certain specified human indications in India and 140 other countries largely in developing regions (the "Transferred Assets").

As a result of the execution of the Glenmark Transition Agreement, we, through Napo, now control commercial rights for Mytesi for all indications, territories and patient populations globally, and also hold commercial rights to the existing regulatory approvals for crofelemer in Brazil, Ecuador, Zimbabwe and Botswana.

In consideration for Glenmark's assignment and transfer of the Transferred Assets to Napo, Napo agreed to pay Glenmark in cash, within 45 days after receipt by Napo, 25% of any payment that Napo receives from a third party to whom Napo grants a license or sublicense or with whom Napo partners in respect of, or sells or otherwise transfers any of the Transferred Assets, subject to certain limitations, until Glenmark has received a total of $7 million. As additional consideration for the assignment and transfer of the Transferred Assets, Napo agreed (i) to enter into, within 90 days after the Transfer Date, a manufacturing and supply agreement with Glenmark for crofelemer, which will be manufactured at either or both of Glenmark's facilities in India and (ii) to transfer and assign to Glenmark all right, title and interest in and to certain required dedicated equipment used to manufacture crofelemer located at Glenmark's Ankleshwar facility, subject to certain limitations.

License Agreement with Luye Pharmaceuticals, Inc.

In 2005, Napo entered into a license agreement with Luye Pharmaceuticals ("Luye") for the development of crofelemer for the indications of HIV/AIDS diarrhea, pediatric diarrhea and adult acute infectious diarrhea for the People's Republic of China including Macao and Hong Kong. The license agreement provided for Napo to receive royalties on net sales of crofelemer derived products. Annual royalty payments will be a specified percentage of net sales, ranging from the low single digits to low double digits but in no case exceeding 15% of net sales, depending on the annual amount of net sales. To date, Luye has not developed crofelemer for any indications in its licensed territory and the Company has not received any royalty income from Luye. In 2010, Napo amended the license agreement to provide Napo the opportunity to sub-license rights granted to Luye under the license agreement, including providing commercial rights to Napo, thereby expanding Napo's control of commercial rights to all human indications of crofelemer.

Table of Contents

License Agreement with Insmed Incorporated

In 2007, Napo entered into a license agreement with Insmed Incorporated ("Insmed"), pursuant to which Insmed granted Napo a perpetual, world-wide license to use Insmed's patent and other intellectual property rights to Masoprocal in the field of use relating to diabetes, cardiac disease, hypertension, vascular disease, metabolic disease, Syndrome X and all other clinical syndromes related to insulin resistance, but excluding all rights in the field of use to all indications relating to the field of oncology, which were retained by Insmed. Under the terms of the agreement, Napo made an upfront payment to Insmed upon execution of the agreement and will make additional payments to Insmed ranging from the low six figures to $1,000,000 upon the achievement of certain milestones. In addition, Napo is required to make royalty payments to Insmed, which will be a specified percentage of net sales, ranging from the low single digits to high single digits, depending on the annual amount of net sales and the geographical location of such sales. Napo's obligation to make royalty payments continues until the longer of (a) the maximum length of time that Masoprocal is protected by a licensed patent and (b) five years from the date upon which Napo receives FDA approval of the new drug application or foreign equivalent for any Masoprocal product or Masoprocal product formulation developed, manufactured and commercialized by or for Napo or Insmed, subject to certain limitations described therein.

License Agreement with Elanco US Inc.

As we announced on January 31, 2017, we signed an agreement with Elanco US Inc., a subsidiary of Eli Lilly and Company, to license, develop, co-promote, and commercialize Canalevia, our drug product candidate under investigation for treatment of acute diarrhea and CID in dogs. The agreement grants Elanco exclusive global rights to Canalevia for use in companion animals. On November 1, 2017, Elanco notified the Company of its intention to terminate the agreement, effective January 30, 2018. On the effective date of termination of the agreement, all licenses granted by us to Elanco under the agreement will be revoked and the rights granted thereunder revert back to us.

Patent Portfolio

Napo

Napo owns a portfolio of patents and patent applications covering formulations of and methods of treatment with proanthocyanidin polymers isolated from *Croton* spp or *Calophyllum* spp., including Mytesi (crofelemer). The patent family related to International Patent publication WO1998/16111 relates to enteric protected formulations of proanthocyanidin polymers isolated from Croton spp or Calophyllum spp., including crofelemer, and methods of treating watery diarrhea using these enteric-protected formulation. There are three U.S. patents in this family, including, US 7,323,195, which has a term until at least June 7, 2018, US 7,341,744, which has a term until at least January 11, 2018, and US 8,574,634, which has a term until at least January 11, 2018. The United States Patent and Trademark Office (USPTO) issued on December 16, 2006, a notice of recalculation of the patent term adjustment for US 7,341,744 for 842 days, for an expiration date of February 5, 2019; however, the USPTO has not issued a certificate of correction to correct the patent term adjustment accorded to this patent. In addition, on February 20, 2017, Napo has filed a Request for Reconsideration of the patent term adjustment of US 7,341,744, requesting recalculation resulting in 1032 days or, alternatively, 980 days of patent term adjustment. Napo has elected to extend the term of US 7,341,744 under 35 U.S.C. 156, and the United States Patent and Trademark Office has issued a Notice of Final Determination that the patent term extension for US 7,341,744 is 1075 days. Based upon the January 11, 2018 expiration date, the patent would be extended to June 2021, to account for regulatory delay in obtaining human marketing approval for crofelemer. Napo has requested that the USPTO not issue the final Patent Term Extension certificate until final resolution of the number of days of patent term adjustment accorded to US 7,341,744. Patent protection for enteric protected formulations of

Table of Contents

crofelemer and methods of use has also been obtained outside the United States, including in Australia, Korea, Mexico, New Zealand and Taiwan, with terms extending until October 14, 2017 in these jurisdictions.

Napo additionally owns a family of patents arising from International Patent Application Publication WO2012058664 that cover methods of treating HIV associated diarrhea and HAART associated diarrhea with proanthocyanidin polymers isolated from *Croton* spp or *Calophyllum* spp., including crofelemer. In the U.S., there are two issued patents, US 8,962,680 and US 9,585,868, both of which expire October 31, 2031 and one pending application. Outside the U.S., patent protection for methods of treating HIV associated diarrhea has been obtained in Australia, Japan, Kenya, Kazakhstan, Russia, Ukraine, South Africa and Zimbabwe, with expiration dates of October 31, 2031, and Napo has pending applications in Brazil, Canada, China, Europe, Hong Kong, India, Japan, Mexico, and Malaysia. Napo also has patent families related to methods of treating diarrhea-predominant irritable bowel syndrome, constipation-predominant irritable bowel syndrome, and inflammatory bowel disease, familial adenomatous polyposis and colon cancer, with proanthocyanidin polymers isolated from *Croton* spp or *Calophyllum* spp., including crofelemer. In particular, for diarrhea-predominant irritable bowel syndrome, Napo has 1 issued US patent, which expires February 9, 2027, and 1 pending application, issued patents in Australia, Japan, South Korea, Mexico, New Zealand, Singapore, and Taiwan and pending applications in Bangladesh, Bolivia, Canada, Chile, Europe, Gulf States, Mexico, Panama, Peru, Paraguay, Thailand, and Taiwan, all of which are estimated to expire April 30, 2027; for constipation-predominant irritable bowel syndrome, Napo has 3 issued US patents, with terms of at least April 30, 2027, patents in Australia, Europe, Mexico, New Zealand, Singapore and pending applications in Canada, and India, all of which are estimated to expire April 30, 2027; and for inflammatory bowel disease, familial adenomatous polyposis and/or colon cancer, Napo has 1 issued US patent, which has an expiration date of October 9, 2029 and 1 pending application, issued patents in Australia, Europe and a pending application in Canada, which have estimated expiration dates of April 30, 2027.

Napo also co-owns with Glenmark, issued patents in India, South Africa and Eurasia patents that expire August 24, 2030, and cover a method of manufacturing with proanthocyanidin polymers isolated from *Croton* spp or *Calophyllum* spp., including crofelemer). Napo holds two US patents covering a formulation of NP-500 (nordihydroguiaretic acid (NDGA)) and its use in treating a metabolic disorder that have terms until April 23, 2031 Napo has filed a PCT provisional application for the treatment of Chemotherapy induced diarrhea (CID) with crofelemer.

