UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2017
or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____
Commission file number: 001-36075

Evoke Pharma, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-8447886**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
420 Stevens Avenue, Suite 370 Solana Beach, California	**92075**
(Address of Principal Executive Offices)	**(Zip Code)**

858-345-1494
(Registrant's Telephone Number, Including Area Code)
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.0001 per share	**The Nasdaq Capital Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). ☒ Yes ☐ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of the last business day of the registrant's most recently completed second fiscal quarter was approximately $32.9 million, based on the closing price of the registrant's common stock on the Nasdaq Capital Market of $2.56 per share.

The number of outstanding shares of the registrant's common stock, par value $0.0001 per share, as of February 28, 2018 was 15,493,368.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2017 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant's fiscal year ended December 31, 2017.

EVOKE PHARMA, INC.

FORM 10-K — ANNUAL REPORT

For the Fiscal Year Ended December 31, 2017

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PART I

Forward-Looking Statements and Market Data

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, regulatory developments, research and development costs, timing and likelihood of success, 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 statement. The forward-looking statements are contained principally in the sections entitled "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business." In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. Although we believe the expectations reflected in these forward-looking statements are reasonable, such statements are inherently subject to risk and we can give no assurances that our expectations will prove to be correct. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K. You should read this Annual Report on Form 10-K completely. As a result of many factors, including without limitation those set forth under "Risk Factors" under Item 1A of this Part I below, and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements. Except as required by applicable law, we undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date of this report or to reflect actual outcomes. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for Gimoti™, including data regarding the estimated size of those markets, their projected growth rates, the incidence of certain medical conditions, statements that certain drugs or classes of drugs are the most widely prescribed in the United States or other markets, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources

We use our registered trademarks, EVOKE PHARMA and Gimoti, in this Annual Report on Form 10-K. This Annual Report on Form 10-K also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this Annual Report on Form 10-K appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, 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.

Unless the context requires otherwise, references in this Annual Report on Form 10-K to "Evoke," "we," "us" and "our" refer to Evoke Pharma, Inc.

Item 1. Business

Overview

We are a specialty pharmaceutical company focused primarily on the development of drugs to treat gastrointestinal, or GI, disorders and diseases. We are developing Gimoti, an investigational metoclopramide nasal spray for the relief of symptoms associated with acute and recurrent diabetic gastroparesis in women. Diabetic gastroparesis is a GI disorder afflicting millions of individuals worldwide and is characterized by slow or delayed gastric emptying and evidence of gastric retention in the absence of mechanical obstruction and can cause various serious digestive system symptoms and other complications. Metoclopramide tablets and injection are the only products currently approved in the United States to treat the symptoms associated with acute and recurrent diabetic gastroparesis. Gimoti is a novel nasal spray formulation of metoclopramide designed to provide systemic delivery of the molecule through the nasal mucosa.

In individuals with gastroparesis, food remains in the stomach for a longer time than normal, leading to a variety of GI symptoms and systemic metabolic complications. Gastroparesis frequently occurs in individuals with diabetes, but is also observed in patients with prior gastric surgery, a preceding infectious illness, pseudo-obstruction, collagen vascular disorders and anorexia nervosa. In some patients with gastroparesis, no cause can be identified, which is referred to as idiopathic gastroparesis. According to the American Motility Society Task Force on Gastroparesis, the prevalence of gastroparesis is estimated to be up to 4% of the United States population. Signs and symptoms of gastroparesis may include nausea, early satiety, bloating, prolonged fullness, upper abdominal pain, vomiting and retching. Patients may experience any combination of signs and symptoms with varying degrees of severity.

Patients with diabetic gastroparesis may experience impaired glucose control due to unpredictable gastric emptying and altered absorption of orally administered hypoglycemic drugs, which may affect the severity of their signs and symptoms. Severe signs and symptoms may cause complications such as malnutrition, esophagitis, and Mallory-Weiss tears. Gastroparesis adversely affects the lives of patients with the disease, resulting in decreased social interaction, poor work functionality, and the development of anxiety and/or depression.

We believe nasal spray administration has the potential to provide our target population of female diabetic gastroparesis patients with a preferred treatment option over the tablet formulation for several important reasons: (1) unlike metoclopramide tablets which may be absorbed erratically due to gastroparesis itself, Gimoti is designed to bypass the digestive system to allow for more predictable absorption without needing to determine if a patient's stomach is functioning (2) during episodes of vomiting Gimoti provides predictable drug absorption through the nasal mucosa; and (3) for gastroparesis patients experiencing nausea and are not wanting to swallow a pill or water, a nasal spray may be better tolerated than an oral medication.

We have evaluated Gimoti in a multicenter, randomized, double-blind, placebo-controlled parallel group, dose-ranging Phase 2b clinical trial in 287 male and female subjects with diabetic gastroparesis where Gimoti doses of 10 mg and 14 mg were effective in improving the characteristic and clinically-relevant symptoms associated with gastroparesis in women while exhibiting a favorable safety profile in men and women. Subjects received either Gimoti or placebo four times daily for 28 days.

In July 2016, we announced results from a Phase 3 clinical trial of Gimoti in female subjects with symptoms associated with acute and recurrent diabetic gastroparesis. This trial was a multicenter, randomized, double-blind, placebo-controlled, parallel group clinical trial to evaluate the efficacy, safety and population pharmacokinetics, or PK, of 10 mg Gimoti in adult female subjects with symptomatic diabetic gastroparesis and delayed gastric emptying by gastric emptying scintigraphy, or GES. Subjects received either Gimoti or placebo four times daily for 28 days. The primary endpoint was the change in symptoms from the baseline period to Week 4 as measured using a proprietary Patient Reported Outcome, or PRO, instrument. On a daily basis, subjects reported the frequency and severity of their gastroparesis signs and symptoms using a telephone diary. The subjects' daily symptom scores were the basis for calculating their weekly scores using the PRO instrument. A total of 205 subjects were randomized in this trial. Results of the trial showed that Gimoti did not achieve its primary endpoint of a symptom improvement at Week 4 in the intent to treat, or ITT, population.

Although the Phase 3 trial failed to achieve its primary endpoint, Gimoti demonstrated efficacy in patients with moderate to severe symptoms at baseline, which included 105 of the 205 patients (51%) enrolled in the study. In these patients with higher symptom severity, statistically significant benefits were demonstrated for those treated with Gimoti versus those receiving placebo. These statistically significant benefits were observed at Weeks 1, 2 and 3 in the ITT population and at all four weeks in the per protocol population. There were also clinically and statistically significant improvements in nausea and upper abdominal pain, two of the more severe and debilitating symptoms of gastroparesis, at all four weeks.

In September 2016, we announced the completion of a pre-New Drug Application, or pre-NDA, meeting with the U.S. Food and Drug Administration, or FDA. The purpose of the meeting was to discuss a proposed NDA and to confirm various regulatory, chemistry, manufacturing, and control, or CMC, and non-clinical requirements for our potential NDA submission for Gimoti. At the pre-NDA meeting, the FDA reviewed a portion of our data package being prepared for the NDA submission. Based on the review, discussion, and minutes received, we believe that such data package could be used with the submission of those portions of an NDA utilizing the 505(b)(2) pathway.

In December 2016, we had another pre-NDA meeting with FDA, in which FDA agreed that a comparative exposure PK trial was acceptable as a basis for submission of a Gimoti NDA. In March 2017, we had a type A meeting with FDA to finalize the design of the comparative exposure PK trial and reach agreement on certain other chemistry, manufacturing and controls-related items associated with the proposed NDA submission.

In October 2017, we announced positive topline results from the comparative exposure PK trial. The objective of the trial was to identify a dose of Gimoti that met the criteria for bioequivalence compared to the Listed Drug, Reglan Tablets after nasal and oral administration to healthy volunteers under fasted conditions.

The comparative exposure PK trial was an open label, 4-way crossover and enrolled 108 healthy male and female volunteers who each received one Reglan Tablet dose and three different doses of Gimoti in a random sequence. Following discussions at pre-NDA meetings with FDA, we planned to select a Gimoti dose based on criteria that included a 90% confidence interval for the ratio of area under the plasma concentration curve, or AUC, falling within the exposure equivalence range of 80-125% of Reglan Tablets. Though only one dose was needed to meet the dose selection criteria, the comparative exposure PK trial was designed to test three different strengths of Gimoti. Based on results of the study, two of the three doses tested met the dose selection criteria for the pooled data in women and men. The maximum observed plasma concentration, or C_{max}, for Gimoti was slightly lower than the equivalence range, but was anticipated and had been previously discussed with FDA as a likely outcome given the different route of administration and prior Gimoti PK trial results. Additionally, data showed the AUC and C_{max} increased in a dose related manner across all three strengths tested. Relative to safety, all Gimoti doses were well tolerated with no clinically significant adverse events reported following any of the doses.

Additional analysis of the PK data by sex revealed statistically significant differences in exposure between women and men given the same metoclopramide dose (nasal and oral). Based on this further analysis of results from the comparative exposure PK trial, statistically significantly lower AUC's were found in men compared to women. The findings were not explicitly attributable to differences in body mass index (BMI) or weight. Similarly sex-based differences were observed in a previous healthy volunteer study we conducted, irrespective of the route of metoclopramide administration (nasal, oral and IV).

In the most recent comparative exposure PK trial, results for women independently met equivalence criteria for $AUC_{0\text{-}inf}$ and $AUC_{0\text{-}t}$ at the tested Gimoti dose to be proposed in the NDA. We plan to submit our NDA for a female-only indication based on a dose in women with equivalent exposure to Reglan Tablets and will submit supporting efficacy and safety data from our Phase 2b and Phase 3 trials, specifically for women, at doses similar or lower than the dose to be proposed in the NDA.

In parallel, we recently held a pre-NDA meeting with FDA to discuss and clarify its expectations of items being prepared for inclusion in the NDA for Gimoti. The planned NDA will include our proposal for a risk management strategy and a post-approval safety study that will be designed to confirm prior safety findings and rule-out possible differences in side effects compared to the Reglan Tablet over 8 weeks. We expect to discuss the details of the post-marketing safety trial with FDA during the NDA review process. With the new sex-based PK findings, and to incorporate the feedback received by FDA at the most recent pre-NDA meeting, we expect to file the Gimoti NDA in the second quarter of 2018.

In March 2018, we announced that FDA granted the Company's request for a small business waiver of the Prescription Drug User Fee Act, or PDUFA, fee of approximately $2.4 million for its 505(b)(2) NDA for Gimoti.

We have no products approved for sale, and we have not generated any revenue from product sales or other arrangements. We have primarily funded our operations through the sale of our convertible preferred stock prior to our initial public offering, or IPO, in September 2013, borrowings under our bank loans and the sale of shares of our common stock on the Nasdaq Capital Market. We have incurred losses in each year since our inception. Substantially all of our operating losses resulted from expenses incurred in connection with advancing Gimoti through development activities and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We may never become profitable, or if we do, we may not be able to sustain profitability on a recurring basis.

Business Strategy

Our objective is to develop and bring to market products to treat acute and chronic GI motility disorders that are not satisfactorily treated with current therapies and that represent significant market opportunities. Our business strategy is to:

- *Pursue regulatory approval for Gimoti.* We have completed our Phase 3 trial of Gimoti in female subjects suffering from diabetic gastroparesis and a comparative exposure PK trial to serve as a basis for submission of an NDA for Gimoti. We expect to submit our NDA during the second quarter of 2018.
- *Seek partnerships to accelerate and maximize the potential for Gimoti.* Following our planned NDA submission for Gimoti, we will continue to evaluate partnering opportunities with pharmaceutical companies that have established development and sales and marketing capabilities to potentially enhance and accelerate the development and commercialization of Gimoti.
- *Explore building in-house capabilities to potentially commercialize Gimoti in the United States.* In addition to partnering opportunities, we are evaluating the development of a specialty sales force and marketing capabilities, either internally or externally, to allow us to directly market Gimoti in the United States, if approved by FDA. We have partnered with Syneos Health, Inc. (formerly inVentiv Commercial Services LLC), to build our commercial infrastructure as we prepare for the potential commercialization of Gimoti, including to potentially hire, train, retain and deploy a direct sales force.
- *Explore regulatory approval of Gimoti outside the United States*. We will initially seek approval of Gimoti in the United States and then will evaluate the market opportunity in other countries.

- *Evaluate the development and/or commercialization of other therapies for GI motility disorders*. Similar to our initial focus on gastroparesis, we will evaluate opportunities to in-license or acquire other product candidates, as well as commercial products, to treat patients suffering from predominantly GI disorders, seeking to identify areas of high unmet medical needs with limited treatment options.

The Gastrointestinal Market

The health of the GI system has a major effect on an individual's daily activities and quality of life. A retrospective review published by the National Institute of Diabetes and Digestive and Kidney Diseases estimated that in 2004 there were more than 72 million ambulatory care visits with a diagnosis of a GI disorder in the United States alone. The annual cost of these GI disorders in 2004, not including digestive cancers and viral diseases, was estimated to be greater than $114 billion in direct and indirect expenditures, including hospital, physician and nursing services as well as over-the-counter and prescription drugs.

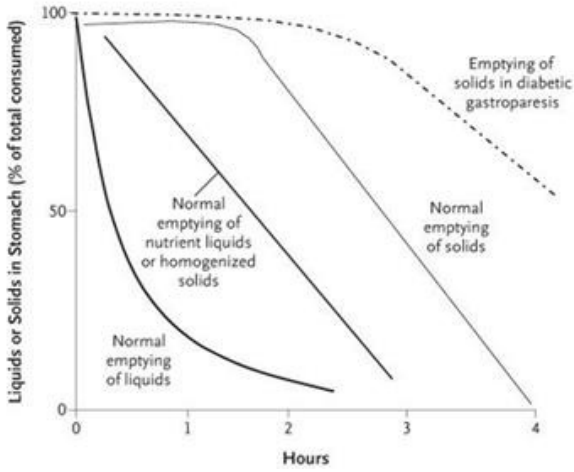
In 2004, the total cost of GI prescription drugs in the United States was $12.3 billion, and over half of this cost ($7.7 billion) was associated with drugs prescribed for gastroesophageal reflux disease, or GERD. Peptic ulcer disease, hepatitis C, irritable bowel syndrome, or IBS, and inflammatory bowel disease, or IBD, were major contributors to the remaining drug cost. Historically GI product development efforts have focused on indications with the largest patient populations such as GERD, constipation, peptic ulcers and IBS. As a result, limited innovation has occurred in other segments of the GI market, such as upper GI motility disorders, even though these disorders affect several million patients worldwide. Consequently, due to the limited treatment options available for upper GI motility disorders, we believe there is a substantial market opportunity for us to address significant unmet medical needs, initially for diabetic gastroparesis.

GI Motility Disorders

Motility disorders are one of the most common GI disorders. Motility disorders affect the orderly contractions or relaxation of the GI tract which move contents forward and prevent backward egress. This is important in the normal movement of food through the GI tract. Motility disorders are sometimes referred to as functional GI disorders to highlight that many abnormalities in stomach function can occur even when anatomic structures appear normal. Functional GI disorders affect the upper and lower GI tract and include gastroparesis, GERD, functional dyspepsia, constipation and IBS. It has been estimated by the International Foundation for Functional Gastrointestinal Disorders that one in four people in the United States suffer from functional GI disorders, having signs and symptoms such as abdominal pain, nausea, constipation, diarrhea, bloating, decreased appetite, early satiety, swallowing difficulties, heartburn, vomiting and/or incontinence.

Gastroparesis

Gastroparesis is a debilitating, chronic condition that has a significant impact on patients' lives. It is characterized by slow or delayed gastric emptying and evidence of gastric retention in the absence of mechanical obstruction. Muscular contractions in the stomach, which move food into the intestine, may be too slow, out of rhythm or erratic. The following graph depicts the timing associated with the emptying of solids in patients with diabetic gastroparesis compared to normal individuals:



Camilleri M. New England Journal of Medicine 2007

The stomach is a muscular sac between the esophagus and the small intestine where the digestion of food begins. The stomach makes acids and enzymes referred to as gastric juices which are mixed with food by the churning action of the stomach muscles. Peristalsis is the contraction and relaxation of the stomach muscles to physically breakdown food and propel it forward. The crushed and mixed food is liquefied to form chyme and is pushed through the pyloric canal into the small intestine in a controlled and regulated manner.

In gastroparesis, the stomach does not perform these functions normally, causing characteristic flares of signs and symptoms that include nausea, early satiety, prolonged fullness, bloating, upper abdominal pain, vomiting and retching. As a result of these signs and symptoms, patients may limit their food and liquid intake leading to poor nutrition, dehydration and electrolyte disturbances, and have poor blood glucose control, ultimately requiring hospitalization. If left untreated or not adequately treated, gastroparesis causes significant acute and chronic medical problems, including additional diabetic complications resulting from poor glucose control.

Gastroparesis in the Hospital Setting

When patients experience a flare of their gastroparesis symptoms that cannot be adequately managed by oral medications, they may be hospitalized for hydration, parenteral nutrition, and correction of abnormal blood glucose or electrolyte levels. In this setting, intravenous metoclopramide is the first line of treatment. Typically, these diabetic patients with gastroparesis symptoms remain in the hospital until they are stabilized and able to be effectively treated with oral metoclopramide. These hospitalizations are costly and expose patients to increased risks, including hospital-acquired infections. The number of patients with gastroparesis that require hospitalization due to their disease is growing, according to a study published in the *American Journal of Gastroenterology* in 2008. Additionally, the study reported, from 1995 to 2004, total hospitalizations with a primary diagnosis of gastroparesis increased 158%. Hospital admissions for patients with gastroparesis as the secondary diagnosis increased 136%. The average length of stay for a patient is approximately six days at an estimated cost of approximately $22,000. Compared to the other four most common upper GI admission diagnoses (GERD, gastric ulcer, gastritis or nonspecific nausea/vomiting), gastroparesis had the longest length of stay and one of the highest total charges per stay. Additionally, the study estimates that costs associated with gastroparesis as the primary or secondary diagnosis for admission exceeded $3.5 billion in 2004.

A study of patients in clinics at the University of Pittsburgh Medical Center between January 2004 and December 2008, published in the *Journal of Gastroenterology and Hepatology*, showed that patients with diabetic or post-surgical gastroparesis had significantly more emergency room visits than other gastroparesis groups. The study reinforced the view that gastroparesis constitutes a significant burden for patients and the healthcare system, with more than one-third of patients requiring hospitalization. The number of emergency room visits and annual days of inpatient treatment were comparable to patients with Crohn's disease. The study indicated that patients received an average of 6.7 prescriptions on admission. Eighty percent of the patients identified in the University of Pittsburgh study were women. According to a recent study conducted by Baylor College of Medicine and published in *Gastroenterology & Endoscopy* in December 2017, hospitalizations for gastroparesis have risen significantly since the early 1990s.

This study noted that the number of hospitalizations increased from roughly 900 in 1994 to 16,400 in 2014, with median costs climbing from $6,000 to approximately $24,500 during the period. The number of people who visited the emergency department because of gastroparesis rose from 15,549 in 2006 to 39,470 in 2014, with an average annual increase of nearly 13% over that time.

Etiology

Gastroparesis can be a manifestation of many systemic illnesses, arise as a complication of select surgical procedures, or develop due to unknown causes. Any disease inducing neuromuscular dysfunction of the GI tract can result in gastroparesis, with diabetes being one of the leading known causes. In a 2007 study published in *Current Gastroenterology Reports*, 29% of gastroparesis cases were found in association with diabetes, 13% developed as a complication of surgery and 36% were due to unknown causes. According to the American Motility Society Task Force on Gastroparesis, up to 4% of the U.S. population experiences symptomatic manifestations of gastroparesis. As the incidence of diabetes rises worldwide, the prevalence of gastroparesis is expected to rise correspondingly.

The most common identified cause of gastroparesis is diabetes mellitus. The underlying mechanism of diabetic gastroparesis is unknown, though it is thought to be related in part to neuropathic changes in the vagus nerve and/or the myenteric plexus. Prolonged elevated serum glucose levels are also associated with vagus nerve damage. The vagus nerve controls the movement of food through the digestive tract and when it is damaged, movement of food through the GI tract may be abnormal. The prevalence of diabetes in the United States is rapidly rising, with the Centers for Disease Control estimating that one in ten adults currently suffer from the disease. Sedentary lifestyles, poor dietary habits and a consequent rising prevalence of obesity are expected to cause this number to grow substantially. According to a study published in the *Journal of Gastrointestinal and Liver Diseases* in July 2010, between 25% and 55% of type 1 and 15% and 30% of type 2 diabetics suffer from symptoms associated with the condition and diabetics are 29% of the total gastroparesis population.

A 2007 study published in *Current Gastroenterology Reports* states that approximately 36% of gastroparesis patients suffer from idiopathic gastroparesis. The development of idiopathic gastroparesis is thought to be related to loss of myenteric ganglion cells in the distal large bowel (myenteric hypoganglionosis) and reduction in the interstitial cells of Cajal, which help control contraction of the smooth muscle in the GI tract.

Post-surgical gastroparesis is a smaller subset of the total patient pool and accounts for approximately 13% of all cases of the disease, according to a 2007 study published in Current Gastroenterology Reports. Post-surgical gastroparesis is often associated with peptic ulcer surgery, bariatric procedures or esophageal procedures and is thought to result from damage/desensitization of the vagus nerve.

Prevalence

In 2012, the American Diabetes Association estimated that diabetes affects approximately 29.1 million people of all ages in the United States, equating to about 9.3% of the population. Based on prevalence data, the potential gastroparesis patient pool in the United States is approximately 12 to 16 million adults with women making up 82% of this population, according to a 2007 study published in *Current Gastroenterology Reports*.

There are 2.3 million diabetic patients with moderate or severe gastroparesis symptoms who are seeking treatment in the United States by a health care professional, according to a study presented at the Digestive Disease Week 2013 conference in Orlando, Florida. When patients do receive treatment for gastroparesis, multiple medications are frequently used to address the individual signs and symptoms of gastroparesis. For example, patients may receive anti-emetics for nausea and vomiting and opioids for abdominal pain, which can exacerbate delayed gastric emptying in patients with gastroparesis.

Unmet Needs in Gastroparesis Treatment

Market research and physician interviews demonstrate that existing treatment options for diabetic gastroparesis are inadequate and there is a high level of interest in effective outpatient options for managing patients with gastroparesis symptoms. The market is currently served by oral metoclopramide, intravenous metoclopramide, and the oral disintegrating tablet, or ODT, formulation of metoclopramide (Metozolv® ODT), with approximately 4.0 million prescriptions in the United States per year, according to IMS Health (2015).

Due to the limited availability of FDA-approved treatments for gastroparesis, physicians may resort to using medications “off-label” in an attempt to address individual symptoms experienced by patients. Off-label therapies are pharmaceuticals prescribed by physicians for an unapproved indication or in an unapproved age group, unapproved dose or unapproved form of administration. Examples of drugs used without FDA approval in gastroparesis include erythromycin and Botox® injected via endoscopic procedure directly into the lower gastric sphincter. Previously-approved drugs, such as cisapride and tegaserod, are no longer commercially available in the United States because of safety concerns. Domperidone has never been approved by FDA but is obtained through certain compounding pharmacies for individual patients under special FDA usage rules.

Gimoti is a non-oral, promotility and anti-emetic treatment that we believe has the potential to significantly improve the standard of care for female gastroparesis patients. If metoclopramide nasal spray is approved for the treatment of diabetic gastroparesis in women, patients and physicians will have access to an outpatient therapy that could be administered and absorbed even when patients are experiencing delayed gastric emptying or nausea and vomiting.

Our Solution: Gimoti (Metoclopramide Nasal Spray)

We are developing Gimoti, a dopamine antagonist / mixed 5-HT3 antagonist / 5-HT4 agonist with promotility and anti-emetic effects, for the relief of symptoms associated with acute and recurrent diabetic gastroparesis in women. Since oral metoclopramide was approved by FDA in 1980, oral and intravenous metoclopramide have been the only products approved in the United States to treat gastroparesis. Gimoti is a novel formulation of metoclopramide offering systemic delivery by nasal spray administration.

We are developing the nasal formulation of metoclopramide to provide our targeted patient population with acute or recurrent symptoms of diabetic gastroparesis with a product that can be systemically delivered as an alternative to the oral or intravenous routes of administration. Nasal delivery is possible because the mucosa of the nasal cavity is a single epithelial cell layer which is well-vascularized and allows metoclopramide molecules to be transferred directly to the systemic circulation. There is no first pass liver metabolism required prior to onset of action. Since gastroparesis is a disease that halts or slows the movement of the contents of the stomach to the small intestine, oral drug administration is often compromised. The nasal formulation may also provide a predictable and consistent means of delivering metoclopramide in patients with delayed gastric emptying and/or frequent vomiting. Also, unlike the oral tablet formulation of metoclopramide, we believe that Gimoti may be tolerated even when patients are experiencing nausea.

A nasal spray formulation of metoclopramide could offer an alternative route of administration for female patients with severe symptoms of diabetic gastroparesis receiving the parenteral formulation of metoclopramide. Following hospitalization for intravenous metoclopramide, a nasal spray formulation would also provide a non-oral option for the transition to an outpatient treatment.

Comparative Exposure PK Trial

In October 2017, we announced positive topline results from the comparative exposure PK trial. The objective of the trial was to identify a dose of Gimoti that met the criteria for bioequivalence compared to the Listed Drug, Reglan Tablets after nasal and oral administration to healthy volunteers under fasted conditions.

The comparative exposure PK trial was an open label, 4-way crossover and enrolled 108 healthy male and female volunteers who each received one Reglan Tablet dose and three different doses of Gimoti in a random sequence. Following discussions at pre-NDA meetings with FDA, we planned to select a Gimoti dose based on criteria that included a 90% confidence interval for the ratio of AUC falling within the equivalence range of 80-125% of Reglan Tablets. Though only one dose was needed to meet the dose selection criteria, the comparative exposure PK trial was designed to test three different strengths of Gimoti. Based on results of the study, two of the three doses tested met the dose selection criteria for the pooled data in men and women. The C_{max} for Gimoti was slightly lower than the equivalence range, but was anticipated and had been previously discussed with FDA as a likely outcome given the different route of administration and prior Gimoti PK trial results. Additionally, data showed the AUC and C_{max} increased in a dose related manner across all three strengths tested. Relative to safety, all Gimoti doses were well tolerated with no clinically significant adverse events reported following any of the doses.

Additional analysis of the PK data by sex revealed statistically significant differences in exposure between women and men given the same metoclopramide dose (nasal and oral). Based on this further analysis of results from the comparative exposure PK trial, statistically significantly lower AUC's were found in men compared to women. The findings were not explicitly attributable to differences in body mass index (BMI) or weight. Similarly sex-based differences were observed in a previous healthy volunteer study we conducted, irrespective of the route of metoclopramide administration (nasal, oral and IV).

In the most recent comparative exposure PK trial, results for women independently met equivalence criteria for $AUC_{0\text{-}inf}$ and $AUC_{0\text{-}t}$ at the tested Gimoti dose to be proposed in the NDA. We plan to submit our NDA for a female-only indication based on a dose in women with equivalent exposure to Reglan Tablets and will submit supporting efficacy and safety data from our Phase 2b and Phase 3 trials, specifically for women, at doses similar or lower than the dose to be proposed in the NDA.

Phase 3 Clinical Trial

In July 2016, we announced results from a Phase 3 clinical trial of Gimoti in female patients with symptoms associated with acute and recurrent diabetic gastroparesis. This U.S.-based, multicenter, randomized, double-blind, placebo-controlled, parallel group clinical trial evaluated the efficacy, safety and population PK of Gimoti in adult female patients with symptomatic diabetic gastroparesis and delayed gastric emptying by GES. Subjects received either Gimoti or placebo four times daily for 28 days. The primary endpoint was the change in symptoms from the baseline period to Week 4 as measured using a proprietary PRO instrument. On a daily basis,

subjects reported the frequency and severity of their gastroparesis signs and symptoms using a telephone diary. The subjects' daily symptom scores were the basis for calculating their weekly scores using the PRO instrument.

A total of 205 women (mean age 52.7 years, 88% with type 2 diabetes; 79% postmenopausal, 51% using insulin, mean duration of diabetes 12.9 years, mean baseline glycosylated hemoglobin (HbA1c) 7.5%) were randomized and 93% completed the study. The primary endpoint for the ITT population was not statistically significant (p=0.881); however, in exploratory analyses, a treatment effect was seen at Weeks 1 to 3 for patients with higher baseline symptom scores (moderate to severe) in the ITT population (n=105) and for all four weeks for the per protocol population (see Table 1 below). There were also clinically and statistically significant improvements in nausea and abdominal pain, which are two of the more severe and debilitating symptoms of gastroparesis (see Table 2 below).

In July 2015, FDA issued a draft guidance document regarding the clinical evaluation of drugs for the treatment of gastroparesis, in which FDA states that in order to optimize the ability to demonstrate a treatment effect, clinical trials in this indication should enroll patients with higher symptom severity (moderate to severe). The improvements observed in our exploratory analyses of our Phase 3 study focused on this subset of patients enrolled in the study. At the time this draft guidance was issued, our Phase 3 study, designed to include patients with a range of symptom severity, had been actively enrolling for more than a year. The overall efficacy results were not significant, due in large part to the patients with less severe symptoms who responded to placebo. Importantly, patients with more severe symptoms experienced a statistically-significant treatment effect with Gimoti, consistent with the recommendation in the draft guidance on clinical studies of gastroparesis.

Reports of treatment-emergent adverse events were similar in both groups (36% Gimoti and 35% placebo) and most were mild or moderate in severity. There were slightly more reports of nasal irritation in subjects receiving placebo than in subjects receiving Gimoti. In particular, there were no adverse events of special interest, such as the central nervous system, or CNS, effects observed (see Table 3 below).

These safety results were consistent with findings from previous Gimoti studies that showed the nasal formulation of metoclopramide has a favorable safety profile and is well-tolerated by healthy volunteers and patients with diabetic gastroparesis. There have been no reports of tardive dyskinesia among the more than 1,400 exposed healthy volunteers and patients over the metoclopramide nasal spray clinical development program.