Jaguar

We have exclusive rights in the veterinary field to an international patent family related to International Patent Application WO1998/16111 as set forth above in the disclosure of the Napo patent portfolio. The patents and patent applications in this family are directed to enteric protected formulations of proanthocyanidin polymers isolated from *Croton spp* or *Calophyllum spp.* (such as crofelemer and Neonorm), and methods of treating watery diarrhea using the enteric protected formulations for both human and veterinary uses. As such, the patents and patent applications of this family cover certain formulations of crofelemer, including Canalevia, as well as the standardized botanical extract in Neonorm, and methods of treating diarrhea using these formulations.

Certain Napo patents and patent applications, 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 Mytesi (formerly known as Fulyzaq) were returned to Napo and the collaboration agreement between Salix and Napo (the "Salix Collaboration Agreement"), was terminated. Napo has the responsibility to file, prosecute and maintain the Napo Patents. There are three issued Napo Patents in the United States that cover, collectively, enteric protected

Table of Contents

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.

We have filed and have currently three applications pending under the PCT, and seven U.S. non-provisional patent applications relating to veterinary uses of *Croton* proanthocyanidin polymer compositions, including crofelemer, Neonorm and Canalevia, and product combinations under development. These applications are directed to treatment of watery diarrhea in newborn and young animals, including methods of improving mortality and weight gain in newborn animals, treatment of stress-induced diarrhea in animals, and treatment of watery diarrhea caused by salmonella in animals. These applications also focus on the treatment of diarrhea in companion animals such as dogs and cats. In addition, an application has been submitted for the treatment of ulcers and related symptoms in animals with an emphasis on ulcers in horses. An application has also been filed on a prebiotic effect of crofelemer in bovine and other animal species based on research findings that indicate a prebiotic enhancement of the gut bacteria in animals. One other patent application has been filed combining crofelemer with rifaximin, a non-absorbed antibiotic for the treatment of bacteria induced diarrhea in multiple animal species. Applications have been filed relating to treatment of porcine epidemic virus in piglets and treatment of diarrhea in livestock with a formulation that is not enteric protected. Patents that may issue based upon these applications should have terms that extend until at least May 2035.

Government Regulation

Human Health Business

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of prescription drugs such as those Napo is developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of Napo's drug product candidates. To comply with the regulatory requirements in each of the jurisdictions in which Napo is seeking to market and subsequently sell its prescription products, Napo is establishing processes and resources to provide oversight of the development, approval processes and launch of its products and to position those products in order to gain market share.

U.S. Government Regulation

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), and its implementing regulations.

The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;

Table of Contents

submission to the FDA of an investigational new drug application, or IND, which must become approved before human clinical trials may begin;

approval by an institutional review board, or IRB, of the study protocol and informed consent forms for the clinical site before each trial may be initiated. Multiple sites may necessitate the involvement of multiple IRBs and submissions;

performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;

submission to the FDA of an NDA which would include the study reports of the clinical trials, chemistry and manufacturing of the active pharmaceutical ingredient and the final dosage form as well as other required sections to be included in the NDA;

satisfactory completion of an FDA advisory committee review, if applicable;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and

FDA review and approval of the NDA.

Pre-clinical Studies

Pre-clinical studies include laboratory evaluation of the drug product's chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects pursuant to a clinical protocol, under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives or endpoints of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA under the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.govwebsite.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution,

Table of Contents

excretion and, if possible, to gain an early indication of its effectiveness depending on the endpoints set forth in the protocol.

Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Special Protocol Assessment

The special protocol assessment, or SPA, process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate issues related to the adequacy of certain clinical trials, including Phase 3 clinical trials that can form the primary basis for a drug product's efficacy claim in an NDA. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

public health concerns emerge that were unrecognized at the time of the protocol assessment;

the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;

a sponsor fails to follow a protocol that was agreed upon with the FDA; or

the relevant data, assumptions, or information provided by the sponsor in a request for SPA change, are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

Table of Contents

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of a NDA requesting approval to market the product for one or more indications. In most cases, the submission of a NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act ("PDUFA"), guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003 ("PREA"), as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations; this would include information which supports dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA may also require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA may also require other information as part of the NDA filing such as an environmental impact statement. The FDA can waive some or delay compliance with some of these requirements.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept a NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews a NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter must contain a statement of specific items that prevent the FDA from approving the

Table of Contents

application and will also contain conditions that must be met in order to secure final approval of the NDA and may require additional clinical or pre-clinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. New secondary indications must be supported by clinical trials or data. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition

Table of Contents

of distribution or other restrictions under a REMS program. Other potential consequences include, include, but are not limited to:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In addition the FDA regulates the purity and or consistency of the approved product. Products, if deemed adulterated can lead to serious consequences as set forth above as well as civil and criminal penalties.

Foreign Government Regulation

To the extent that any of Napo's product candidates, once approved, are sold in a foreign country, Napo may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

In order to market Napo's future products in the EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein) and many other foreign jurisdictions, a sponsor must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- the Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Table of Contents

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

In the EEA, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

Other U.S. Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security and physician payment and drug pricing transparency laws.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the U.S. federal Anti-Kickback

Table of Contents

Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

Additionally, the intent standard under the U.S. federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, or off-label, uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Violations of fraud and abuse laws, including federal and state anti-kickback and false claims laws, may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, the ACA broadened the reach of certain

Table of Contents

criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year and up to an aggregate of $1 million per year for "knowing failures." Covered manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

Napo may also be subject to data privacy and security regulation by both the federal government and the states in which Napo conducts its business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical products for which Napo obtains regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use Napo's products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of Napo's products. Sales of any products for which Napo receives regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations. In the United States, the process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover Napo's product candidates

Table of Contents

could reduce physician utilization of Napo's products once approved and have a material adverse effect on Napo's sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable Napo to maintain price levels sufficient to realize an appropriate return on Napo's investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require Napo to provide scientific and clinical support for the use of Napo's products to each payor separately and will be a time-consuming process.

In the EEA, governments influence the price of products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider Napo's products to be cost-effective compared to other available therapies, they may not cover Napo's products after FDA approval or, if they do, the level of payment may not be sufficient to allow Napo to sell its products at a profit.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; creation of the Independent Payment Advisory Board, once empaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. Since its enactment, the U.S. federal government has delayed

Table of Contents

or suspended implementation of certain provisions of the ACA. In addition, there have been judicial and Congressional challenges to certain aspects of the ACA, and Napo expects there will be additional challenges and amendments to the ACA in the future. For example, in January 2017, the U.S. House of Representatives and Senate passed legislation, which, if signed into law, would repeal certain aspects of the ACA. In addition, Congress could consider subsequent legislation to replace those elements of the ACA if so repealed.

Napo expects that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that Napo receives for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. The implementation of cost containment measures or other healthcare reforms may prevent Napo from being able to generate revenue, attain profitability or commercialize Napo's drugs.

Additionally, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional action is taken by Congress. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny recently over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products.

Napo expects that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Napo's products once approved or additional pricing pressures.

Animal Health Business

The development, approval and sale of animal health products are governed by the laws and regulations of each country in which we intend to seek approval, where necessary, to market and subsequently sell our prescription drug and non-drug products. To comply with these regulatory requirements, we are establishing processes and resources to provide oversight of the development, approval processes and launch of its products and to position those products in order to gain market share in each respective market.

United States

Certain federal regulatory agencies are charged with oversight and regulatory authority of animal health products in the United States. These agencies, depending on the product and its intended use may include the FDA, the USDA and the Environmental Protection Agency. In addition, the Drug Enforcement Administration regulates animal therapeutics that are classified as controlled substances.

Table of Contents

In addition, the Federal Trade Commission may in the case of non-drug products, regulate the marketing and advertising claims being made.

The approval of prescription drugs intended for animal use is regulated by the FDA's Center for Veterinary Medicine ("CVM"). The CVM consists of six offices that work together to, in part, approve new drugs for commercialization and thereafter monitor those commercialized drugs once in the market. The Office of New Animal Drug Evaluation ("ONADE"), is the lead office for reviewing novel drug candidates. We, as the sponsor of a novel drug candidate, commence the development and approval process by initiating communication with the ONADE and opening an INAD file. As part of this process, we will also schedule a discussion of the novel drug's development plan in order to obtain agreement from the CVM for the number, type and design of studies needed to obtain FDA approval of the novel drug.