Table 1: Phase 3 Change from Baseline in Daily Total Symptom Scores by Week in Analysis Populations with Moderate to Severe Symptoms at Baseline

Population	Time Period	Placebo[1]	Gimoti[1]	p-value[2]
		(N = 53)	**(N = 52)**	
Intent-to-Treat	Week 1	-0.387	-0.588	**0.036**
	Week 2	-0.614	-0.950	**0.025**
	Week 3	-0.749	-1.096	**0.039**
	Week 4	-0.856	-1.220	0.085*
		(N = 40)	**(N = 38)**	
Per Protocol	Week 1	-0.362	-0.623	**0.019**
	Week 2	-0.625	-1.040	**0.015**
	Week 3	-0.714	-1.286	**0.003**
	Week 4	-0.841	-1.373	**0.014**

Table 2: Phase 3 Change from Baseline in Daily Nausea and Upper Abdominal Pain Scores by Week in Intent-to-Treat Population with Moderate to Severe Symptoms at Baseline

Symptom	Time Period	Placebo[1] (N = 53)	Gimoti[1] (N = 52)	p-value[2]
Nausea	Week 1	-0.370	-0.859	**0.001**
	Week 2	-0.696	-1.149	**0.032***
	Week 3	-0.818	-1.242	**0.043**
	Week 4	-0.905	-1.404	**0.027**
Upper Abdominal Pain	Week 1	-0.394	-0.641	**0.025**
	Week 2	-0.554	-0.990	**0.016**
	Week 3	-0.690	-1.194	**0.008**
	Week 4	-0.791	-1.218	**0.047**

1 LSMean from ANCOVA

2 p-value is obtained from an ANCOVA model with fixed effect for treatment group and the baseline value as a covariate. If the normality assumption was not met, the p-value was obtained from a rank ANCOVA test and denoted with an *.

Table 3: Selected Treatment-Emergent Adverse Events Reported by More than 2 Subjects in Any Treatment Group

Adverse Event	Placebo (N = 103)	Gimoti (N = 102)
Headache	7 (7%)	5 (5%)
Nasal discomfort	4 (4%)	1 (1%)
Epistaxis	2 (2%)	1 (1%)
Fatigue	1 (1%)	2 (2%)

In December 2016, we announced the completion of a second pre-NDA meeting with FDA. The purpose of the meeting was to discuss efficacy and safety results from the Phase 3 clinical trial and submission strategies for an NDA. At the pre-NDA meeting the FDA agreed that a comparative exposure PK trial was acceptable as a basis for submission of a Gimoti NDA. The comparative exposure PK trial will serve as a portion of the full 505(b)(2) data package to include prior efficacy and safety data developed by us and the FDA's prior findings of safety and efficacy for the Listed Drug, Reglan Tablets.

In the first pre-NDA meeting with FDA held in August 2016, we confirmed various regulatory, CMC, and non-clinical requirements for our potential NDA submission. In February 2017, we announced that we received a letter from FDA exempting Gimoti from HG Validation study requirements prior to submission of the NDA.

Male Companion Trial

We also conducted a companion clinical trial with Gimoti in male patients with symptoms associated with acute and recurrent diabetic gastroparesis to assess the safety and efficacy of Gimoti in men. This trial was requested by FDA to confirm the Phase 2b trial results and to capture additional safety data in men. The design of the male study was the same as the study in women and was initiated in April 2014 at sites also enrolling the Phase 3 study in women. Given that diabetic gastroparesis is predominately a female disorder, enrollment was challenging and the trial spontaneously stopped enrolling with 53 randomized male subjects (26 on Gimoti).

In November 2016, the data from the study were analyzed and futility was demonstrated. Results confirmed that even if the trial had fully enrolled, the results would not have differed. As we anticipated at the beginning of the trial, based on the prior Phase 2b data, the results showed no statistically significant efficacy in men. The safety profile for Gimoti was well-tolerated and the safety profile was comparable to placebo. The male trial is not required for submission of the Gimoti NDA for women; however, we expect to include safety data from this study in the NDA submission.

Phase 2b Clinical Trial

We have evaluated Gimoti in a multicenter, randomized, double-blind, placebo-controlled parallel group, dose-ranging Phase 2b clinical trial in 287 subjects (71% female) with diabetic gastroparesis. Subjects in the trial were between the ages of 18 and 75, with a history of diabetes (type 1 and type 2) and diabetic gastroparesis, who had a baseline modified Gastroparesis Cardinal Symptom Index Daily Diary, or mGCSI-DD, of >2 and <4 for the seven days prior to randomization to blinded study drug (Gimoti or placebo).

In the pre-specified analysis of the primary endpoint, mean mGCSI-DD total score change from Baseline to Week 4, by gender, there was a benefit demonstrated in female subjects that was clinically and statistically significant ($p<0.025$) while male subjects demonstrated a high placebo response rate. This improvement in mGCSI-DD was supported by secondary and exploratory measures of efficacy in females across the majority of parameters evaluated. Due to the results in men, the primary objective of statistical significance in the overall population was not achieved ($p=0.15$).

We believe this Phase 2b trial is the largest ever conducted in a diabetic gastroparesis population for any approved metoclopramide dosage forms (oral tablet, orally disintegrating tablet and injection). Previous metoclopramide studies enrolled small numbers of subjects and did not evaluate treatment effects by gender. For example, fewer than 130 gastroparesis subjects were enrolled across all studies included in the NDA for Reglan Tablets, a branded form of metoclopramide currently marketed in the United States by Ani Pharmaceuticals.

The results of our Phase 2b trial are consistent with what is known about the gender effects in other GI motility disorders. GI motility and functional GI disorders, including gastroparesis, are more common in females than in males. Also, healthy females generally have slower gastric emptying rates. In a study conducted at Temple University (Parkman, et al), gastric emptying of solid food in normal young women was shown to be slower than in age-matched men, even in the first 10 days of the menstrual cycle when estrogen and progesterone levels are low, and the delay in gastric emptying of solids in women appears to be primarily due to altered distal gastric motor function. One explanation may be that less vigorous antral contractions may contribute to slower breakdown of food particles and thus delay the rate of emptying.

Gastrointestinal disorders present differently in males and females and responses to therapy vary by gender. There is general consensus among thought leaders in GI motility that women have a higher prevalence of symptoms, their neural and sensory pathways differ, and hormones, such as estrogen and progesterone, play a role. While the Gimoti Phase 2b trial is the first report of a gender- based difference in response to metoclopramide among subjects with diabetic gastroparesis, gender effects have been reported in drug studies for other GI disorders, such as IBS. For example, products such as Lotronex® (alosetron), Zelnorm® (tegaserod) and Amitiza® (lubiprostone) were approved by FDA based on effectiveness in women, but not in men.

Phase 2b Trial Design

The Phase 2b clinical trial consisted of up to a 23-day screening period and a seven-day washout period, followed by 28 days of treatment with study drug. We evaluated two dosage strengths of Gimoti: 10 mg and 14 mg; as well as placebo. The study drug was administered for the 28-day treatment period as a single nasal spray four times daily, 30 minutes before meals and at bedtime. Subjects recorded the severity of their gastroparesis symptoms in a telephonic diary using an interactive voice response system once each day. The symptoms were analyzed using a patient reported outcomes instrument, the Gastroparesis Cardinal Symptom Index Daily Diary, or GCSI-DD, developed for collecting and analyzing data to evaluate the effectiveness of treatments for gastroparesis.

The GCSI-DD contains nine signs and symptoms (nausea, retching, vomiting, stomach fullness, not able to finish a normal sized meal, feeling excessively full after meal, loss of appetite, bloating, and stomach or belly visibly larger) grouped in three subscales. The daily score is calculated as a mean of three subscale means. Additional signs and symptoms collected in the daily diary included abdominal pain, abdominal discomfort, number of hours of nausea, number of episodes of vomiting, and overall severity of gastroparesis symptoms. In close collaboration with the staff of FDA's Division of Gastroenterology and Inborn Errors Products and the Clinical Outcome Assessments, or COA, these additional symptom data were used to further refine the patient reported outcome instrument.

The result is the mGCSI-DD comprised of four symptoms (nausea, early satiety, bloating, and upper abdominal pain) rated from zero (none) to five (very severe). The instrument has been optimized to detect symptom variability on a severity continuum from nausea to vomiting.

Phase 2b Efficacy Results

Two patient reported outcome endpoints (mGCSI-DD and GCSI-DD) were examined in ITT population based on the protocol design and FDA communications:

- The primary efficacy endpoint was the change from seven-day baseline to Week 4 of the treatment period in the mGCSI-DD total score (mean of four symptoms).
- The second efficacy endpoint analyzed was the change from seven-day baseline to Week 4 of the treatment period in the GCSI-DD total score (mean of three subset means with a total of nine symptoms).

Although an overall improvement in symptoms was observed in Gimoti-treated subjects with diabetic gastroparesis compared to placebo, the difference was not statistically significant due to a high placebo response among male subjects. However, statistically significant improvement in gastroparesis symptoms was observed in female subjects with diabetic gastroparesis as measured by the mGCSI-DD and GCSI-DD total scores for both doses of Gimoti compared to the placebo. The beneficial effect of treatment in females appears to be uniform. The results are consistent across the overall endpoints, the individual components, and the two dose groups.

The observed differences in efficacy were based on gender and were not due to severity of baseline disease or other demographic characteristics. No statistically significant differences were observed in efficacy between the 10 mg and 14 mg Gimoti doses; thus the 10 mg dose was considered the lowest effective dose in this study. The table below summarizes the p-values observed for both doses of Gimoti compared to placebo in the Phase 2b clinical trial across all subjects and for male and female subjects separately.

Gimoti Phase 2b Clinical Trial
Gastroparesis Study Endpoint Points P-Value Summary
(Gimoti vs. Placebo: Change from Baseline to Week 4)

	Gimoti 10 mg p-values	Gimoti 14 mg p-values
mGCSI-DD Total Score (per FDA guidance) (1)		
All Subjects	0.1504	0.3005
Females	**0.0247**	**0.0215**
Males	0.4497	0.2174
GCSI-DD Total Score (per trial protocol) (2)		
All Subjects	0.2277	0.5266
Females	**0.0485**	**0.0437**
Males	0.4054	0.0972

P-values for pairwise comparisons are obtained from an analysis of covariance, or ANCOVA, model with effects for treatment group and Baseline value as a covariate.

(1) The mGCSI-DD was comprised of four symptoms collected on a severity rating scale of 0 to 5. Baseline was seven days prior to treatment or qualifying days during washout and Week 4 was days 21 to 27 of treatment.

(2) The GCSI-DD was comprised of nine symptoms collected on a severity rating scale of 0 to 5. Baseline was seven days prior to treatment or qualifying days during washout and Week 4 was days 21 to 27 of treatment.

The table below summarizes the key data from the trial across all subjects and for female and male subjects separately:

Gimoti Phase 2b Clinical Trial
Primary Endpoint: Mean mGCSI-DD Total Score Change
from Baseline to Week 4 by All Subjects and Gender
(intent-to-treat, last observation carried forward on treatment)

Time Point	Placebo (N=95)	Metoclopramide 10 mg IN (N=96)	Metoclopramide 14 mg IN (N=96)
ALL SUBJECTS			
Baseline (1)			
N	95	96	96
Mean (SD)	2.8 (0.57)	2.9 (0.60)	2.8 (0.62)
Week 4			
N	95	96	96
Mean (SD)	1.8 (1.00)	1.6 (1.06)	1.7 (0.90)
Change from Baseline to Week 4			
N	95	96	96
Mean (SD)	- 1.0 (0.89)	-1.2 (1.18)	-1.2 (0.94)
Difference of Least Square Means (95% CI)		-0.20 (-0.47, 0.07)	-0.14 (-0.42, 0.13)
Pairwise p-value vs. Placebo (2)		0.1504	0.3005
Difference of Least Square Means (95% CI)			0.06(-0.22, 0.33)
Pairwise p-value vs. Metoclopramide 10 mg (2)			0.6830
FEMALES			
Baseline (1)			
N	68	65	70
Mean (SD)	2.7 (0.54)	2.9 (0.62)	2.9 (0.62)
Week 4			
N	68	65	70
Mean (SD)	1.9 (1.02)	1.6 (1.08)	1.7(0.94)
Change from Baseline to Week 4			
N	68	65	70
Mean (SD)	- 0.8 (0.79)	-1.2 (1.18)	-1.3(0.98)
Difference of Least Square Means (95% CI)		-0.38 (-0.71, -0.05)	-0.38 (-0.71, -0.06)
Pairwise p-value vs. Placebo (2)		**0.0247**	**0.0215**
Difference of Least Square Means (95% CI)			-0.00 (-0.33, 0.32)
Pairwise p-value vs. Metoclopramide 10 mg (2)			0.9864
MALES			
Baseline (1)			
N	27	31	26
Mean (SD)	2.9 (0.63)	2.8(0.54)	2.5 (0.56)
Week 4			
N	27	31	26
Mean (SD)	1.4 (0.84)	1.6(1.05)	1.7 (0.79)
Change from Baseline to Week 4			
N	27	31	26
Mean (SD)	- 1.4 (0.98)	-1.2 (1.21)	-0.9 (0.78)
Difference of Least Square Means (95% CI)		0.18 (-0.30, 0.66)	0.32 (-0.19, 0.83)
Pairwise p-value vs. Placebo (2)		0.4497	0.2174
Difference of Least Square Means (95% CI)			0.14 (-0.35, 0.63)
Pairwise p-value vs. Metoclopramide 10 mg (2)			0.5805

(1) Baseline is defined as the mean mGCSI-DD total score during the washout period
(2) p-values for pairwise comparisons are obtained from an ANCOVA model with effects for treatment group and baseline value as a covariate

Phase 2b Safety Observations

In the Phase 2b clinical trial, Gimoti 10 mg and 14 mg doses were well-tolerated and no differences in the safety profiles were observed between the two doses administered. No serious adverse events occurred related to study treatment. In addition, there were no clinically-meaningful differences observed in clinical laboratory parameters, physical examination findings, or electrocardiogram recordings.

Adverse events that occurred more commonly in both Gimoti 10 mg and 14 mg doses compared to placebo (≥2% difference between treated compared to placebo groups) were dysgeusia, headache, nasal discomfort, rhinorrhea, throat irritation, fatigue, hypoglycemia and hyperglycemia. The majority of adverse events were mild to moderate and transient in nature.

Treatment-Emergent Adverse Events Reported by More than Two Subjects in Any Treatment Group

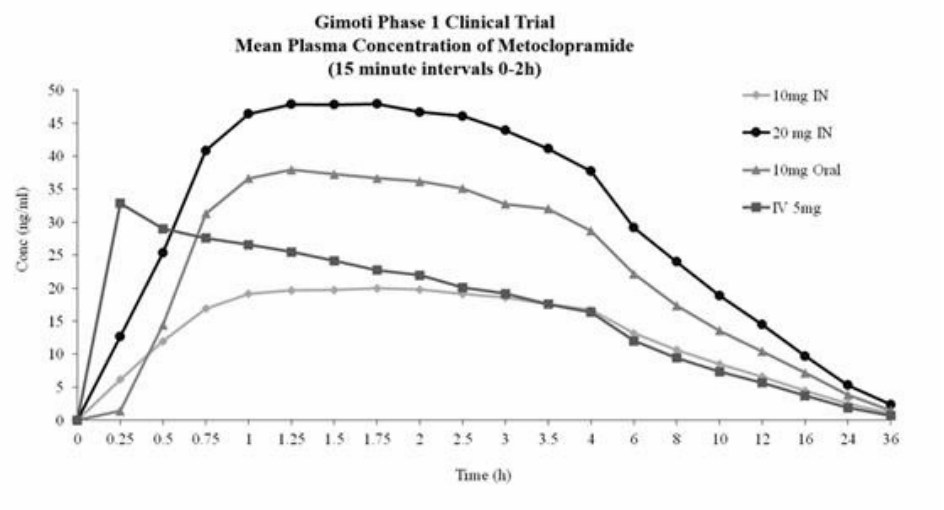
	All Subjects		
System Organ Class Preferred Term	**Placebo (N = 95)**	**Gimoti 10 mg (N = 95)**	**Gimoti 14 mg (N = 95)**
Nervous System Disorders			
Dysgeusia	4(4.2%)	12(12.6%)	13(13.7%)
Headache	4(4.2%)	7(7.4%)	8(8.4%)
Dizziness	2(2.1%)	3(3.2%)	3(3.2%)
Gastrointestinal Disorders			
Diarrhea	9(9.5%)	3(3.2%)	2(2.1%)
Nausea	4(4.2%)	1(1.1%)	4(4.2%)
Gastroesophageal reflux disease	1(1.1%)	4(4.2%)	0(0.0%)
Respiratory, Thoracic, and Mediastinal Disorders			
Epistaxis	2(2.1%)	2(2.1%)	3(3.2%)
Cough	2(2.1%)	0(0.0%)	3(3.2%)
Nasal discomfort	0(0.0%)	3(3.2%)	2(2.1%)
Rhinorrhea	1(1.1%)	1(1.1%)	3(3.2%)
Throat irritation	1(1.1%)	0(0.0%)	3(3.2%)
Infections and Infestations			
Upper respiratory tract infection	4(4.2%)	0(0.0%)	2(2.1%)
Nasopharyngitis	1(1.1%)	3(3.2%)	1(1.1%)
General Disorders and Admin Site Conditions			
Fatigue	1(1.1%)	5(5.3%)	6(6.3%)
Metabolism & Nutrition Disorders			
Hyperglycemia	1(1.1%)	1(1.1%)	3(3.2%)
Hypoglycemia	1(1.1%)	1(1.1%)	3(3.2%)
Psychiatric Disorders			
Depression	3(3.2%)	0(0.0%)	0(0.0%)

Phase 1 Comparative Bioavailability Bridging Study

Our Phase 1 clinical trial of Gimoti was an open-label, four-treatment, four-period, four-sequence crossover study conducted at a single study center. Forty healthy volunteers were enrolled and randomly assigned to one of four treatment sequences. After an overnight fast, subjects received a single dose of each of the metoclopramide treatments (10 mg Gimoti, 20 mg Gimoti, 10 mg Reglan tablet, and 5 mg/mL Reglan injection) in random sequence with a seven-day washout period between doses. Thirty nine subjects received at least one dose of metoclopramide. The pharmacokinetic analysis population consisted of 37 subjects who received all four treatments and two subjects who received three of the four treatments.

After nasal spray administration of the 10 mg and 20 mg doses of Gimoti, mean plasma metoclopramide concentrations increased in a dose-related manner, as did mean values for C_{max} and AUC_{inf}. The absolute bioavailability of Gimoti after nasal spray administration was comparable for the 10 mg (47.4%) and 20 mg (52.5%) doses as were the bioavailabilities relative to the oral tablet (60.1% and 66.5%, respectively).

The graphs below illustrate the mean plasma concentrations of the active ingredient in the two doses of Gimoti as well as the oral and injection forms.



Thorough ECG (QT/QTc) Study

We conducted a randomized, double-blind, double-dummy, four-way crossover thorough ECG (QT/QTc) study of Gimoti in 2014. The study was designed in accordance with FDA's published guidance on clinical evaluation of QT/QTc interval, and compared the effects of Gimoti on the QT/QTc interval when administered at therapeutic and supratherapeutic doses in 48 healthy female and male volunteers. Moxifloxacin, an antibiotic known to prolong the QT/QTc interval, was used as the positive control.

In December 2014 we reported that data from the study met the pre-specified primary endpoint, demonstrating that Gimoti, at therapeutic and supratherapeutic doses, did not prolong the QT/QTc interval in healthy subjects. The study was conducted to satisfy a safety requirement by FDA in support of our submission of an NDA for Gimoti.

In 2014, we also completed a thorough ECG (QT/QTc) study and reported positive results. Prolongation of the QT interval may increase the risk for cardiac arrhythmias. Data from the thorough ECG (QT/QTc) trial met the pre-specified primary endpoint, demonstrating that Gimoti, at therapeutic and supratherapeutic doses, did not prolong the QT/QTc interval in healthy subjects.

We have also conducted a companion clinical trial with Gimoti in male subjects with symptoms associated with acute and recurrent diabetic gastroparesis to assess the safety and efficacy of Gimoti in men. The male companion trial was initiated in May 2014 and the design was the same as the Phase 3 trial in women. This trial was requested by FDA to confirm the Phase 2b trial results and to capture additional safety data in men. This trial was not required for submission of the Gimoti NDA for women; however, we expect to include safety data from this trial in the NDA submission. During November 2016, we determined the trial showed futility so that even if the trial had fully been enrolled, the results would not have differed. As we anticipated at the beginning of the trial, based on the prior Phase 2b data, the results showed no benefit for Gimoti versus placebo in men. The safety results were consistent with findings from previous Gimoti studies that showed the nasal formulation of metoclopramide has a favorable safety profile and is well tolerated by patients with diabetic gastroparesis.

Prior Development

From 1985 to present, we, or our predecessors, have conducted numerous clinical studies to evaluate the safety and pharmacokinetic profile of nasal spray formulations of metoclopramide in healthy volunteers and the safety, efficacy, and pharmacokinetic profile of metoclopramide nasal spray in patients. More than 1,400 subjects have been exposed to nasal formulations of metoclopramide at doses ranging from 10 mg to 80 mg in these studies.

In one study, a Phase 2A, multicenter, randomized, open-label, parallel design study, Questcor Pharmaceuticals, Inc., or Questcor (now part of Mallinckrodt plc), compared the efficacy and safety of two doses of metoclopramide nasal spray, 10 mg and 20 mg, with FDA-approved 10 mg metoclopramide tablet. For the primary efficacy endpoint in the per protocol population analysis, a statistically significant difference in the total symptom score between baseline and week 6 for both the nasal 10 mg (p=0.026) and nasal 20 mg (p=0.008) cohorts compared to the oral 10 mg group was observed. Metoclopramide nasal spray was initially developed by Nastech Pharmaceutical Company, Inc. in precursor formulations to Gimoti and subsequently acquired and developed by Questcor.

We acquired rights to this product candidate from Questcor in 2007. We then optimized the acquired formulation of metoclopramide nasal spray to improve stability and remove inactive ingredients to improve the palatability and tolerability of Gimoti for subjects. We also developed the current formulation with excipients that are at or below the levels listed in FDA's Inactive Ingredient Database for nasal products.

We evaluated the current formulation of Gimoti with the same nasal spray pump in six completed clinical trials enrolling a total of 746 healthy volunteers and patients with diabetic gastroparesis. Phase 1 (39 and 108), thorough ECG (54), Phase 2 (287), Phase 3 (205) and Companion (53).

The primary container closure system for Gimoti is comprised of an amber glass vial directly attached to a pre-assembled spray pump unit with a protection cap. Each multi dose sprayer system comes preassembled and capable of delivering a 30 day supply (120 doses at 4 doses per day.) The sprayer is a standardized metered sprayer technology utilized in other nasal spray products as well as the amber vial.

Intellectual Property and Proprietary Rights

Overview

We are building an intellectual property portfolio for Gimoti in the United States and abroad. We seek patent protection in the United States and internationally for our product candidate, its methods of use and processes for its manufacture, and for other technologies, where appropriate. Our policy is to actively seek to protect our proprietary position by, among other things, filing patent applications in the United States and abroad relating to proprietary technologies that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our technology.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technologies we consider important to our business, defend our patents, preserve the confidentiality of our trade secrets and operate our business without infringing the patents and proprietary rights of third parties.

Patent Portfolio

Our patent portfolio includes the following U.S. patents and patent applications as of February 28, 2018:

- U.S. Patent 6,770,262—Nasal Administration of Agents for the Treatment of Gastroparesis. This patent expires in 2021.
- U.S. Patent 8,334,281—Nasal Formulations of Metoclopramide. This patent is expected to expire in 2030 and has a pending Continuation application (U.S. Non-Provisional Patent Application No. 15/130,086).
- U.S. Non-Provisional Patent Application No. 13/593.215 —Treatment of Symptoms Associated with Female Gastroparesis. If granted, this patent would be expected to expire in 2032.

We have also been granted European and Canadian patents for the method of use of metoclopramide via nasal delivery for gastroparesis. These patents are expected to expire in 2021. We have also been granted European and Canadian patents for pharmaceutical compositions comprising metoclopramide. These patents are expected to expire in 2030.

The United States patent system permits the filing of provisional and non-provisional patent applications. A non-provisional patent application is examined by the U.S. Patent and Trademark Office, or USPTO, and can mature into a patent once the USPTO determines that the claimed invention meets the standards for patentability. A provisional patent application is not examined for patentability, and automatically expires 12 months after its filing date. As a result, a provisional patent application cannot mature into a patent. The requirements for filing a provisional patent application are not as strict as those for filing a non-provisional patent application. Provisional applications are often used, among other things, to establish an earlier filing date for a subsequent non-provisional patent application. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, or PTA, which compensates a patentee for administrative delays by the USPTO in granting a patent. In view of a recent court decision, the USPTO is under greater scrutiny regarding its calculations where the USPTO erred in calculating the patent term adjustment for the patents in question denying the patentee a portion of the patent term to which it was entitled. Alternatively, a patent's term may be shortened if a patent is terminally disclaimed over another patent.

The effective filing date of a non-provisional patent application is used by the USPTO to determine what information is prior art when it considers the patentability of a claimed invention. If certain requirements are satisfied, a non-provisional patent application can

claim the benefit of the filing date of an earlier filed provisional patent application. As a result, the filing date accorded by the provisional patent application may supersede information that otherwise could preclude the patentability of an invention.

Other Intellectual Property Rights

We currently have registered trademarks for EVOKE PHARMA and GIMOTI in the United States.

Confidential Information and Inventions Assignment Agreements

We require our employees and consultants to execute confidentiality agreements upon the commencement of employment, consulting or collaborative relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances.

In the case of employees, the agreements provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law. Our consulting agreements also provide for assignment to us of any intellectual property resulting from services performed for us.

Sales and Marketing

We plan to commercialize Gimoti in the United States alone, or in partnership with pharmaceutical companies that have established development and sales and marketing capabilities. Our strategy for Gimoti, if approved, will be to establish Gimoti as the prescription product of choice for diabetic gastroparesis in women. If the product candidate is approved, our expectation is that Gimoti would initially be marketed to gastrointestinal and internal medicine specialists, primary care physicians and select health care providers. We have partnered with Syneos Health, Inc., or Syneos (formerly inVentiv Commercial Services LLC), to build our commercial infrastructure, including to potentially hire, train, retain and deploy a direct sales force for the potential commercialization of Gimoti, pending the filing of the NDA and FDA approval. Under terms of the agreement, Syneos may provide services including, but not limited to, sales representatives, sales management, marketing, account management, advertising, medical communications, distribution support, and overall commercial management.

Manufacturing

We do not own or operate manufacturing facilities for the production of Gimoti, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our product development and clinical trials. We currently use a third-party consultant, which we engage on an as-needed, hourly basis, to manage product development and manufacturing contractors.

In April 2015, we announced the completion of production of a commercial scale lot of Gimoti as required by FDA. With the completion of this large-scale production of Gimoti, we believe we have demonstrated our ability to manufacture Gimoti at commercial scale quantities in accordance with CMC. In addition to data from this recent program, we have a three-year registration stability data package from previous studies which have all met proposed specifications. These CMC datasets will be submitted as part of our NDA submission.

In November 2017, we entered into a Manufacturing Services Agreement, or the Manufacturing Agreement, with Patheon UK Limited, or Patheon, a wholly-owned subsidiary of Thermo Fisher, Inc., pursuant to which Patheon has agreed to manufacture commercial quantities of Gimoti. Under the terms of the agreement, we are required to purchase a certain percentage of our requirements for our Gimoti product intended for commercial sale, provided certain terms and conditions are met. The initial term of the agreement commenced in November 2017 and will continue in effect until December 31st of the year that is five years from the date Gimoti first receives approval for marketing from FDA or any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products. This initial term shall be automatically renewed for additional one-year terms, unless either party provides written notice of its intention to terminate the agreement upon notice within a specified time prior to the end of the then current term. Either party may terminate the agreement effective immediately upon written notice to the other in the event that (i) the other party dissolves, is declared insolvent or bankrupt by a court of competent jurisdiction, (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction, or (iii) the agreement is assigned for the benefit of creditors. We may terminate the agreement upon specified prior written notice if any governmental or regulatory authority, including, but not limited to, FDA, takes any action, or raises any objection, that prevents us from importing, exporting, purchasing, or selling Gimoti. Patheon or we may terminate the agreement upon specified prior written notice to the other party if Patheon or we, as applicable, assigns any of our rights under the agreement to an assignee that is (i) not a credit worthy substitute for the assigning party; or (ii) a competitor of assigning party. Moreover, either party may terminate the agreement upon written notice to the other party where the other party has failed to

remedy a material breach of any of its representations, warranties, or other obligations under the agreement within a specified period of time following receipt of a written notice of the breach, subject to specified terms and conditions.

In May 2016, we entered into a Master Supply Agreement with Cosma S.p.A., or Cosma, pursuant to which Cosma will be the exclusive commercial supplier of metoclopramide for the manufacture of Gimoti. Under the supply agreement, Cosma will supply metoclopramide pursuant to purchase orders which we may deliver to Cosma from time to time, and there is no minimum supply requirement. In the event Cosma discontinues supply of metoclopramide for any reason, including by reason of a force majeure event, or materially changes the metoclopramide specifications, then we may require Cosma to supply up to a two years' supply of the metoclopramide based on our purchase orders over the preceding two years. The term of the supply agreement is three years, which term shall be automatically extended (1) for an additional period equivalent to the time elapsing from May 2016 to the date of the first commercial launch of Gimoti and (2) for successive one-year periods thereafter, unless terminated earlier. Either party may terminate the supply agreement on 180 days' written notice to the other party or on 30 days' written notice to the other party for such party's material uncured breach.

Competition

The pharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, coverage pricing and reimbursement.

Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our drugs non-competitive or obsolete.