As required by the FDA, new animal drug products must obtain marketing approval through the NADA process. Under the Administrative New Animal Drug Application, or Administrative NADA, process, a sponsor can engage in a phased submission of the required technical sections of an NADA, known as a rolling NADA, as opposed to submitting the entire application at once with a standard NADA. The requirements for all NADAs are the same regardless of whether a sponsor chooses the rolling NADA or the standard NADA submission. Under the phased review, once all technical sections have been submitted and reviewed, the sponsor submits an Administrative NADA to reflect that all technical sections of the NADA have been submitted and reviewed, each such technical section meets the requirements for approval and the CVM has issued technical section complete letters for each technical section. The phased review and Administrative NADA allow a drug sponsor to engage with the FDA as to each technical section to ensure that each section meets all requirements prior to submission of the application for approval. Phasing of NADA submissions is a voluntary process.

Once the tasks set forth in the development plan have been completed, including the clinical work as well as the chemistry and manufacturing work (feasibility, validation and stability of the drug inclusive), We, as the novel drug sponsor will need to provide to the FDA through the application process, information as to the safety and efficacy of the drug candidate, and, if needed, human food safety studies. These food safety studies are only required for drugs intended for use in production animals, and we currently have no plans to develop drugs for production animals. Additionally, the application will contain a module on CMC, which describes the plan for manufacturing the drug including the API, the final formulation, where it will be made, how it will be made, how the drug will be packaged, how it can be stored, the conditions required for storage and how long it can be stored before expiry. A major part of the CMC section is the analysis we employ to ensure that the manufactured drug is of a high quality, is consistently manufactured under cGMP and is stable. Other significant components to the application we have to complete before receiving drug approval includes a draft label that will list specific information such as dosing information, intended use, warnings, directions for use, and other information as required by the regulations. The package insert that will contain information on studies, warnings, drug interactions, intended use and dosing is considered part of the label in addition to that which is adhering to the container itself. The CVM ensures that the labeling provides all the necessary information to use the drug safely and effectively, and that it clearly discloses the risks associated with the drug.

MUMS Designation

The Minor Use and Minor Species Animal Health Act ("MUMS Act"), became effective in August 2004. The purpose of the MUMS Act was twofold: first, to encourage the development and availability of more animal drugs that are intended to be used in a major species defined as dogs, cats, cattle, horses, chickens, turkeys and pigs to treat diseases which occur infrequently or in limited geographic areas, therefore having an impact on a smaller number of animals on a yearly basis; and second, to encourage the development and availability of animal drugs for use in minor species

Table of Contents

(defined as all animals other than humans that are not one of the major species). The drug sponsor may seek conditional approval of the drug product provided the Office of Minor Use Minor Species ("OMUMS") acknowledges that the intended use fits within a small number of animals treated per annum. A drug does not have to be designated to be eligible for conditional approval, however if OMUMS designates a MUMS drug, certain incentives and exclusivities are available to the sponsor. The MUMS designation is modeled on the orphan drug designation for human drug development and has certain financial incentives available to encourage MUMS drug development such as the availability of grants to help with the cost of the MUMS drug development. Also, drug developers of MUMS drugs are eligible to apply for a waiver of the user fees once the MUMS designation has been given by OMUMS. We believe that we qualify for MUMS designation for Canalevia as a minor use in a major species because the estimated total number of dogs in the United States affected by CID is less than 70,000. We also believe that Canalevia will qualify for MUMS designation for EID because, in our estimate, the total number of dogs in the United States affected by EID on an annual basis is less than 70,000. To obtain conditional approval of a MUMS drug, the company must submit CMC and safety data similar to that required for an NADA, as well as data suggesting a reasonable expectation of effectiveness. After the submission and the review of the application, the FDA through the CVM can then grant a conditional approval (CA-1). This approval allows for a commercialization of the product, while the sponsor continues to collect the substantial evidence of effectiveness required for a full NADA approval. The sponsor has up to five years to demonstrate substantial evidence of effectiveness for a previously conditionally approved drug. Ideally, MUMS designation helps move the product forward in development; however, it may not shorten the time to full commercialization. A sponsor that gains approval or conditional approval for a MUMS designated drug receives seven years of marketing exclusivity.

Protocol Concurrence

As we announced in April 2016, we obtained protocol concurrence from the FDA for our pivotal trial of Canalevia that we initiated in December 2015 for acute diarrhea in dogs. We plan to pursue protocol concurrences from the FDA for future pivotal trials in other indications. Under this process, a protocol is submitted to the FDA voluntarily by a drug sponsor. The FDA review of the protocol for a pivotal study makes it more likely that the study will generate information the sponsor needs to demonstrate whether the drug is safe and effective for its intended use. It creates an expectation by the sponsor that the FDA will not later alter its perspectives on these issues unless public or animal health concerns appear that were not recognized at the time of protocol assessment. Even if FDA issues a protocol concurrence, ultimate approval of an NADA by the FDA is not guaranteed because a final determination that the agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data submitted to the FDA. Even if we were to obtain protocol concurrence, such concurrence does not guarantee that the results of the study will support a particular finding or approval of the new drug.

Marketing Exclusivity

We are currently planning on seeking MUMS designation for some of our prescription drug products and if we receive such a designation, we will be entitled to a seven-year marketing exclusivity, which means that we will face no competition from another sponsor marketing the same drug in the same dosage form for the same intended use. If we were to lose such designation or not receive such designation but our application as a new animal drug is found to be a new chemical entity that meets the criteria described by the FDA, we would be entitled to a five-year marketing exclusivity. In order to receive this five-year exclusivity, the FDA would have to find in its approval of our application that our NADA contains an API not previously approved in another application, that the application itself is an original application, not a supplemental application, and that our application included the following studies: one or more investigations to demonstrate substantial evidence of effectiveness of the drug for

Table of Contents

which we are seeking approval; animal safety studies and human food safety studies (where applicable). If the NADA is seeking approval of a drug for which we have received conditional approval, we, upon approval would still be entitled to a five-year marketing exclusivity provided we meet the criteria as set forth above. If however, our NADA is for a drug for which the FDA has determined that the drug contains an API that has previously been approved, regardless of whether the original approval was for use in humans or not, we may only be entitled to a three-year marketing exclusivity provided that the NADA is an original, not supplemental, application and contains both safety and efficacy studies demonstrating the safety and efficacy of the drug which is the subject of the application. We have received MUMS designation for Canalevia for the indication of Chemotherapy-Induced Diarrhea, or CID, in dogs. Additionally, the FDA has indicated that the use of Canalevia for the treatment of EID in dogs qualifies as a "minor use", which means that Canalevia is eligible for conditional approval for the indication of EID in dogs. If Canalevia is approved for CID and EID in dogs, we expect to conduct the commercial launch of Canalevia for these indications in the first half of 2018.

European Union

The European Union, or EU, definition of a veterinary medicinal product closely matches the definition of an animal drug in the United States. In the EU, a company can market a veterinary medicinal product only after a marketing authorization has been issued by an EU member state, (*i.e.*, approval on a country-by-country basis) or by the EU Commission through the European Medicines Agency, or the EMA. Before the EU member state or the EU Commission issues marketing authorization, we must submit a marketing authorization application, known as the dossier. The dossier includes data from studies showing the product's quality, safety, and efficacy and is similar to an NADA filed with the FDA.

For an animal drug, the Committee for Medicinal Products for Veterinary Use ("CVMP"), is responsible for the scientific evaluation. Experts from all EU member states are on the CVMP. The Rapporteur, or lead reviewer on the dossier, prepares an overview of the committee's scientific evaluation, called the CVMP Assessment Report.

The CVMP Assessment Report:

- summarizes the data submitted by the company on the product's quality, safety, and efficacy;
- explains the assessment done by the CVMP to support the committee's recommendation to the EU Commission to issue a marketing authorization; and
- is the basis for the European Public Assessment Report published on the EMA's website.

Labeling

The FDA plays a significant role in regulating the labeling, advertising and promotion of animal drugs. This is also true of regulatory agencies in the EU and other territories. In addition, advertising and promotion of animal health products is controlled by regulations in many countries. These rules generally restrict advertising and promotion to those claims and uses that have been reviewed and approved by the applicable agency. We will conduct a review of advertising and promotional material for compliance with the local and regional requirements in the markets where it eventually may sell its product candidates.

Our non-prescription products will be labeled in accordance with the health guidelines outlined by the National Animal Supplements Council, an industry organization that sets industry standards for certain non-prescription animal products, including but not limited to product labeling.

Table of Contents

Other Regulatory Considerations

We believe regulatory rules relating to human food safety, food additives, or drug residues in food will not apply to the products we currently are developing because our prescription drug product candidates are not intended for use in production animals, with the exception of horses, which qualify as food animals in Europe and Canada; and our non-prescription products are not regulated by section 201(g) of the Federal Food, Drug, and Cosmetic Act, which the FDA is authorized to administer.

Our prescription drug product candidates currently in development, if approved, may eventually face generic competition in the United States and in the EU after the period of exclusivity has expired. In the United States, a generic animal drug may be approved pursuant to an abbreviated new animal drug application ("ANADA"). With an ANADA, a generic applicant is not subject to the submission of new clinical and safety data but instead must only show that the proposed generic product is a copy of the novel drug product, and bioequivalent to the approved novel product. However, if our product candidates are the first approved by the FDA or the EMA as applicable for use in animals, they will be eligible for a five-year marketing exclusivity in the United States and 10 years in the EU thereby prohibiting generic entry into the market. If the product has MUMS designation it has a seven-year marketing exclusivity.

We do not believe that our non-prescription products are currently subject to regulation in the United States. The CVM only regulates those animal supplements that fall within the FDA's definition of an animal drug, food or feed additive. The Federal Food Drug and Cosmetic Act defines food as "articles used for food or drink for man or other animals and articles used as components of any such article." Animal foods are not subject to pre-market approval and are designed to provide a nutritive purpose to the animals that receive them. Feed additives are defined as those articles that are added to an animal's feed or water as illustrated by the guidance documents. Our non-prescription products are not added to food, are not ingredients in food nor are they added to any animal's drinking water. Therefore, our non-prescription products do not fall within the definition of a food or feed additive. The FDA seeks to regulate such supplements as food or food additives depending on the intended use of the product. The intended use is demonstrated by how the article is included in a food, or added to the animals' intake (*i.e.,* through its drinking water). If the intended use of the product does not fall within the proscribed use making the product a food, it cannot be regulated as a food. There is no intent to make our non-prescription products a component of an animal food, either directly or indirectly. A feed additive is a product that is added to a feed for any reason including the top dressing of an already prepared feed. Some additives, such as certain forage, are deemed to be Generally Recognized as Safe ("GRAS"), and therefore, not subject to a feed Additive Petition approval prior to use. However, the substances deemed GRAS are generally those that are recognized as providing nutrients as a food does. We do not believe that our non-prescription products fit within this framework either. Finally, a new animal drug refers to drugs intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in animals. Our non-prescription products are not intended to diagnose, cure, mitigate, treat or prevent disease and therefore, do not fit within the definition of an animal drug. Our non-prescription products are intended to support a healthy gut, support fluid retention, and normalize stool formation in animals suffering from scours. Additionally, because a previously marketed human formulation of the botanical extract in our non-prescription products was considered a dietary supplement subject to the Dietary Supplement Health and Education Act of 1994 (and not regulated as a drug by the FDA), we do not believe that the FDA would regulate the animal formulation used in our non-prescription products in a different manner. We do not believe that our non-prescription products fit the definition of an animal drug, food or food additive and therefore are not regulated by the FDA at this time.

In addition to the foregoing, we may be subject to state, federal and foreign healthcare and/or veterinary medicine laws, including but not limited to anti-kickback laws, as we may from time to time

Table of Contents

enter consulting and other financial arrangements with veterinarians, who may prescribe or recommend our products. If our financial relationships with veterinarians are found to be in violation of such laws that apply to us, we may be subject to penalties.

Legal Proceedings

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Other than as set forth below, there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

On July 20, 2017, a putative class action complaint was filed in the United States District Court, Northern District of California, Civil Action No. 3:17-cv-04102, by Tony Plant on behalf of pre-Merger shareholders of Jaguar who held shares on June 30, 2017 and were entitled to vote at the 2017 Special Shareholders Meeting, against us and certain individuals who were directors as of the date of the vote, in a matter captioned Tony Plant v. Jaguar Animal Health, Inc., et al. The plaintiff attempts to assert claims arising under Section 14(a) and Section 20(a) of the Exchange Act and Rule 14a-9, 17 C.F.R. § 240.14a-9, promulgated thereunder by the SEC. The plaintiff alleges that material omissions and misstatements were contained in the Joint Proxy Statement/Prospectus on Form S-4 (File No. 333-217364) declared effective by the SEC on July 6, 2017 related to the solicitation of votes from shareholders to approve the Merger and certain transaction related thereto. We believe the claims are without merit. While no monetary damages have been quantified, we intend to vigorously contest this complaint.

The plaintiff has not yet served the complaint and summons on any of the defendants. If plaintiff elected to proceed with the litigation and made service on the defendants, the defendants would move to dismiss the complaint for failure to state a claim on which relief may be granted.

Table of Contents

PLAN OF DISTRIBUTION

We are offering 2,000,000 shares of common stock under this prospectus supplement and the accompanying prospectus directly to L2 Capital, LLC ("L2 Capital") at a price of approximately $0.25 per share.

The shares were offered directly to L2 Capital without a placement agent, underwriter, broker or dealer. We are not paying underwriting discounts or commissions in connection with the offering.

We have entered into a share purchase agreement, dated as of November 24, 2017, with L2 Capital for the full amount of the offering. The share purchase agreement is included as an exhibit to our Current Report on Form 8-K that we will file with the SEC in connection with the consummation of this offering. See "Where You Can Find More Information".

Our obligation to issue and sell shares to L2 Capital is subject to the conditions set forth in the share purchase agreement. L2 Capital's obligation to purchase shares is subject to conditions set forth in the share purchase agreement as well.

We currently anticipate that the sale of the securities offered by this prospectus supplement and the accompanying base prospectus will be completed on or about the date hereof, subject to customary closing conditions. We estimate the total offering expenses of this offering that will be payable by us will be approximately $9,000, which includes legal and printing costs and various other fees. At the closing, The Depository Trust Company will credit the shares of common stock to the account of the purchaser.

Concurrently with this offering, L2 Capital has also entered into a common stock purchase agreement with us on November 24, 2017, in which L2 Capital committed to purchase, at our election, up to an aggregate of 10 million shares of our common stock.

Table of Contents

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by our counsel, Reed Smith LLP, Palo Alto, California.

EXPERTS

The financial statements of the Company as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 incorporated by reference in this prospectus supplement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm (the reports on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

The consolidated financial statements of Napo as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 incorporated by reference in this prospectus supplement have been audited by Macias Gini & O'Connell LLP, as stated in their report incorporated by reference in this prospectus supplement (which report contains an explanatory paragraph regarding Napo's ability to continue as a going concern), and are incorporated by reference in reliance upon such report and upon the authority of such firm as experts in auditing and accounting.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

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

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

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

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. This prospectus supplement omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus supplement. Statements in this prospectus supplement or the accompanying prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

our Annual Report on Form 10-K/A for the fiscal year ended December 31, 2016 filed on May 26, 2017;

our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders held on May 8, 2017, filed on April 17, 2017;

our Quarterly Report on Form 10-Q/A for the fiscal quarter ended March 31, 2017 filed on June 23, 2017, our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2017 filed on August 9, 2017, and our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30,2 017 filed on November 20, 2017;

our Current Reports on Form 8-K filed on January 31, 2017, February 9, 2017, February 24, 2017, March 31, 2017, April 6, 2017, May 2, 2017, May 8, 2017, May 19, 2017, July 3, 2017, July 7, 2017, July 28, 2017, July 31, 2017, August 1, 2017, August 4, 2017, August 16, 2017, August 29, 2017, September 14, 2017, September 15, 2017, September 25, 2017, October 3, 2017, October 26, 2017, and November 7, 2017;

Table of Contents

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

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

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

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

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

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

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

Table of Contents

JAGUAR HEALTH, INC.

$60,000,000

Common Stock

Warrants

Subscription Rights

Units

6,852,998 Shares of Common Stock

Offered by the Selling Shareholders

This prospectus relates to (i) common stock, warrants and subscription rights that we may sell from time to time in one or more offerings up to a total public offering price of $60,000,000 on terms to be determined at the time of sale, which securities may be sold either individually or in units, and (ii) the proposed resale or other disposition from time to time of up to 6,852,998 shares of Jaguar Health, Inc. common stock, $0.0001 par value per share, by the selling shareholders identified in this prospectus. We will not receive any of the proceeds from the sale or other disposition of common stock by the selling shareholders. We and the selling shareholders may offer securities at the same time or in separate transactions.

Each time we sell securities hereunder, we will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

These securities may be offered and sold in the same offering or in separate offerings, directly to purchasers, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See "Plan of Distribution" in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our or the selling shareholders' arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any sale of securities offered by us will also be included in a prospectus supplement.

The selling shareholders or their pledgees, assignees or successors-in-interest may offer and sell or otherwise dispose of the shares of common stock described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling shareholders will bear all commissions and discounts, if any, attributable to the sales of shares. We will bear all other costs, expenses and fees in connection with the registration of the shares. See "Plan of Distribution" beginning on page 21 for more information about how the selling shareholders may sell or dispose of their shares of common stock.