We expect that, if approved, Gimoti will compete directly with metoclopramide oral, erythromycin and domperidone as a treatment for gastroparesis. Metoclopramide is the only product currently approved in the United States to treat gastroparesis. Metoclopramide is available from a number of generic pharmaceutical manufacturers as well in branded form in the United States under the tradename Reglan® Tablets from Ani Pharmaceuticals.

Salix Pharmaceuticals, Inc. launched an orally dissolving tablet formulation of metoclopramide in 2009. Other programs in the gastroparesis pipeline include new chemical entities in earlier-stage clinical trials. In addition to our Gimoti product candidate, we are aware of the following development candidates; all of which are in Phase 2 clinical development.

Gastroparesis Treatment Development Pipeline

Product	Class	Route	Company	Status
Gimoti	dopamine antagonist /mixed 5-HT3 antagonist 5-HT4 agonist	nasal	Evoke Pharma	NDA Preparation
RM-131	ghrelin agonist	sub-cutaneous	Rhythm/Allergan	Phase 2b
Velusetrag/TAK-954	5-HT4 receptor agonist	oral	Theravance/Takeda	Phase 2
Tradipitant	NK-1 antagonist	oral	Vanda	Phase 2
Renzapride	5-HT4 agonist/ 5-HT3 antagonist	oral	Endologic	Phase 2
ATC-1906/TAK-906	D2/D3 antagonist	oral	Takeda	Phase 2
NG-101	D2/D3 antagonist	Oral	Neurogastrx	Phase 1

RM-131 is a small-peptide analog of ghrelin, a hormone produced in the stomach that stimulates gastrointestinal activity. The compound is being developed for GI motility disorders and has shown efficacy in surgical and opiate-induced ileus in animal models due to a direct prokinetic effect. In October 2016, a Phase 2b study failed to reach statistical significance. Following the trial results, Allergan plc. executed its option to acquire Rhythm Holding Company, LLC. RM-131 reverses body weight loss in cachexia models.

TD-5108, or TAK-954, also called Velusetrag, is a 5-HT4 receptor agonist compound under development for the treatment of gastroparesis by Takeda Pharmaceuticals in collaboration with Theravance Biopharma, Inc. Previously, Theravance was in collaboration with Alfa Wassermann S.p.A. for the development TD-5108 for chronic constipation.

Tradipitant is a NK-1 antagonist that has been tested in various other indications by Vanda Pharmaceuticals Inc. No known data related to gastroparesis is available for this program.

Renzapride, a 5-HT4 agonist and 5HT-3 antagonist, has been studied in more than 5,000 patients including one Phase 3 trial for the treatment of constipation-dominant irritable bowel syndrome (IBS-C). Renzapride demonstrated a small but statistically significant benefit in the Phase 3 study in IBS-C, however, the prior owner of the product decided to not continue to pursue development of the drug for this indication. The drug was well tolerated and showed no evidence of cardiotoxicity. A pilot Phase 2 study in patients with diabetic gastroparesis showed that doses of 0.5 mg, 1.0 mg and 2.0 mg, once-daily, showed significant improvement in gastric emptying in a dose-dependent manner. This endpoint does not meet the July 2015 FDA guidance for gastroparesis recommending measurement of symptoms associated with gastroparesis.

Altos Therapeutics LLC, or Altos, was developing the ATC-1906/TAK-906 compound as an oral dopamine D2/D3 receptor antagonist that addresses the symptoms of nausea and vomiting in gastroparesis patients. As part of an agreement, Takeda acquired Altos and assumed control over development and commercialization of ATC-1906/TAK-906.

Neurogastrx is currently developing NG-101. NG-101 is a selective and peripherally restricted dopamine D2/D3 receptor antagonist to treat gastroparesis. It is approved in countries outside the US in other indications.

One additional medication, Motilium (domperidone), a dopamine receptor modulator, is not FDA-approved, but is available in the United States through various compounding pharmacies under a specific FDA restricted-access program. The safety and efficacy of Motilium as a promotility agent is not fully established.

Technology Acquisition Agreement

In June 2007, we acquired all worldwide rights, data, patents and other related assets associated with Gimoti from Questcor pursuant to an asset purchase agreement. We paid Questcor $650,000 in the form of an upfront payment and $500,000 in May 2014 as a milestone payment based upon the initiation of the first patient dosing in our Phase 3 clinical trial for Gimoti. In August 2014, Mallinckrodt plc, or Mallinckrodt, acquired Questcor. As a result of that acquisition, Questcor transferred its rights included in the asset purchase agreement with us to Mallinckrodt. In addition to the payments we made to Questcor, we may also be required to make additional milestone payments to Mallinckrodt totaling up to $51.5 million. These milestones include up to $4.5 million in payments if Gimoti achieves the following development targets:

- $1.5 million upon FDA's acceptance for review of an NDA for Gimoti; and
- $3 million upon FDA's approval of Gimoti.

The remaining $47 million in milestone payments depend on Gimoti's commercial success and will only apply if Gimoti receives regulatory approval. In addition, we will be required to pay to Mallinckrodt a low single digit royalty on net sales of Gimoti. Our obligation to pay such royalties will terminate upon the expiration of the last patent right covering Gimoti, which is expected to occur in 2030.

Government Regulation

FDA Review and Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by FDA. The Federal Food, Drug, and Cosmetic Act, or FFDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA's refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by FDA before a drug may be marketed in the United States generally involves:

- completion of pre-clinical laboratory and animal testing and formulation studies in compliance with FDA's good laboratory practice regulations;
- submission to FDA of an Investigational New Drug Application, or IND, for human clinical testing which must become effective before human clinical trials may begin in the United States;
- approval by an independent institutional review board, or IRB, at each clinical trial site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, regulations to establish the safety and efficacy of the proposed drug product for each intended use;
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with FDA current good manufacturing practices, or cGMP, regulations, including, for devices and device components, the Quality System Regulation, or QSR, and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- submission to FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable; and
- FDA review and approval of the NDA.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Pre-clinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of pre-clinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to FDA. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by FDA, unless FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Further, an IRB covering each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site, and it must monitor the study until completed. FDA, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk or for failure to comply with the IRB's or regulatory requirements, or for other reasons, or FDA or IRB may impose other conditions.

Clinical trials involve the administration of the investigational new drug to human subjects 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. Sponsors of clinical trials generally must register and report, at the National Institutes of Health-maintained website ClinicalTrials.gov, key parameters of certain clinical trials. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- *Phase 1:* The drug is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.
- *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 indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive Phase 3 clinical trials.
- *Phase 3:* These are commonly referred to as pivotal studies. When Phase 2 evaluations demonstrate that a dose range of the product appears to be effective and has an acceptable safety profile, Phase 3 trials are undertaken in large patient populations to further evaluate dosage, to obtain additional evidence of clinical efficacy and safety in an expanded patient population at multiple, geographically-dispersed clinical trial sites, to establish the overall risk-benefit relationship of the drug and to provide adequate information for the labeling of the drug.
- *Phase 4:* In some cases, FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The results of product development, pre-clinical studies and clinical trials are submitted to FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, chemistry, manufacturing and controls, or CMC, and proposed labeling, among other things.

Under federal law, the submission of most NDAs is subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. FDA may request additional information rather than accept an NDA for filing. In this event,

the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. The resubmitted application is also subject to review before FDA accepts it for filing.

Once the submission has been accepted for filing, FDA begins an in-depth substantive review. Under PDUFA, FDA agrees to specific performance goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review NDAs have a goal of being completed within ten months of the date of receipt by FDA (for drugs that do not contain new molecular entities) and ten months of the 60-day filing date (for drugs that contain new molecular entities). A Priority Review designation is given to drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The goal for completing a Priority Review is six months from the date of receipt by FDA (for drugs that do not contain new molecular entities) and six months of the 60-day filing date (for drugs that contain new molecular entities). However, FDA does not always complete its review within these timelines and the review can take substantially longer.

We believe that our product candidate will be granted a Standard Review for a product that does not contain a new chemical entity. The review process may be extended to allow FDA to request and review additional information or obtain clarification regarding information provided in the original submission. FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions.

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

After FDA evaluates the NDA and, in some cases, the related manufacturing facilities, it may issue an approval letter or a Complete Response Letter, or CRL, to indicate that the review cycle for an application is complete or that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for FDA to reconsider the application. Even with submission of this additional information, FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to FDA's satisfaction, FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Once issued, FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. In addition, FDA may require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label, and, even if FDA approves a product, it may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional pre-clinical studies and clinical trials.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by FDA, including, among other things, requirements relating to drug/device listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with FDA and state agencies, and are subject to periodic unannounced inspections by FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and generally require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we 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, FDA may suspend, restrict or withdraw the approval, require a product recall, or impose additional restrictions or limitations 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, among other things:

- 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 FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license 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.

FDA may require post-approval studies and clinical trials if FDA finds that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug. Based on feedback from FDA, we plan to propose a post-marketing safety trial as part of the Gimoti NDA submission. We expect to discuss the details of such a trial with FDA during the NDA review process.

The Food and Drug Administration Amendments Act of 2007 gave FDA the authority to require a Risk Evaluation and Mitigation Strategy, or REMS, from manufacturers to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval. FDA may also impose a REMS requirement on a drug already on the market if FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits continue to outweigh its risks.

In March 2009, FDA informed drug manufacturers that it will require a REMS for metoclopramide drug products. FDA's authority to take this action is based on risk management and post market safety provisions within the Food and Drug Administration Amendments Act. The REMS consists of a Medication Guide, elements to assure safe use (including an education program for prescribers and materials for prescribers to educate patients), and a timetable for submission of assessments of at least six months, 12 months, and annually after the REMS is approved. In 2011, FDA determined that maintaining the Medication Guide as a part of the approved labeling is adequate to address the public health concern and meets the regulatory standards. We intend to follow current labeling procedures to include a medication guide at the time of the NDA submission for Gimoti. Based on feedback from FDA, we intend to propose elements of a REMS to be included in the NDA submission. At this time the elements of the REMS for Gimoti are unclear as there are varying levels of requirements that may include a Medication Guide, similar to the Reglan Tablet, and other elements, such as a communication plan and an implementation plan, designed to ensure safe use, as well as a timetable for submission of post-marketing assessments after the REMS is approved.

FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market, and FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet. While physicians may prescribe for off-label uses, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. 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. Indeed, FDA has very broad enforcement authority under the FFDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials are pre-cleared by FDA, and state and federal civil and criminal investigations and prosecutions.

The distribution of prescription pharmaceutical products is also subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples

and impose requirements to ensure accountability in distribution, including a drug pedigree which tracks the distribution of prescription drugs.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval for modifications to formulations or uses of products previously approved by FDA, an applicant may submit an NDA under Section 505(b)(2) of the FFDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon published literature and FDA's findings of safety and effectiveness based on certain pre-clinical or clinical studies conducted for an approved product. FDA may also require companies to perform additional studies or measurements to support the change from the approved product. FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that a Section 505(b)(2) NDA relies on studies conducted for a previously approved drug product, the applicant is required to certify to FDA concerning any patents listed for the approved product in FDA Orange Book. FDA Orange Book is where patents associated with a FDA-approved product are listed. Specifically, the applicant must certify for each listed patent that (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patent or that such patent is invalid is known as a Paragraph IV certification. If the applicant does not challenge the listed patents through a Paragraph IV certification, the Section 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired. The Section 505(b)(2) NDA application also will not be accepted or approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a New Chemical Entity, listed in the Orange Book for the referenced product has expired.

If the 505(b)(2) NDA applicant has provided a Paragraph IV certification to FDA, the applicant must also send notice of the Paragraph IV certification to the referenced NDA and patent holders once the 505(b)(2) NDA has been accepted for filing by FDA. The NDA and patent holders may then initiate a legal challenge to the Paragraph IV certification. Under the FFDCA, the filing of a patent infringement lawsuit within 45 days of the NDA and patent holders' receipt of a Paragraph IV certification in most cases automatically prevents FDA from approving the Section 505(b)(2) NDA for 30 months, or until a court decision or settlement finding that the patent is invalid, unenforceable or not infringed, whichever is earlier. The court also has the ability to shorten or lengthen the 30-month stay if either party is found not to be reasonably cooperating in expediting the litigation. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its product only to be subject to significant delay and patent litigation before its product may be commercialized.

The 505(b)(2) NDA applicant also may be eligible for its own regulatory exclusivity period, such as three-year exclusivity. Specifically, a product may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, FDA would be precluded from making effective any other application for the same condition of use or for a change to the drug product that was granted exclusivity until after that three-year exclusivity period has expired. Additional non-patent exclusivities may also apply.

Additionally, the 505(b)(2) NDA applicant may have relevant patents in the Orange Book, and if so, it can initiate patent infringement litigation against those applicants that challenge such patents, which could result in a 30-month stay delaying those applicants.

Manufacturing Requirements

We and our third-party manufacturers must comply with applicable FDA regulations relating to FDA's cGMP regulations including applicable QSR requirements. The cGMP regulations include requirements relating to, among other things, organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and our third-party manufacturers are also subject to periodic unannounced inspections of facilities by FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including, among other things, warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties.

Other Regulatory Requirements

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, FDA has broad regulatory and enforcement powers, including, among other things, the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have a material adverse effect on us.

Coverage and Reimbursement

Sales of our products, if approved, will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health care programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly limiting coverage and reducing reimbursements for medical products and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates or a decision by a third-party payor to not cover our drug candidates could reduce physician utilization of our products and have a material adverse effect on our sales, results of operations and financial condition.

Other Healthcare Laws

Although we currently do not have any products on the market, if our drug candidates are approved and we begin commercialization, we will be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. Further, 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 government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal 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.

Additionally, the False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the 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 False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government 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, also created new 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 federal Anti-Kickback Statute, 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.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our 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.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes new reporting requirements on certain drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $165,786 per year (or up to an aggregate of $1.105 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit reports to the government by the 90th day of each calendar year. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of marketing expenditures and pricing information, as well as gifts, compensation and other remuneration to physicians.

The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance and/or reporting requirements in multiple jurisdictions increase the possibility that a healthcare company may violate one or more of the requirements. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Healthcare Reform

In March 2010, the Affordable Care Act, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States, was signed into law and significantly affected the pharmaceutical industry. The Affordable Care Act contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the Affordable Care Act increases the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs; and addresses 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. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several 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 drug products. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Employees

As of February 28, 2018, we had seven full-time employees and several consultants in the regulatory, clinical, manufacturing and finance areas. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good.

Research and Development

We incurred $7.1 million and $7.0 million in research and development expenses for the years ended December 31, 2017 and 2016, respectively.

About Evoke

We were formed as a Delaware corporation in January 2007. Our principal executive offices are located at 420 Stevens Avenue, Suite 370, Solana Beach, California 92075, and our telephone number is (858) 345-1494.

Financial Information about Segments

We have one operating segment, which is the development of pharmaceutical products. See Note 2 to our financial statements included in this Annual Report on Form 10-K. For financial information regarding our business, see "Management's Discussion and Analysis of Financial Condition and Results of Operations" and those financial statements and related notes.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended. We make available copies of these reports, free of charge, on our website at *www.evokepharma.com*, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov. The information in or accessible through the SEC and our website are not incorporated into, and are not considered part of, this report. Further, our references to the URLs for these websites are intended to be inactive textual references only.