Our voting common stock is listed on the NASDAQ Capital Market, under the symbol "JAGX." On September 11, 2017, the last reported sale price of our voting common stock on the NASDAQ Capital Market was $0.44 per share.

As of July 31, 2017, the aggregate market value of the voting and non-voting common equity held by non-affiliates, computed by reference to the price at which the common equity was last sold or the average bid and asked price of such common equity on that date, was approximately $37,422,042.56, based on 67,430,585 shares of outstanding common stock, of which 66,825,076 were held by non-affiliates. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below $75.0 million. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus.

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 5 of this prospectus under the caption "Risk Factors" and in the documents incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is September 14, 2017.

Table of Contents

TABLE OF CONTENTS

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total public offering price of $60,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The prospectus supplement may also add to, update or change information contained in this prospectus.

The selling shareholders may also use the registration statement to offer and sell or otherwise dispose of up to an aggregate of 6,852,998 shares of our common stock from time to time in the public market. Neither we nor the selling shareholders have authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any of our securities other than the securities covered hereby, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy any securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about, and to observe, any restrictions as to the offering and the distribution of this prospectus applicable to those jurisdictions.

We further note that the representations, warranties and covenants made in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front cover of this prospectus or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or securities are sold or otherwise disposed of on a later date. It is important for you to read and consider all information contained in this prospectus, including the Information Incorporated by Reference herein, and any prospectus supplement in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions "Where You Can Find More Information" and "Incorporation of Information by Reference" in this prospectus.

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

Table of Contents

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the SEC. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Overview

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

We are pursuing a follow-on indication for Mytesi in chemotherapy-induced diarrhea, an important supportive care indication for patients undergoing primary or adjuvant chemotherapy for cancer treatment. Mytesi is in development for orphan-drug indications for infants and children with congenital diarrheal disorders and short bowel syndrome; as a second-generation anti-secretory agent for use in cholera patients; and for supportive care for irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). Mytesi® has demonstrated benefit to D-IBS patients in published Phase 2 studies.

Canalevia is our lead veterinary prescription drug product candidate, intended for treatment of various forms of diarrhea in dogs. We achieved statistically significant results in a multicenter canine proof-of-concept study completed in February 2015, supporting the conclusion that Canalevia treatment is superior to placebo. As we announced in December 2015, the pivotal clinical field study to evaluate the safety and effectiveness of Canalevia for acute diarrhea in dogs is underway. Two-hundred dogs were enrolled in the Canalevia pivotal study, which completed enrollment in January 2017. We have received Minor Use in a Minor Species (MUMS) designation for Canalevia for Chemotherapy-Induced Diarrhea (CID) in dogs, and we are pursuing MUMS designation for Canalevia for the indication of exercise-induced diarrhea (EID) in dogs. If Canalevia is approved for CID in dogs, we expect to conduct the commercial launch of Canalevia for this indication in 2018.

Canalevia is a canine-specific formulation of crofelemer, an active pharmaceutical ingredient isolated and purified from the *Croton lechleri* tree, which is sustainably harvested. Members of our management team developed crofelemer while at Napo, which was our parent company until May 13, 2015. Canalevia utilizes the same mechanism of action as Mytesi, as do Neonorm Foal and Neonorm Calf our lead non-prescription products. 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 its low risk strategy of extending the clinical success in humans to preweaned dairy calves, foals, piglets, and dogs; and we believe these clinical benefits will continue to be confirmed in other mammalian species.

Neonorm is a standardized botanical extract derived from the *Croton lechleri* tree. The reception among users of Neonorm Calf and Neonorm Foal, an anti-diarrheal product we launched for newborn horses in early 2016 has been positive. We launched Neonorm Calf in the United States at the end of 2014 for preweaned dairy calves. In June 2017 we launched neonorm.com, a commercial website for

Table of Contents

both Neonorm products. As we announced on June 14, 2017, the Organic Materials Review Institute (OMRI) has reviewed Neonorm Calf and determined that it is allowed for use in compliance with the U.S. Department of Agriculture National Organic Program. OMRI is an international nonprofit organization that determines which input products are allowed for use in organic production and processing.

The clinically-proven performance of Neonorm Foal, in combination with our heightened understanding of market needs within the global equine space, is driving our increased focus on equine product development. Equilevia is our non-prescription product for total gut health in equine athletes. Gut health is important in horses, as colic can cause an otherwise healthy horse to die in a matter of hours. Although we are still assessing the size of this opportunity, we expect to launch sales of Equilevia in the fall of 2017. Equilevia is a pharmaceutical formulation of a standardized botanical extract.

Canalevia, Equilevia and Neonorm are distinct products formulated to address specific species and market channels. We have filed nine investigational new animal drug applications, or INADs, with the FDA and intend to develop species-specific formulations of Neonorm in six additional target species, and Canalevia for both cats and dogs.

We, through Napo, own the intellectual property rights and technology related to our products and product candidates, including rights to a library of over 2,300 medicinal plants, for all veterinary treatment uses and indications for all species of animals. This includes rights to Neonorm, Canalevia, and other distinct prescription drug product candidates in our pipeline along with the corresponding existing preclinical and clinical data packages. We also recently expanded this intellectual property portfolio to include combinations of our proprietary anti-secretory product lines, Canalevia and Neonorm, with the non-absorbed antibiotic, rifaximin, for gastrointestinal indications in all animals.

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.

About Mytesi

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

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

Corporate Information

We were incorporated in the State of Delaware on June 6, 2013. Our principal executive offices are located at 201 Mission Street, Suite 2375, San Francisco, CA 94015 and our telephone number is (415) 371-8300. Our website address is www.jaguaranimalhealth.com. The information contained on, or that can be accessed through, our website is not part of this prospectus. Our voting common stock is

Table of Contents

listed on the NASDAQ Capital Market and trades under the symbol "JAGX." On July 31, 2017, we completed the acquisition of Napo (the "Merger") pursuant to the Agreement and Plan of Merger, dated March 31, 2017, by and among the Company, Napo, Napo Acquisition Corporation, and Napo's representative (the "Merger Agreement").

Jaguar Health, our logo, Canalevia, Neonorm and Mytesi are our trademarks that are used in this prospectus. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ©, ® or symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

The Offering

This prospectus relates to the offer by us of up to $60,000,000 of common stock, warrants, subscription rights or units in one or more offerings and in any combination.

This prospectus also relates to the resale of up to 6,852,998 shares of our common stock held by the selling shareholders identified in this prospectus, including its transferees, pledgees, donees or successors. See "Selling Shareholders." The selling shareholders may offer to sell these shares at fixed prices, at prevailing market prices at the time of sale, at varying prices or at negotiated prices. We have agreed to register the offer and sale of the common stock to satisfy registration rights we have granted to the selling shareholders. We will not receive any proceeds from the sale of the securities by the selling shareholders.

Table of Contents

RISK FACTORS

Please carefully consider the risk factors described in our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus. Additional risks and uncertainties not presently known to us or that we deem currently immaterial may also impair our business operations or adversely affect our results of operations or financial condition.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

Table of Contents

UNAUDITED PRO FORMA CONSOLIDATED FINANCIAL INFORMATION

Incorporated by reference herein is the unaudited pro forma consolidated financial information reflecting the consummation of the Merger and related transactions. This financial information is included in Exhibit 99.2 to our Current Report on Form 8-K, filed with the SEC on August 29, 2017 and consists of (i) the unaudited pro forma combined condensed statement of operations for the six months ended June 30, 2017, (ii) the unaudited pro forma consolidated balance sheet, as of June 30, 2017 and (iii) the unaudited pro forma combined condensed statement of operations, for the year ended December 31, 2016. The unaudited pro forma consolidated financial information should be read in conjunction with the historical consolidated financial statements and the related notes of the Company, included in the Company's periodic reports filed with the SEC, and of Napo, included in Exhibit 99.2 to our Current Report on Form 8-K/A, filed with the SEC on August 4, 2017, and Exhibit 99.1 to our Current Report on Form 8-K, filed with the SEC on August 29, 2017, each of which are incorporated by reference herein. See "Incorporation of Information by Reference."

Table of Contents

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of the securities offered by us for working capital and other general corporate purposes, and possibly acquisitions of other companies, products or technologies. Working capital and other general corporate purposes may include research and development expenditures, capital expenditures, operating and administrative expenditures, and any other purpose that we may specify in any prospectus supplement. While we have no current plans for any specific acquisitions at this time, we believe opportunities may exist from time to time to expand our current business through strategic alliances or acquisitions with other companies, products or technologies. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of the securities offered by us. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities. Our plans to use the estimated net proceeds from the sale of the securities offered by us may change, and if they do, we will update this information in a prospectus supplement.