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Annual Report on Form 10-K and our other public filings with the Securities and Exchange Commission, or SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risks Related to our Business, including the Development, Regulatory Approval and Potential Commercialization of our Product Candidate, Gimoti

Our business is entirely dependent on the success of Gimoti, which failed to achieve the primary endpoint of symptom improvement in a Phase 3 clinical trial in female patients with symptoms associated with diabetic gastroparesis. While we are continuing to pursue regulatory approval based on the results of our completed comparative exposure PK trial, we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, Gimoti.

To date, we have devoted all of our research, development and clinical efforts and financial resources toward the development of Gimoti, our patented nasal delivery formulation of metoclopramide for the relief of symptoms associated with acute and recurrent diabetic gastroparesis in adult women. Gimoti is our only product candidate. In July 2016, we announced topline results from our Phase 3 clinical trial that evaluated the efficacy and safety of Gimoti in women with symptoms associated with diabetic gastroparesis. In this study, Gimoti did not achieve its primary endpoint of symptom improvement in the Intent-to-Treat (ITT) group at Week 4.

In December 2016, we announced the completion of a pre-NDA meeting with FDA, in which FDA agreed that a comparative exposure PK trial was acceptable as a basis for submission of a Gimoti NDA. Data from the comparative exposure PK trial will serve as a portion of the 505(b)(2) data package to include prior efficacy and safety data developed by us and FDA's prior findings of safety and efficacy for the Listed Drug, Reglan Tablets. In October 2017, we announced positive topline results from the comparative exposure PK trial. In addition, based on feedback received from FDA at an additional pre-NDA meeting, we plan to propose a risk mitigation strategy and post-approval safety trial as part of our NDA submission. In order to incorporate the feedback received by FDA at the additional pre-NDA meeting, we expect to submit the Gimoti NDA in the second quarter of 2018, though FDA may require the conduct of additional efficacy or safety trials, and we may be unable to submit an NDA on this timeframe, or potentially at all.

Because our business is entirely dependent on the success of Gimoti, if we are unable to successfully complete development of and receive regulatory approval of this product candidate, we will be required to curtail all of our activities and may be required to liquidate, dissolve or otherwise wind down our operations. Any of these events could result in the complete loss of an investment in our securities.

In addition to the above factors, the future regulatory and commercial success of Gimoti is subject to a number of additional risks, including the following:

- we may not have sufficient financial and other resources to complete clinical development for Gimoti;
- we may not be able to provide acceptable evidence of safety and efficacy for Gimoti, including as a result of the proposed duration of use for Gimoti being shorter as compared to the maximum approved dosing duration for the referenced Listed Drug, Reglan Tablets;
- FDA may disagree with the design of our comparative exposure PK trial or any other future clinical trials, if any are necessary;
- variability in subjects, adjustments to clinical trial procedures and inclusion of additional clinical trial sites;
- FDA may not agree with the analysis of our clinical trial results, including our analysis of the results of the PK trial;
- the results of our clinical trials may not meet the level of statistical or clinical significance or other bioequivalence parameters required by FDA for marketing approval, including C_{max} falling below the equivalence range in the comparative exposure PK trial;
- we may be required to undertake additional clinical trials and other studies of Gimoti before we can submit an NDA, to FDA or receive approval of the NDA;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to Gimoti, such as dysgeusia, headache, diarrhea, nasal discomfort, tremor, myoclonus, somnolence, rhinorrhea, throat irritation, and fatigue;

- if approved, Gimoti will compete with well-established products already approved for marketing by FDA, including oral and intravenous forms of metoclopramide, the same active ingredient in the nasal spray for Gimoti;
- we may not be able to obtain, maintain and enforce our patents and other intellectual property rights; and
- we may not be able to maintain commercial manufacturing arrangements with third-party manufacturers or establish and maintain commercial-scale manufacturing capabilities.

Of the large number of drugs in development in this industry, only a small percentage result in the submission of an NDA to FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market Gimoti, any such approval may be subject to limitations on the indicated uses for which we may market the product.

We will require substantial additional funding and may be unable to raise capital when needed, which would force us to liquidate, dissolve or otherwise wind down our operations.

Our operations have consumed substantial amounts of cash since inception. We believe, based on our current operating plan, that our existing cash and cash equivalents will be sufficient to fund our operations into October 2018, although there can be no assurance in that regard. We will be required to raise additional funds in order to continue as a going concern beyond that time.

Our estimates of the amount of cash necessary to fund our activities may prove to be wrong and we could spend our available financial resources much faster than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

- the need for, and the progress, costs and results of, any additional clinical trials of Gimoti that may be required by FDA, including any pre-approval or post-approval trials FDA or other regulatory agencies may require evaluating the efficacy or safety of Gimoti;
- the outcome, costs and timing of seeking and obtaining regulatory approvals from FDA, and any similar regulatory agencies;
- the costs and timing of completion of outsourced commercial manufacturing supply arrangements for Gimoti;
- the costs of establishing or outsourcing sales, marketing and distribution capabilities;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with Gimoti;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish; and
- costs associated with any other product candidates that we may develop, in-license or acquire.

Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. Furthermore, the issuance of additional shares or other securities by us, or the possibility of such issuance, may cause the market price of our shares to decline and dilute the holdings of our existing stockholders. If we raise additional funds by incurring debt, the terms of the debt may involve significant cash payment obligations, as well as covenants and specific financial ratios that may restrict our ability to operate our business. We cannot provide any assurance that our existing capital resources will be sufficient to enable us to identify or execute a viable plan for continued clinical development of Gimoti or to otherwise survive as a going concern.

Topline data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose topline or interim data from time to time, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. For example, while we believe that the AUC measurement was the most clinically relevant PK parameter for our comparative exposure PK trial, FDA may disagree or may emphasize other data such as C_{max} falling below the equivalence range of Reglan Tablets. Any contrary views by FDA would impact our dose selection and FDA's review of our planned NDA submission. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. Further, although we reported positive topline data for the PK trial, FDA may still require the conduct of additional efficacy or safety trials prior to our planned NDA submission.

If we are not able to obtain regulatory approval for Gimoti, we will not be able to commercialize this product candidate and our ability to generate revenue will be limited.

We have not submitted an NDA or received regulatory approval to market any product candidates in any jurisdiction. We are not permitted to market Gimoti in the United States until we receive approval of an NDA for the product candidate in a particular indication from FDA. To date, we have completed a Phase 1 bioavailability and pharmacokinetics trial, a comparative exposure PK trial, a Phase 3 clinical trial in female subjects, a Phase 3 clinical trial in male subjects, a Thorough ECG (QT/QTc) study, a Phase 2b clinical trial and we acquired the results from a separate Phase 2 clinical trial in diabetic subjects with gastroparesis. In the Phase 2b clinical trial that we performed ourselves, which concluded in 2011, Gimoti failed to meet the primary endpoint for the trial. Although an overall improvement in symptoms was observed in Gimoti-treated subjects with diabetic gastroparesis compared to placebo in this Phase 2b clinical trial, the difference was not statistically significant due to a high placebo response among male subjects. The earlier Phase 2 clinical trial performed by Questcor was a multicenter, randomized, open-label, parallel design study. This head-to-head study compared the efficacy and safety of two doses of metoclopramide nasal spray, 10 mg and 20 mg, with FDA-approved 10 mg metoclopramide tablet. Although data from the earlier Phase 2 clinical trial will be referenced in the Gimoti NDA, the open-label study design limits the importance of the efficacy results in the NDA.

We completed our Phase 3 clinical trial in female subjects with symptoms associated with acute and recurrent diabetic gastroparesis and announced in July 2016 that Gimoti did not achieve its primary endpoint of symptom improvement at Week 4. While we are planning to submit the results from the comparative exposure PK trial as a portion of the 505(b)(2) NDA submission that will include prior efficacy and safety data developed by us along with FDA's prior findings of safety and efficacy for the Listed Drug, Reglan Tablets, there is no guarantee that regulators will agree with our assessment of the clinical trials for Gimoti conducted to date, including the comparative exposure PK trial. In addition, we have only limited experience in filing the applications necessary to gain regulatory approvals and expect to rely on consultants and third party contract research organizations to assist us in this process. FDA and other regulators have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional clinical trials, or preclinical or other studies.

Varying interpretation of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Furthermore, we have acquired our rights to Gimoti from Questcor, who acquired its rights from a predecessor. Thus, much of the preclinical and a portion of the clinical data relating to Gimoti that we would expect to submit in an NDA for Gimoti was obtained from studies conducted before we owned the rights to the product candidate and, accordingly, was prepared and managed by others. These predecessors may not have applied the same resources and given the same attention to this development program as we would have if we had been in control from inception.

Gimoti and the activities associated with its development and potential commercialization, including its testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory marketing approval for Gimoti will prevent us from commercializing the product candidate, and our ability to generate revenue will be materially impaired.

FDA may impose requirements on our clinical trials that are difficult to comply with, which could harm our business.

In July 2015 FDA published draft guidance intended to assist sponsors in the clinical development of drugs for the treatment of diabetic and idiopathic gastroparesis clinical trials, *Gastroparesis: Clinical Evaluation of Drugs for Treatment – Guidance for Industry*. We believe that FDA Guidance is consistent with the advice FDA provided to us regarding trial design and study endpoints for our completed Phase 3 trials. In addition, FDA Guidance explicitly states that there is an urgent medical need for development of drugs with a favorable risk-benefit profile to treat patients with gastroparesis and acknowledges that "patients with diabetic gastroparesis may experience further derangement of glucose control because of unpredictable gastric emptying and altered absorption of orally administered hypoglycemic drugs." FDA Guidance, however, does not create or confer any rights for or on any person and do not operate to bind FDA or the public, and FDA may ultimately disagree with our interpretation regarding the meaning or applicability of any published Guidance documents.

We conducted a Phase 3 trial in adult female subjects with diabetic gastroparesis, which failed to reach its primary endpoint. However, following our second pre-NDA meeting with FDA in December 2016, FDA agreed that a comparative exposure PK trial, along with prior efficacy and safety data from other completed Gimoti studies, would be appropriate for NDA submission seeking an indication of treatment of symptoms associated with diabetic gastroparesis in women. Although we believe the results from the comparative exposure PK trial along with the prior data will be sufficient to allow us to submit an NDA for Gimoti, it is possible FDA will require additional clinical testing before submission or approval of the NDA. In addition, based on discussions with FDA, we also conducted a similar study for safety and efficacy in adult male subjects with diabetic gastroparesis. A portion of the safety and efficacy data from this trial will be submitted as a part of the NDA submission. If we are unable to comply with FDA's requirements, we will not be able to obtain approval for Gimoti and our ability to generate revenue will be materially impaired.

Any termination or suspension of, or delays in the completion of, any future clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Delays in the completion of any future clinical trials for Gimoti could significantly affect our product development costs. We do not know whether any trials will produce data on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- FDA placing a clinical trial on hold;
- subjects failing to remain in our trial at the rate we expect (for example, due to variable patient frequency and severity of disease and variability in gastric emptying testing);
- subjects choosing an alternative treatment for the indication for which we are developing Gimoti, or participating in competing clinical trials;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing Gimoti, or any of its components, being ordered by FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of FDA's current good manufacturing practices or other applicable requirements, or infections or cross-contaminations of product candidate in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing their license or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practice and regulatory requirements, or other third parties not performing data collection and analysis in a timely or accurate manner;
- inspections of clinical trial sites by FDA or the finding of regulatory violations by FDA or an independent institutional review board, or IRB, that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial, or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or any of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of Gimoti, or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of or if we, FDA or other regulatory authorities, the IRB, or other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for our product candidate may be harmed and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Also, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of Gimoti could be significantly reduced.

Delays in the completion of any clinical trials and studies we may conduct for Gimoti could be harmful to our business and cause us to require additional funding.

Final marketing approval for Gimoti by FDA or other regulatory authorities for commercial use may be delayed, limited, or denied, any of which would adversely affect our ability to generate operating revenues.

We plan to submit an NDA for Gimoti during the second quarter of 2018. However, we cannot provide any assurance as to whether or when we will submit an NDA, or whether or when we will obtain regulatory approval to commercialize Gimoti. We cannot, therefore, predict the timing of any future revenue. Because Gimoti is our only product candidate this risk is particularly significant for us. We cannot commercialize Gimoti until the appropriate regulatory authorities have reviewed and approved marketing applications for this product candidate. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for Gimoti. In addition, we may experience delays or the application may be rejected based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. For example, in 2009 following an FDA review of metoclopramide spontaneous safety reports, FDA required a boxed warning be added to the metoclopramide product label concerning the chance of tardive dyskinesia, or TD, for patients taking these products. FDA requires a boxed warning (sometimes referred to as a "Black Box" Warning) for products that have shown a significant risk of severe or life-threatening adverse events. Recently, the European Medicines Agency's Committee on Medicinal Products for Human Use, or CHMP, has reviewed and has proposed labeling changes for marketed metoclopramide products in the European Union based on age, dosing guidelines or indications. Based on their assessment of the limited efficacy and safety data currently available to the CHMP, the CHMP recommended to the European Medicines Agency that indications with limited or inconclusive efficacy data, including GERD, dyspepsia and gastroparesis, be removed from the approved product label in the European Union. There can be no assurance as to whether FDA will re-review approved metoclopramide product labels as a result of any such regulatory actions in the European Union or otherwise. If marketing approval for Gimoti is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

If FDA does not conclude that Gimoti satisfies the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements under Section 505(b)(2) are not as we expect, the approval pathway for our primary product candidate will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We intend to seek FDA approval through the Section 505(b)(2) regulatory pathway for our primary product candidate, Gimoti. Gimoti is a drug/device combination product that will be regulated under the drug provisions of the FFDCA, enabling us to submit an NDA for its approval. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

If FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for Gimoti, and the complications and risks associated with our lead product candidate, would likely substantially increase. We may need to obtain additional funding, which could result in significant dilution to the ownership interests of our then existing stockholders to the extent we issue equity securities or convertible debt. We cannot assure you that we would be able to obtain such additional financing on terms acceptable to us, if at all. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in competitive products reaching the market before Gimoti, which could impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that Gimoti or any future product candidates will receive the requisite approvals for commercialization.

Even if we obtain marketing approval for Gimoti, it could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidate, when and if Gimoti is approved.

Even if U.S. regulatory approval is obtained, FDA may still impose significant restrictions on Gimoti's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. For example, FDA has requested us to include a proposal for a post-marketing safety trial as part of our planned NDA submission. Gimoti will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for Gimoti fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product, or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

FDA has the authority to require a REMS as a condition of approval of an NDA or following approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. In March 2009, FDA informed drug manufacturers that it will require a REMS for metoclopramide drug products, including a Medication Guide, elements to assure safe use (including an education program for prescribers and materials for prescribers to educate patients), and a timetable for submission of assessments of at least six months, 12 months, and annually after the REMS is approved. In addition, FDA has requested we include a proposal for a risk mitigation strategy in our planned NDA submission. We intend to propose elements of a REMS and our proposal for a post-approval safety trial at the time of the NDA submission for Gimoti. At this time the elements of the REMS for Gimoti are unclear as there are varying levels of requirements that may include a Medication Guide, similar to the Reglan Tablet, and other elements, such as a communication plan and an implementation plan, designed to ensure safe use, as well as a timetable for submission of post-marketing assessments after the REMS is approved.