We will not receive any of the proceeds from the sale of shares of our common stock by the selling shareholders. The selling shareholders will receive all of the proceeds from such sale. The selling shareholders will pay any underwriting discounts and commissions and expenses incurred by the selling shareholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling shareholders in disposing of the shares held by them. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, fees and expenses of our counsel and our independent registered public accountants.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

General

The following is a summary of the rights of our common stock and preferred stock and of certain provisions of our third amended and restated certificate of incorporation and amended and restated bylaws. This summary is not complete. For more detailed information, please see the third amended and restated certificate of incorporation and amended and restated bylaws, each of which is incorporated by reference into the registration statement of which this prospectus is a part.

We will describe in a prospectus supplement the specific terms of any common stock we may offer pursuant to this prospectus. If indicated in a prospectus supplement, the terms of such common stock or preferred stock may differ from the terms described below.

Our authorized capital stock consists of 310,000,000 shares, all with a par value of $0.0001 per share, of which 250,000,000 shares are designated as voting common stock, 50,000,000 shares are designated as non-voting common stock, and 10,000,000 shares are designated as preferred stock.

Voting Common Stock and Non-Voting Common Stock

As of August 11, 2017, we had 24,797,637 shares of voting common stock outstanding held by 24 stockholders of record, 42,903,218 shares of non-voting common stock outstanding held by 6 stockholders of record, and zero shares of preferred stock outstanding.

As of August 11, 2017, there were outstanding options to purchase 2,952,039 shares of our voting common stock with a weighted-average exercise price of $2.48 per share and outstanding RSUs for 5,893,849 shares of our voting common stock.

As of August 11, 2017, there were outstanding warrants exercisable for 6,656,333 shares of our voting common stock with a weighted-average exercise price of $1.15 per share.

Voting Rights

The holders of our voting common stock are entitled to one vote per share on all matters to be voted on by our stockholders. The holders of our non-voting common stock are not entitled to vote on matters submitted to our stockholders, other than in connection with a change of control of the Company.

Dividends

Subject to preferences that may be applicable to any outstanding our preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. We are required to obtain the prior written consent of Nantucket Investments Limited ("Nantucket") before the issuance of dividends to holders of our voting common stock and/or non-voting common stock for so long as Nantucket or its affiliates own any shares of our non-voting common stock.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our voting common stock and non-voting common stock will be entitled to share ratably in the net assets legally available for distribution to our stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of our preferred stock.

Table of Contents

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights. There are no redemption or sinking fund provisions applicable to our common stock.

Shares of our non-voting common stock are convertible into shares of our voting common stock on a one-for-one basis (i) at the option of the respective holders thereof, at any time and from time to time on or after April 1, 2018 or (ii) automatically, without any payment of additional consideration by the holder thereof, (x) upon a transfer of such shares to any person or entity that is neither an affiliate of Nantucket nor an investment fund, investment vehicle or other account, that is, directly or indirectly, managed or advised by Nantucket or any of its affiliates pursuant to a sale of such stock to a third-party for cash in accordance with the terms and condition set forth in the Investor Rights Agreement, dated March 31, 2017, between the Company and Nantucket, or (y) upon the release or transfer of such shares to the registered holders of Napo's outstanding shares of common stock immediately prior to the consummation of the Merger (the "Napo Legacy Stockholders").

The rights, preferences and privileges of the holders of our voting common stock and non-voting common stock are subject to and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of our preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. We have no current plan to issue any shares of preferred stock.

Warrants

As of August 11, 2017, we had outstanding warrants to purchase an aggregate of 6,656,333 shares of our voting common stock, 207,664 of which are exercisable at a price of $2.53 per share and expire on February 5, 2019; 16,666 of which are exercisable at a price of $0.69 per share and expire on June 26, 2020; 178,569 of which are exercisable at a price of $5.60 per share and expire on June 3, 2020; 58,035 of which are exercisable at a price of $5.60 per share and expire December 31, 2017; 111,605 of which are exercisable at a price of $5.60 per share and expire December 31, 2017; 143,000 of which are exercisable at a price of $8.75 per share and expire on May 13, 2020; 120,000 of which are exercisable at a price of $0.01 per share and expire on or before July 28, 2022; 1,800,001 of which are exercisable at a price of $0.75 per share and expire on May 29, 2022; 1,666,668 of which are exercisable at a price of $0.90 per share and expire on November 29, 2017; 758,334 of which are exercisable at a price of $1.00 per share and expire on May 29, 2018; 370,916 of which are exercisable at a price of $0.51 per share and expire on January 31, 2019; 145,457 of which are exercisable at a price of $0.08 per share and expire on December 31, 2018; and 1,079,418 of which are exercisable at a price of $0.08 per share and expire on December 31, 2025.

Table of Contents

Registration Rights

Pursuant to the Registration Rights Agreement, dated November 22, 2016, we are required to file one or more registration statements as permissible and necessary to register under the Securities Act, the resale of the shares of our voting common stock and shares of our voting common stock underlying warrants sold to the investors pursuant to the securities purchase agreement, dated November 22, 2016, between us and certain institutional investors.

Pursuant to the Registration Rights Agreement, dated June 8, 2016, we are required to file one or more registration statements as permissible and necessary to register under the Securities Act, the resale of the shares of our voting common stock sold to Aspire Capital Fund LLC ("Aspire Capital") under the common stock purchase agreement, dated June 8, 2016, between us and Aspire Capital.

Pursuant to the Commitment Letter, dated February 21, 2017, signed by Invesco Asset Management Limited ("Invesco"), and the Share Purchase Agreement, dated July 31, 2017, between us and Invesco, we are required to register the resale of the shares of our voting common stock sold to Invesco thereunder. We are registering the resale of such shares pursuant to the registration statement of which this prospectus forms a part.

Pursuant to the Note Purchase Agreement, dated March 1, 2017, by and among Napo, MEF I, LP and Riverside Merchant Partners, Napo is required to include in the Merger Agreement provisions, consistent with the terms set forth in Annex II of the Note Purchase Agreement, that we register the shares of our voting common stock issuable upon exchange of the Exchangeable Promissory Notes issuable thereunder.

Pursuant to the Amended and Restated Note Purchase Agreement, dated March 31, 2017, by and among Napo, Kingdon Associates, M. Kingdon Offshore Master Fund L.P. and Kingdon Family Partnership, L.P., we are required to register the shares of our voting common stock issuable upon conversion of the Conversion Stock (as defined therein), together with any shares of our voting common stock issuable in connection with interest payments under the Convertible Promissory Notes issuable thereunder.

Pursuant to the settlement agreements with Nantucket, Dorsar Investment Company, Alco Investment Company, Two Daughters LLC, Boies Schiller Flexner LLP and Dan Becka on or about March 31, 2017, Napo agreed to cause us to register the shares of our voting common stock, the shares of our voting common stock issuable upon conversion of the shares of our non-voting common stock, and the shares of our voting common stock underlying the warrants, in each case as issuable under the settlement agreements. We are registering the resale of shares of voting stock issuable upon conversion of shares of non-voting common stock held by Dan Becka pursuant to the registration statement of which this prospectus forms a part.

Pursuant to the share purchase agreements, each entered on or about June 23, 2017, between us and the investors named therein, relating to the issuance of $100,000 of our voting common stock, we are required to file one or more registration statements as permissible and necessary to register under the Securities Act the resale of the shares of our voting common stock sold to the investors thereto.

Pursuant to the Securities Purchase Agreement, dated June 29, 2017, between us and Chicago Venture Partners L.P., we are required to register the shares of our voting common stock issuable upon conversion of the Convertible Promissory Note, due August 2, 2018, issued thereunder.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Delaware Law

Certain provisions of Delaware law and our third amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could have the effect of

Table of Contents

delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed in part to encourage anyone seeking to acquire control of us to negotiate with our board of directors. We believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Third Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our third amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;

specify that special meetings of our stockholders can be called only by our board of directors, the chairman of our board of directors, the chief executive officer or the president;

establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;

provide that directors may be removed only for cause;

provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;

establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms;

specify that no stockholder is permitted to cumulate votes at any election of our board of directors; and

require approval of the stockholders of at least 75% of the shares and a majority of the board of directors to amend certain of the above-mentioned provisions.