In addition, if Gimoti is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by FDA as reflected in the product's approved labeling. If we receive marketing approval for Gimoti, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. 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 sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including FDA, which prohibits FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. Although certain positions at FDA may be exempt from the freeze, an under-staffed FDA could result in delays in FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all.

Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Even if we receive regulatory approval for Gimoti, we still may not be able to successfully commercialize it and the revenue that we generate from its sales, if any, will be limited.

Gimoti's commercial success will depend upon the acceptance of the product candidate by the medical community, including physicians, patients and health care payors. The degree of market acceptance of our product candidate will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the limitation of our targeted patient population to women-only;
- limitations or warnings contained in any FDA-approved labeling, including the potential boxed warning on all metoclopramide product labels concerning the chance of TD for patients taking these products, or any limitations with respect to metoclopramide product labels in the European Union;
- acceptance of a new formulation by health care providers and their patients;
- the prevalence and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating or may reduce the incidences of diabetic gastroparesis;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If Gimoti is approved, but does not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not generate sufficient revenue, and we may not be able to achieve or sustain profitability. Our efforts to educate the medical community and third-party payors on the benefits of Gimoti may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend the intellectual property of our products.

It will be difficult for us to profitably sell Gimoti if coverage and reimbursement are limited.

Market acceptance and sales of our product candidate will depend on coverage and reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. 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 medications. Increasingly, third-party payors have been challenging the prices charged for products. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which FDA has granted marketing approval. This trend may impact the reimbursement for treatments for GI disorders especially, including Gimoti, as physicians typically focus on symptoms rather than underlying conditions when treating patients with these disorders and drugs are often prescribed for uses outside of their approved indications. In instances where alternative products are available, it may be required that those alternative treatment options are tried before coverage and reimbursement are available for Gimoti. Although Gimoti is a novel nasal spray formulation of metoclopramide, this is the same active ingredient that is already available in other formulations approved for the treatment of gastroparesis that are already widely available at generic prices. We cannot be sure that coverage will be available for Gimoti and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, this product candidate. In addition, in certain foreign countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize our product candidate.

We rely and will continue to rely on outsourcing arrangements for many of our activities, including clinical development and supply of Gimoti.

As of February 28, 2018, we had only seven full-time employees and, as a result, we rely on outsourcing arrangements for a significant portion of our activities, including clinical research, data collection and analysis and manufacturing, as well as functioning as a public company. We also rely on a third-party CRO to manage the preparation and submission of our planned NDA, and any failure of such CRO to effectively manage the process could adversely affect the timing and quality of the NDA submission. We may have limited control over these third parties and we cannot guarantee that they will perform their obligations in an effective and timely manner.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. We do not own or operate manufacturing facilities for the production of any component of Gimoti, including metoclopramide, the nasal spray device or associated bottle, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials, drug substance and drug product for our clinical trials and pre-commercialization activities, and will continue to rely on such third parties for commercial production if Gimoti is approved for marketing. We are currently using, and relying on, single suppliers and single manufacturers for starting materials, the final drug substance and nasal spray delivery device for Gimoti, including Cosma S.p.A. as the sole-source supplier of metoclopramide and Thermo Fisher Scientific Inc., as the sole manufacturer of Gimoti. Although potential alternative suppliers and manufacturers for some components have been identified, we have not qualified these vendors to date. If we were required to change vendors, it could result in a failure to meet regulatory requirements or projected timelines and necessary quality standards for successful manufacturing of the various required lots of material for our development and commercialization efforts.

If we change to other manufacturers in the future, FDA and comparable foreign regulators must approve these manufacturers' facilities and processes prior to use, which could require new clinical studies, testing and compliance inspections, and the new manufactures would have to be educated in, or demonstrate successful technology transfer of, the processes necessary for the production of Gimoti.

In addition, our reliance on third party CROs and contract manufacturing organizations, or CMOs, entails further risks including:

- non-compliance by third parties with regulatory and quality control standards;
- breach by third parties of our agreements with them;
- termination or non-renewal of an agreement with third parties; and
- sanctions imposed by regulatory authorities if compounds supplied or manufactured by a third party supplier or manufacturer fail to comply with applicable regulatory standards.

We face substantial competition, which may result in others selling their products more effectively than we do, and in others discovering, developing or commercializing product candidates before, or more successfully, than we do.

Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of Gimoti. We anticipate that Gimoti, if approved, would compete directly with metoclopramide, erythromycin and domperidone, each of which is available under various trade names sold by several major pharmaceutical companies, including generic manufacturers. Metoclopramide is the only molecule currently approved in the United States to treat gastroparesis. Metoclopramide is generically-available and indicated for the relief of symptoms associated with acute and recurrent diabetic gastroparesis, without the limitation of use in women only.

Many of our potential competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we successfully:

- assure health care providers, patients and health care payors that Gimoti is beneficial compared to other products in the market;
- obtain patent and/or other proprietary protection for Gimoti;
- obtain and maintain required regulatory approvals for Gimoti; and
- collaborate with others to effectively market, sell and distribute Gimoti.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidate obsolete. In addition to our Gimoti product candidate, we are aware of other development candidates in clinical development. Any of these product candidates could advance through clinical development faster than Gimoti and, if approved, could attain faster and greater market acceptance than our product candidate. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

We have no internal sales, marketing or distribution capabilities currently and we may not be able to effectively market, sell and distribute Gimoti, if approved.

Currently, we have no internal sales, marketing or distribution capabilities. If Gimoti ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We will have to invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that Gimoti will be approved, or engage third parties to provide these services. We have entered into an agreement with Syneos Health, Inc., or Syneos (formerly inVentiv Commercial Services LLC), to build our commercial infrastructure for the potential commercial launch of Gimoti, including to potentially retain, train and deploy a direct sales force, but we have no experience operating or managing a third-party sales force. There can be no assurance that the capabilities of the Syneos sales organization will be more effective than an internally developed sales organization. In addition, Syneos can terminate our agreement under certain circumstances. If Syneos fails to hire, train, and retain qualified sales personnel, market our product successfully or on a cost effective basis or otherwise terminates our relationship, our ability to generate revenue will be limited and we will need to identify and retain an alternative organization, or develop our own sales and marketing capability. This could involve significant delays and costs, including the diversion of our management's attention from other activities. We will also need to retain additional consultants or external service providers to assist us in sales, marketing and distribution functions, and may be unsuccessful in retaining such services on acceptable financial terms or at all.

If we do perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- inability to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenues generated by Gimoti or any other product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

If we are unsuccessful in building and managing a sales and marketing infrastructure internally or through a third-party partner for any approved product, we will have difficulty commercializing the product, which would adversely affect our business and financial condition.

If we fail to attract and retain senior management and key commercial personnel, we may be unable to successfully complete the development of Gimoti and commercialize this product candidate.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and commercial personnel. We are highly dependent upon our senior management team composed of three individuals: David A. Gonyer, R.Ph., our President and Chief Executive Officer, Matthew J. D'Onofrio, our Executive Vice President and Chief Business Officer,

and Marilyn Carlson, D.M.D., M.D., our Chief Medical Officer. The loss of services of any of these individuals could delay or prevent the successful development of Gimoti or the commercialization of this product candidate, if approved.

We will need to hire and retain qualified personnel to pursue the potential commercialization of Gimoti. We could experience problems in the future attracting and retaining qualified employees. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense, particularly in the San Diego, California area where we are headquartered. We may not be able to attract and retain quality personnel on acceptable terms who have the expertise we need to sustain and grow our business.

We may encounter difficulties in managing our growth and expanding our operations successfully.

Because we only had seven full-time employees as of February 28, 2018, we will need to grow our organization substantially to pursue the potential commercialization of Gimoti and to potentially conduct additional unplanned development activities. As we seek to commercialize Gimoti, we will need to expand our regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain additional internal capabilities. Our future financial performance and our ability to commercialize Gimoti and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize Gimoti and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for Gimoti, restrict or regulate post-approval activities and affect our ability to profitably sell our product candidate, assuming we obtain marketing approval.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of Gimoti, if any, may be. In addition, increased scrutiny by the U.S. Congress of FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, was signed into law. The Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Affordable Care Act, among other things, increased the Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program for both branded and generic drugs and revised the definition of "average manufacturer price" for reporting purposes, which could further increase the amount of Medicaid drug rebates to states. Further, the law imposes a significant annual fee on companies that manufacture or import branded prescription drug products, increased the number of entities eligible for discounts under the 340B program and included a 50% discount on brand name drugs for Medicare Part D beneficiaries in the coverage gap, or "donut hole." Substantial provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act. We expect that President Trump's administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. Most recently, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with Affordable Care Act's individual mandate to carry health insurance. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the Affordable Care Act. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of two percent per fiscal year, which went into effect on April 1, 2013, and due to subsequent legislative amendments, will remain in effect through 2025, unless additional Congressional action is taken. 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.

Recently there has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. These laws and the regulations and policies implementing them, as well as other healthcare reform measures that may be adopted in the future, may have a material adverse effect on our industry generally and on our ability to successfully develop and commercialize our products, if approved.

If we market products in a manner that violates healthcare laws, or if we violate government price reporting laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict business activities in the pharmaceutical industry, including certain marketing practices. These laws include false claims, anti-kickback, data privacy and security and physician payment transparency laws and regulations. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Further, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the criminal healthcare fraud statutes that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. Over the past few years, several pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as: allegedly providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion that caused claims to be submitted to Medicaid for non-covered, off-label uses; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Most states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

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. Like the federal Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Once our products are approved and we commence sales in the United States, we will also be required to comply with the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by physicians (as defined above) and their immediate family members. Manufacturers are required to report such data to the government by the 90th calendar day of each year. There are also several states with similar laws that require drug manufacturers to report information related to payments and other transfers of

value to physicians and other healthcare providers or marketing expenditures and pricing information, and/or require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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 attorneys' fees and costs associated with pursuing federal civil actions.

The risk of our being found in violation of these laws and regulations is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from governmental health care programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Gimoti.

We face an inherent risk of product liability as a result of the clinical testing of Gimoti and will face an even greater risk if we commercialize the product candidate. For example, we may be sued if Gimoti allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts.

In particular, products containing metoclopramide have been reported to cause side effects, including TD. It is possible that a patient taking Gimoti will be found to experience a variety of side effects. In 2009, FDA required a boxed warning on all metoclopramide product labels concerning the chance of TD for patients taking these products. We expect that the label for Gimoti, if approved, will likely contain a similar warning regarding TD. Several manufactures of metoclopramide products have been sued by patients regarding TD.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidate. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for Gimoti;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize Gimoti; and
- a decline in our stock price.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of Gimoti. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face

significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for Gimoti because third parties may view the development or commercialization risk of Gimoti as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction.

Our business and operations would suffer in the event of system failures, including cyberattacks.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors and consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development program for Gimoti and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture Gimoti and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed, or otherwise adversely affected.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our Gimoti. Our ability to obtain clinical supplies of Gimoti could be disrupted, if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our operations are located in Solana Beach, California near major earthquake faults and fire zones. The ultimate impact on us, our significant suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

As part of our growth strategy, we plan to evaluate the development and/or commercialization of other therapies for GI motility disorders. Similar to our initial focus on gastroparesis, we will evaluate opportunities to in-license or acquire other product candidates as well as commercial products to treat patients suffering from predominantly GI disorders, seeking to identify areas of high unmet medical needs with limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, extensive clinical trials and approval by FDA and applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the drug candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.

From time to time we have considered, and we will continue to consider in the future, strategic business initiatives intended to further the development of our business. These initiatives may include acquiring businesses, technologies or products or entering into a business combination with another company. If we do pursue such a strategy, we could, among other things:

- issue equity securities that would dilute our current stockholders' percentage ownership;
- incur substantial debt that may place strains on our operations;
- spend substantial operational, financial and management resources in integrating new businesses, technologies and products; and
- assume substantial actual or contingent liabilities.

We may be unable to maintain sufficient product liability insurance.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering

our clinical studies. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the commercial launch of any product, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Risks Relating to Our Intellectual Property

It is difficult and costly to protect our intellectual property rights, and we cannot ensure the protection of these rights. Any impairment of our intellectual property rights may materially affect our business.

We place considerable importance on obtaining patent protection for new technologies, products and processes because our commercial success will depend, in large part, on obtaining patent protection for new technologies, products and processes, successfully defending these patents against third-party challenges and successfully enforcing our patents against third party competitors. To that end, we have acquired and will file applications for patents covering formulations containing or uses of Gimoti or our proprietary processes as well as other intellectual property important to our business. One of our patent families related to Gimoti was acquired from Questcor. The method of use patents in this patent family were not written by us or our attorneys, and we did not have control over the drafting and prosecution of these patents. Further, Questcor and other predecessors might not have given the same attention to the drafting and prosecution of these patents as we would have if we had been the owners of the patents and application and had control over the drafting and prosecution.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unresolved. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. In recent years patent rights have been the subject of significant litigation, in particular due to *inter partes* review, introduced by the America Invents Act of 2012, which allows for quicker patent challenges decided by the U.S. Patent and Trademark Office's Patent Trial and Appeal Board rather than a lay jury. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our predecessors were the first to make the inventions claimed in our owned and licensed patents or pending patent applications, or that we or our predecessors were the first to file for patent protection of such inventions One or more of these factors could possibly result in findings of invalidity or unenforceability of one or more of the patents we own.

The patent rights we own covering Gimoti are directed to specific methods of use and formulations of metoclopramide. As a result, our ability to prevent others from marketing products related to Gimoti may be limited by the lack of patent protection for the active ingredient itself and other metoclopramide formulations may be developed by competitors. The active ingredient in Gimoti is metoclopramide. No patent protection is available for metoclopramide itself. As a result, competitors who develop and receive required regulatory approval for competing products using the same active ingredient as Gimoti may market their competing products so long as they do not infringe any of the method or formulation patents owned by us.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours, or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we will not be involved in interference, opposition or invalidity proceedings before U.S. or foreign patent offices.

We have focused our intellectual property efforts on the United States. To the extent that our patent portfolio differs from country to country outside the United States, this may make protecting Gimoti as a product outside the United States even more difficult and unpredictable. Various countries maintain their own standards and interpretation of intellectual property law, potentially creating additional patent risk beyond even that experienced within the United States.

We also rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we require employees, consultants and other contractors to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information. Our research collaborators and scientific advisors may have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborators and advisors, our ability to receive patent protection or protect our proprietary information may be imperiled.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patent applications which may issue as patents that may be infringed by commercialization of Gimoti. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and would likely:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing Gimoti until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology; and/or
- require us to enter into royalty or licensing agreements.