Exclusive Jurisdiction

Under the provisions of our third amended and restated certificate of incorporation, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of us; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our third amended and restated certificate of incorporation or amended and restated bylaws; or (iv) any action asserting a claim against us governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our third amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Table of Contents

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

prior to the date of the transaction, our board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon the closing of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers, and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

at or subsequent to the date of the transaction, the business combination is approved by our board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66^{2}/_{3}\%$ of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage business combinations or other attempts that might result in the payment of a premium over the market price for the shares of common stock held by our stockholders.

The provisions of Delaware law and our third amended and restated certificate of incorporation and amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company N.A. The transfer agent and registrar's address is 250 Royall St., Canton, MA 02021. The transfer agent's telephone number is (800) 962-4284.

Listing

Our voting common stock is listed on The NASDAQ Capital Market under the symbol "JAGX." On August 22, 2016, we received notice from NASDAQ, which indicated that under NASDAQ Listing Rule 5550(b)(1), we are required to maintain a minimum of $2,500,000 in stockholders' equity for continued listing. For the year ended December 31, 2016, we reported stockholders' deficit of

Table of Contents

$2,454,185. Based on the plan that we submitted to regain compliance, the SEC granted us an extension until February 21, 2017 to regain compliance.

On February 22, 2017, we received a letter from NASDAQ stating that NASDAQ determined that we did not meet the terms of the extension and that our securities are subject to delisting from NASDAQ unless we timely request a hearing before the NASDAQ Hearings Panel. We timely requested a hearing before the Panel, and at the hearing on April 20, 2017, we presented our plan to evidence compliance with the $2,500,000 stockholders' equity requirement (or the alternatives of market value of listed securities of $35 million or net income from continuing operations) concurrent with the Merger and requested the continued listing of our common stock on NASDAQ pending our return to compliance. On April 27, 2017, we were notified that the Panel determined to grant our request for continued listing on NASDAQ. On July 31, 2017, we notified NASDAQ that we successfully completed our acquisition of Napo and, as a result, believe we have stockholders' equity in excess of $2.5 million as of the date thereof.

On May 16, 2017, we received notice from NASDAQ, which indicated that our closing bid price was less than $1.00 per share for 30 consecutive business days. We have a 180 calendar day grace period, or until November 13, 2017, to regain compliance with the minimum bid price requirement. The minimum bid price requirement will be met if our common stock has a minimum closing bid price of at least $1.00 per share for a minimum of 10 consecutive business days during the 180 calendar day grace period.

Table of Contents

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock. Warrants may be issued independently or together with common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of warrants or beneficial owners of warrants. This summary of some provisions of the warrants is not complete. You should refer to the warrant agreement, including the forms of warrant certificate representing the warrants, relating to the specific warrants being offered for the complete terms of the warrant agreement and the warrants. That warrant agreement, together with the terms of the warrant certificate and warrants, will be filed with the SEC in connection with the offering of the specific warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the title of such warrants;

the aggregate number of such warrants;

the price or prices at which such warrants will be issued;

the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;

the price at which the securities purchasable upon exercise of such warrants may be purchased;

the date on which the right to exercise such warrants will commence and the date on which such right shall expire;

any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;

if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;

if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;

if applicable, the date on and after which such warrants and the related securities will be separately transferable;

information with respect to book-entry procedures, if any; and

any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax considerations.

Warrants for the purchase of common stock will be offered and exercisable for U.S. dollars only. Securities warrants will be issued in registered form only.

Each warrant will entitle its holder to purchase the number of shares of common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised warrants will become void. We will specify the place or places where, and the manner in which, warrants may be exercised in the applicable prospectus supplement.

Table of Contents

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Prior to the exercise of any warrants to purchase common stock, holders of the warrants will not have any of the rights of holders of common stock purchasable upon exercise, including the right to vote or to receive any payments of dividends on the common stock purchasable upon exercise.

Table of Contents

DESCRIPTION OF SUBSCRIPTION RIGHTS

The following is a general description of the terms of the subscription rights we may issue from time to time. Particular terms of any subscription rights we offer will be described in the prospectus supplement or free writing prospectus relating to such subscription rights, and may differ from the terms described herein.

We may issue subscription rights to purchase our securities. These subscription rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering. The applicable prospectus supplement will describe the specific terms of any offering of subscription rights for which this prospectus is being delivered, including the following:

- whether common stock or warrants for those securities will be offered under the stockholder subscription rights;
- the price, if any, for the subscription rights;
- the exercise price payable for each security upon the exercise of the subscription rights;
- the number of subscription rights issued to each stockholder;
- the number and terms of the securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities;
- if appropriate, a discussion of material U.S. federal income tax considerations; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the SEC if we offer subscription rights.

Explanation of Responses:

Table of Contents

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, warrants, or subscription rights in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under "Description of Capital Stock," "Description of Warrants," and "Description of Subscription Rights" will apply to each unit, as applicable, and to any common stock, warrant, or subscription right included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or

Table of Contents

trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Table of Contents

SELLING SHAREHOLDERS

The shares of common stock being offered by the selling shareholders are those previously issued to the selling shareholders. We are registering the shares of common stock in order to permit the selling shareholders to offer the shares for resale from time to time.

The following table sets forth:

- the selling shareholders and other information regarding the beneficial ownership of the shares of common stock by the selling shareholders;
- the number of shares of common stock beneficially owned by the selling shareholders as of August 24, 2017, without regard to any limitations on exercises prior to the sale of the shares covered by this prospectus;
- the number of shares that may be offered by the selling shareholders pursuant to this prospectus;
- the number of shares to be beneficially owned by the selling shareholders and their respective affiliates following the sale of any shares covered by this prospectus; and
- the percentage of our issued and outstanding common stock to be beneficially owned by the selling shareholders and their respective affiliates following the sale of all shares covered by this prospectus.

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

Name of Selling Shareholder	Number of shares of Common Stock Owned Prior to Offering	Maximum Number of shares of Common Stock to be Sold Pursuant to this Prospectus	Number of shares of Common Stock Owned After Offering(1)	
			Number	Percent
Invesco Ltd.(2)	6,297,603	6,297,603	0	
Daniel Becka(3)	618,288	555,395	62,893	*

* Less than 1%.

(1) Assumes that each selling shareholder sells all shares of common stock registered under this prospectus held by such selling shareholder.

(2) As it previously reported on Amendment No. 1 to its Schedule 13G, Invesco Ltd, in its capacity as an investment adviser, may have been deemed to beneficially own 1,974,360 shares. On June 27, 2017, Invesco Ltd., in its capacity as an investment adviser, acquired beneficial ownership of 1,080,000 shares for $0.50 per share on the open market. Invesco Ltd. in its capacity as an investment adviser, beneficially acquired 3,243,243 shares for $0.925 in a private purchase from the Company on July 31, 2017. In addition, prior to the Merger, Invesco Asset Management Limited held 38,878,169 shares of common stock of Napo, representing approximately 35.9% of the outstanding shares of Napo common stock. Pursuant to the terms of the Merger Agreement, upon consummation of the Merger, such shares of Napo common stock were exchanged for contingent rights to receive shares of our voting common stock, which contingent rights are excluded from the shares listed in the table above. Invesco Asset Management Limited is a subsidiary of Invesco Ltd.

(3) Consists of (i) 62,893 shares of voting common stock and (ii) 555,395 shares of voting common stock issuable upon conversion of the shares of non-voting common stock held by Daniel Becka.

Table of Contents

PLAN OF DISTRIBUTION

We or the selling shareholders may offer and sell the securities from time to time in one or more of the following transactions:

to or through underwriters, brokers or dealers (acting as agent or principal);

on the NASDAQ Capital Market, in the over-the-counter market or on any other national securities exchange on which our shares are then listed or traded;

directly to one or more other purchasers;

upon the exercise of rights distributed or issued to our security holders;

through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction;

in "at the market" offerings within the meanings of Rule 415(a)(4) under the Securities Act of 1933 or through a market maker or into an existing market, on an exchange, or otherwise;

directly to purchasers, through a specific bidding or auction process, on a negotiated basis or otherwise;

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

through the writing or settlement of options (including put or call options), whether the options are listed on an options exchange or otherwise;

through the distribution of the common stock by the selling stockholders to their partners, members or stockholders;

through agents on a best-efforts basis;

through any other method permitted pursuant to applicable law; or

otherwise through a combination of any of the above methods of sale.

In addition, we or the selling shareholders may enter into option, share lending or other types of transactions that require us or the selling shareholders, as applicable, to deliver shares of common stock to an underwriter, broker or dealer, who will then resell or transfer the shares of common stock under this prospectus. We or the selling shareholders may also enter into hedging transactions with respect to our securities or the securities of such selling shareholders, as applicable. For example, we or the selling shareholders may:

enter into transactions involving short sales of the shares of common stock by underwriters, brokers or dealers;

sell shares of common stock short and deliver the shares to close out short positions;

enter into option or other types of transactions that require us or the selling shareholders, as applicable, to deliver shares of common stock to an underwriter, broker or dealer, who will then resell or transfer the shares of common stock under this prospectus; or

loan or pledge the shares of common stock to an underwriter, broker or dealer, who may sell the loaned shares or, in the event of default, sell the pledged shares.

The selling shareholders will act independently of us in making decisions with respect to the timing, manner and size of each sale of shares of common stock covered by this prospectus.

Table of Contents

We or the selling shareholders may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or the selling shareholders, as applicable, or borrowed from us, the selling shareholders or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us or the selling shareholders in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the applicable prospectus supplement (or a post-effective amendment). In addition, we or the selling shareholders may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or the securities of the selling shareholders, as applicable, or in connection with a concurrent offering of other securities.

Shares of common stock may also be exchanged for satisfaction of the selling shareholders' obligations or other liabilities to its creditors. Such transactions may or may not involve brokers or dealers.

If we or the selling shareholders use any underwriter, we will provide a prospectus supplement that will name any underwriter involved in the offer and sale of the securities. The prospectus supplement will also set forth the terms of the offering, including:

- the purchase price of the securities and the proceeds we or the selling shareholders, as applicable, will receive from the sale of the securities;
- any underwriting discounts and other items constituting underwriters' compensation;
- any public offering or purchase price and any discounts or commissions allowed or re-allowed or paid to dealers;
- any commissions allowed or paid to agents;
- any securities exchanges on which the securities may be listed;
- the method of distribution of the securities;
- the terms of any agreement, arrangement or understanding entered into with the underwriters, brokers or dealers; and
- any other information we think is important.

If underwriters or dealers are used in the sale, the securities will be acquired by the underwriters or dealers for their own account. The securities may be sold from time to time by us or the selling shareholders in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices;

at varying prices determined at the time of sale; or

at negotiated prices.

Explanation of Responses: 83

Table of Contents

Such sales may be effected:

- in transactions on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in transactions in the over-the-counter market;
- in block transactions in which the broker or dealer so engaged will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction, or in crosses, in which the same broker acts as an agent on both sides of the trade;
- through the writing of options; or
- through other types of transactions.

The securities may be offered to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more of such firms. Unless otherwise set forth in the prospectus supplement, the obligations of underwriters or dealers to purchase the securities offered will be subject to certain conditions precedent and the underwriters or dealers will be obligated to purchase all the offered securities if any are purchased. Any public offering price and any discount or concession allowed or reallowed or paid by underwriters or dealers to other dealers may be changed from time to time.

We may also make direct sales through subscription rights distributed to our existing stockholders on a pro rata basis, which may or may not be transferable. In any distribution of subscription rights to our stockholders, if all of the underlying securities are not subscribed for, we may then sell the unsubscribed securities directly to third parties or may engage the services of one or more underwriters, dealers or agents, including standby underwriters, to sell the unsubscribed securities to third parties. In addition, whether or not all of the underlying securities are subscribed for, we may concurrently offer additional securities to third parties directly or through underwriters, dealers or agents.

The selling shareholders might not sell any shares of common stock under this prospectus. In addition, any shares of common stock covered by this prospectus that qualify for sale pursuant to Rule 144 under the Securities Act of 1933 may be sold under Rule 144 rather than pursuant to this prospectus.

The securities may be sold directly by us or the selling shareholders or through agents designated by us or the selling shareholders, as applicable, from time to time. Any agent involved in the offer or sale of the securities in respect of which this prospectus is delivered will be named, and any commissions payable by us or the selling shareholders, as applicable, to such agent will be set forth in, the prospectus supplement. Unless otherwise indicated in the prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

Offers to purchase the securities offered by this prospectus may be solicited, and sales of the securities may be made by us or by the selling shareholders directly to institutional investors or others, who may be deemed to be underwriters within the meaning of the Securities Act of 1933 with respect to any resale of the securities. The terms of any offer made in this manner will be included in the prospectus supplement relating to the offer.

If indicated in the applicable prospectus supplement, underwriters, dealers or agents will be authorized to solicit offers by certain institutional investors to purchase securities from us pursuant to contracts providing for payment and delivery at a future date. Institutional investors with which these contracts may be made include, among others:

- commercial and savings banks;
- insurance companies;

23

Explanation of Responses:

Table of Contents

pension funds;

investment companies; and

educational and charitable institutions.

In all cases, these purchasers must be approved by us or the selling shareholders, as applicable. Unless otherwise set forth in the applicable prospectus supplement, the obligations of any purchaser under any of these contracts will not be subject to any conditions except that (a) the purchase of the securities must not at the time of delivery be prohibited under the laws of any jurisdiction to which that purchaser is subject, and (b) if the securities are also being sold to underwriters, we or the selling shareholders, as applicable, must have sold to these underwriters the securities not subject to delayed delivery. Underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

Some of the underwriters, dealers or agents used by us or the selling shareholders in any offering of securities under this prospectus may be customers of, engage in transactions with, and perform services for us or the selling shareholders, as applicable, or affiliates of ours or theirs, as applicable, in the ordinary course of business. Underwriters, dealers, agents and other persons may be entitled under agreements which may be entered into with us or the selling shareholders to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, and to be reimbursed by us or the selling shareholders for certain expenses.

Any securities initially sold outside the U.S. may be resold in the U.S. through underwriters, dealers or otherwise.

Any underwriters to which offered securities are sold by us or the selling shareholders for public offering and sale may make a market in such securities, but those underwriters will not be obligated to do so and may discontinue any market making at any time.

The anticipated date of delivery of the securities offered by this prospectus will be described in the applicable prospectus supplement relating to the offering.

In compliance with the guidelines of the Financial Industry Regulatory Authority ("FINRA"), the aggregate maximum discount, commission, agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the offering proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

No FINRA member may participate in any offering of securities made under this prospectus if such member has a conflict of interest under FINRA Rule 5121, including if 5% or more of the net proceeds, not including underwriting compensation, of any offering of securities made under this prospectus will be received by a FINRA member participating in the offering or affiliates or associated persons of such FINRA members, unless a qualified independent underwriter has participated in the offering or the offering otherwise complies with FINRA Rule 5121.

To comply with the securities laws of some states, if applicable, the securities may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the securities may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities.

We agreed to keep this prospectus effective until the earlier of (i) the date on which all registrable securities covered by this prospectus have been sold hereunder or (ii) the date on which all of the remaining registrable securities are eligible to be sold without compliance with the volume limitations

Table of Contents

or public information requirements of Rule 144 under the Securities Act. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

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

Table of Contents

LEGAL MATTERS

The validity of the securities offered by this prospectus will be based upon by Reed Smith LLP, Palo Alto, California.

EXPERTS

The financial statements of the Company as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 incorporated by reference in this prospectus and the registration statement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm (the reports on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

The consolidated financial statements of Napo as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 incorporated by reference in this prospectus and the registration statement have been audited by Macias Gini & O'Connell LLP, as stated in their report incorporated by reference in this registration statement (which report contains an explanatory paragraph regarding Napo's ability to continue as a going concern), and are incorporated by reference in reliance upon such report and upon the authority of such firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

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

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

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

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement and any prospectus supplement filed hereafter, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration

Table of Contents

statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- our Annual Report on Form 10-K/A for the fiscal year ended December 31, 2016 filed on May 26, 2017;
- our definitive proxy statement and definitive additional materials, on Schedule 14A, relating to our Annual Meeting of Stockholders held on May 8, 2017, filed on April 17, 2017;
- our Quarterly Report on Form 10-Q/A for the fiscal quarter ended March 31, 2017 filed on June 23, 2017 and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2017 filed on August 9, 2017;
- our Current Reports on Form 8-K filed on January 31, 2017, February 9, 2017, February 24, 2017, March 31, 2017, April 6, 2017, May 2, 2017, May 8, 2017, May 19, 2017, July 3, 2017, July 7, 2017, July 28, 2017, July 31, 2017, August 1, 2017, August 4, 2017, August 16, 2017 and August 29, 2017;
- the description of our common stock contained in our registration statement on Form 8-A filed on October 30, 2014 (Registration No. 001-36714) with the SEC, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

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

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

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

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

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

Table of Contents

2,000,000 Shares of Common Stock

PROSPECTUS SUPPLEMENT

November 24, 2017