Although no third party has asserted a claim of infringement against us, others may hold proprietary rights that could prevent Gimoti from being marketed. Any patent-related legal action against us claiming damages or seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and could require us to obtain a license to continue to manufacture or market Gimoti, or, if no such license were available on commercially viable terms, could require us to cease manufacturing and marketing of Gimoti. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing Gimoti, which could harm our business, financial condition and operating results. Whatever the outcome, any patent litigation would be costly and time consuming, could be distracting to our management, and could have a material adverse effect on our business.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is commonplace in our industry, we employ and consult with individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject in the future to claims that our employees or consultants are subject to a continuing obligation to their former employers or clients (such as non-competition or non-solicitation obligations) or claims that our employees, our consultants or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers or clients. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to Our Financial Position and Need for Capital

Our recurring losses from operations have raised substantial doubt regarding our ability to continue as a going concern.

Our recurring losses from operations raise substantial doubt about our ability to continue as a going concern, and as a result, our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements as of and for the year ended December 31, 2017 with respect to this uncertainty. This doubt about our ability to continue as a going concern could materially limit our ability to raise additional funds through the issuance of new debt or equity securities or otherwise. Future reports on our financial statements may also include an explanatory paragraph with respect to our ability to continue as a going concern. We have incurred significant losses since our inception and have never been profitable, and it is possible we will never achieve profitability. We have devoted our resources to developing Gimoti, but it cannot be marketed until regulatory approvals have been obtained. Based upon our currently expected level of operating expenditures, we expect to be able to fund our operations into October 2018. This period could be shortened if there are any significant increases in planned spending on our Gimoti development program than anticipated. There is no assurance that other financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

We have incurred significant operating losses since inception, and we expect to incur losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2007 and expect to incur significant losses for the next several years related to completing development for Gimoti, and seeking regulatory approval from FDA to manufacture and commercialize Gimoti. Our net loss for the year ended December 31, 2017, was approximately $12.3 million. As of December 31, 2017, we had an accumulated deficit of approximately $71.0 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses, especially since we became a public company in September 2013. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if Gimoti is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in our incurring further significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize Gimoti or other marketable drugs. As a result, there can be no assurance that we will ever generate revenues or achieve profitability, which could impair our ability to sustain operations or obtain any required additional funding. If we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize Gimoti.

We will require substantial additional future capital in order to finance any additional development activities for Gimoti, including any requirements requested by FDA, as well as for pre-commercial activities, including marketing and manufacturing of Gimoti. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the need for, and the progress, costs and results of, any additional clinical trials of Gimoti required by FDA, including any additional trials FDA or other regulatory agencies may require evaluating the safety of Gimoti;
- the outcome, costs and timing of seeking and obtaining regulatory approvals from FDA, and any similar regulatory agencies;
- the timing and costs associated with manufacturing Gimoti for clinical trials and other studies and, if approved, for commercial sale;
- our need and ability to hire additional management, development and scientific personnel;
- the cost to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the timing and costs associated with establishing sales and marketing capabilities;
- market acceptance of Gimoti;
- the extent to which we are required to pay milestone or other payments under our Mallinckrodt asset purchase agreement and the timing of such payments;
- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

Some of these factors are outside of our control. We cannot provide any assurance that our existing capital will be sufficient to enable us to fund any additional clinical development required for Gimoti, and, in any event, we will need to raise additional capital to complete such clinical development, as well as to prepare to commercialize Gimoti should we receive product approval. We may need to raise additional funds in the near future for commercialization for Gimoti.

We may seek additional funding through collaboration agreements, public or private equity financings, debt financings or receivables financings. For example, we currently may sell from time to time, at our option, up to an aggregate of $16.0 million of shares of our common stock through B. Riley FBR, or FBR, as sales agent pursuant to an At Market Issuance Sales Agreement, or the FBR Sales Agreement, with FBR. Sales pursuant to the FBR Sales Agreement are registered pursuant to a shelf registration statement on Form S-3 which was declared effective by the SEC on December 28, 2017. However, there can be no assurance that FBR will be successful in consummating future sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate.

Under current SEC regulations, at any time during which the aggregate market value of our common stock held by non-affiliates, or public float, is less than $75 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements, including sales under the FBR Sales Agreement, is limited to an aggregate of one-third of our public float. As of February 28, 2018, our public float was approximately $36.1 million which means we may only sell

approximately $12.0 million of securities using our shelf registration statements. If our public float decreases, the amount of securities we may sell under our Form S-3 shelf registration statement will also decrease. In addition, FBR is permitted to terminate the Sales Agreement in its sole discretion upon ten days' notice, or at any time in certain circumstances, including the occurrence of an event that would be reasonably likely to have a material adverse effect on our assets, business, operations, earnings, properties, condition (financial or otherwise), prospects, stockholders' equity or results of operations.

Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline and dilute the holdings of our existing stockholders. If we raise additional funds by incurring debt, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business.

If we are unable to obtain funding on a timely basis, if required, we will be unable to complete additional clinical development of Gimoti and may be required to significantly curtail all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidate or some of our technologies or otherwise agree to terms unfavorable to us.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and may be subject to further limitation as a result of the transactions completed in connection with our initial public offering.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. As a result of our most recent private placement and other transactions that have occurred over the past three years, we may have experienced an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2017, we had federal and state net operating loss carryforwards of approximately $61.9 million and $41.7 million, respectively, and federal research and development credits of approximately $2.0 million which could be limited if we experience an "ownership change." Furthermore, under recently enacted U.S. tax legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond may only offset 80% of our taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

Recently enacted U.S. tax legislation has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, adopting elements of a territorial tax system, imposing a one-time transition tax (or "repatriation tax") on all undistributed earnings and profits of certain U.S.-owned foreign corporations, revising the rules governing net operating losses and the rules governing foreign tax credits, and introducing new anti-base erosion provisions. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service ("IRS"), any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities.

While our analysis and interpretation of this legislation is ongoing, based on our current evaluation, we have reflected a write-down of our deferred income tax assets (including the value of our net operating loss carryforwards and our tax credit carryforwards) due the reduction of the U.S. corporate income tax rate. Based on currently available information, we recorded a reduction of approximately $7.9 million in the fourth quarter of 2017 related to the revaluation of our deferred tax assets, which did not result in additional tax expense in the quarter as our deferred tax assets have a full valuation allowance. This amount may be subject to further adjustment in subsequent periods throughout 2018 in accordance with subsequent interpretive guidance issued by the SEC or the IRS. Further, there may be other material adverse effects resulting from the legislation that we have not yet identified.

While some of the changes made by the tax legislation may adversely affect the Company in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation.

Risks Related to Ownership of Our Common Stock

An active trading market for our common stock may not develop or be sustained.

Prior to our initial public offering in September 2013, there was no public market for our common stock. An active trading market may never develop or be sustained. If an active trading market does not develop or is not sustained, it may be difficult to sell shares of our common stock at a price that is desirable or at all. In addition, an inactive market may impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration, which, in turn, could materially adversely affect our business. Since the commencement of trading in connection with our initial public offering in September 2013 through February 28, 2018, the sale price per share of our common stock on The Nasdaq Capital Market has ranged from a low of $1.35 to a high of $14.25.

The price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price at which they purchased the shares. The market price for our common stock may be influenced by many factors, including:

- regulatory developments in the United States and foreign countries, including a potential NDA submission;
- the timing, progress and results of any additional trials we may conduct, and the results of trials of our competitors or those of other companies in our market sector;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and 5% stockholders;
- trading volume of our common stock;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our Gimoti development program, including NDA preparation and pre-commercialization costs;
- addition or termination of clinical trials;

- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting Gimoti; and
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- permitting our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

We do not intend to pay dividends on our common stock and, consequently, the ability of our stockholders to achieve a return on their investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Persons who were our stockholders prior to the sale of shares in our initial public offering in September 2013 continue to hold a substantial number of shares of our common stock that they are able to sell in the public market, subject in some cases to certain legal restrictions. Significant portions of these shares are held by a small number of stockholders. Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

As of February 28, 2018, we had 15,493,368 shares of common stock outstanding. All of these shares are freely tradable without restriction in the public market, except for 2,555,192 shares that are held by directors, executive officers and other affiliates that are subject to volume limitations under Rule 144 under the Securities Act. In addition, shares of common stock that are either subject to

outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

As of February 28, 2018, the holders of 1,509,789 shares of our common stock are entitled to reasonable best efforts registration rights with respect to the registration of their shares under the Securities Act. In addition, holders of 84,000 shares of common stock issuable upon the exercise of warrants are also entitled to reasonable best efforts registration rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following 2013, the year in which we completed our initial public offering, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately. Unless we lose our status as an emerging growth company earlier, we will cease being an emerging growth company on December 31, 2018. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

We will continue to incur significant costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses under the Sarbanes-Oxley Act and the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as rules adopted by the SEC and The Nasdaq Stock Market. These rules impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls, changes in corporate governance practices, proxy access and "say on pay" votes. As an "emerging growth company," we are permitted to implement many of these requirements over a longer period of time. While we are taking advantage of this option to delay implementation, we cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies have substantially increased our legal and financial compliance costs and made some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult

and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We currently have limited research coverage by securities and industry analysts. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

If we fail to continue to meet all applicable Nasdaq Capital Market requirements and Nasdaq determines to delist our common stock, the delisting could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease.

Our common stock is listed on the Nasdaq Capital Market. In order to maintain our listing, we must meet minimum financial and other requirements, including requirements for a minimum amount of capital, a minimum price per share and continued business operations so that we are not characterized as a "public shell company." In the event that our common stock is delisted from the Nasdaq Capital Market and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. Also, it may be difficult for us to raise additional capital if we are not listed on a major exchange.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We occupy approximately 3,000 square feet of office space in Solana Beach, California under a lease that we entered into in December 2016. This facility lease expires in December 2018. We believe that our facility is adequate to meet our needs and that, if necessary, additional space can be leased to accommodate any future growth on commercially reasonable terms.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been traded on the Nasdaq Capital Market since September 25, 2013 under the symbol "EVOK." Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales price of our common stock, as reported by the Nasdaq Capital Market for the period indicated:

	High	Low
Year Ended December 31, 2017		
Fourth Quarter	$ 4.09	$ 2.20
Third Quarter	$ 3.69	$ 2.19
Second Quarter	$ 3.67	$ 2.40
First Quarter	$ 4.55	$ 1.87
Year Ended December 31, 2016		
Fourth Quarter	$ 2.52	$ 1.35
Third Quarter	$ 11.11	$ 1.52
Second Quarter	$ 7.15	$ 4.57
First Quarter	$ 5.48	$ 2.37

Holders of Common Stock

As of February 28, 2018, there were 17 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain available cash to finance ongoing operations and the potential growth of our business. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Unregistered Sales of Equity Securities

None.

Issuer Repurchases of Equity Securities

None.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Item 6. Selected Financial Data.

The following selected financial data should be read in conjunction with our financial statements and the related notes thereto appearing elsewhere in this Annual Report on Form 10-K and in the section of this Annual Report on Form 10-K entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations." We have derived the statements of operations data for the years ended December 31, 2017 and 2016 and the balance sheet data as of December 31, 2017 and 2016, from our audited financial statements appearing elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of the results to be expected in any future period.

	Year Ended December 31,	
	2017	2016
Statement of Operations Data:		
Research and development	$ 7,137,493	$ 6,951,600
General and administrative	$ 4,093,189	$ 3,592,825
Change in fair value of warrant liability	$ 1,005,349	$ (597,615)
Net loss	$ (12,229,512)	$ (10,544,425)
Net loss per common share, basic(1)	$ (0.82)	$ (1.15)
Net loss per common share, diluted(1)	$ (0.90)	$ (1.15)
Weighted-average shares outstanding, basic	14,897,885	9,338,068
Weighted-average shares outstanding, diluted	14,951,036	9,338,068

(1) See Note 2 to our audited financial statements included elsewhere in this Annual Report on Form 10-K for an explanation of the method used to calculate the historical net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

	As of December 31,	
	2017	2016
Balance Sheet Data:		
Cash and cash equivalents	$ 7,679,267	$ 9,007,071
Working capital	$ 5,855,476	$ 7,871,106
Total assets	$ 7,941,864	$ 9,294,330
Current liabilities	$ 2,074,838	$ 1,411,673
Warrant liability	$ 3,701,279	$ 4,095,019
Accumulated deficit	$ (71,038,655)	$ (58,809,143)
Total stockholders' equity	$ 2,165,749	$ 3,787,638

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including, but not limited to, those set forth under "Risk Factors" under Item 1A of Part I of this Annual Report on Form 10-K and elsewhere in this Annual Report on Form 10-K.

Overview

We are a specialty pharmaceutical company focused primarily on the development of drugs to treat gastrointestinal, or GI, disorders and diseases. We are developing Gimoti, an investigational metoclopramide nasal spray for the relief of symptoms associated with acute and recurrent diabetic gastroparesis in women. Diabetic gastroparesis is a GI disorder afflicting millions of people worldwide and is characterized by slow or delayed gastric emptying and evidence of gastric retention in the absence of mechanical obstruction and can cause various serious digestive system symptoms and other complications. Metoclopramide tablets and injection are the only products currently approved in the United States to treat the symptoms associated with acute and recurrent diabetic gastroparesis. Gimoti is a novel nasal spray formulation of metoclopramide and designed to provide systemic delivery of the molecule through the nasal mucosa.

In July 2016, we announced results from a Phase 3 clinical trial of Gimoti in female subjects with symptoms associated with acute and recurrent diabetic gastroparesis. The trial was a multicenter, randomized, double-blind, placebo-controlled, parallel group clinical trial to evaluate the efficacy, safety and population pharmacokinetics, or PK, of 10 mg Gimoti in adult female subjects with symptomatic diabetic gastroparesis and delayed gastric emptying scintigraphy, or GES. Subjects received either Gimoti or placebo four times daily for 28 days. The primary endpoint was the change in symptoms from the baseline period to Week 4 as measured using a proprietary Patient Reported Outcome, or PRO, instrument. On a daily basis, subjects reported the frequency and severity of their gastroparesis signs and symptoms using a telephone diary. The subjects' daily symptom scores were the basis for calculating their weekly scores using the PRO instrument. A total of 205 subjects were randomized in this trial. Results of the trial showed that Gimoti did not achieve its primary endpoint of a symptom improvement at Week 4 in the intent to treat, or ITT, population.

Although the Phase 3 trial failed to achieve its primary endpoint, Gimoti demonstrated efficacy in patients with moderate to severe symptoms at baseline, which included 105 of the 205 patients (51%) enrolled in the study. In these patients with higher symptom severity, statistically significant benefits were demonstrated for those treated with Gimoti versus those receiving placebo. These statistically significant benefits were observed at Weeks 1, 2 and 3 in the ITT population and at all four weeks in the per protocol population. There were also clinically and statistically significant improvements in nausea and upper abdominal pain, two of the more severe and debilitating symptoms of gastroparesis, at all four weeks.

We have also conducted a companion clinical trial with Gimoti in male subjects with symptoms associated with acute and recurrent diabetic gastroparesis to assess the safety and efficacy of Gimoti in men. The male companion trial was initiated in May 2014 and the design was the same as the Phase 3 trial in women. This trial was requested by FDA to confirm the Phase 2b trial results and to capture additional safety data in men. This trial was not required for submission of the Gimoti NDA for women; however, we expect to include safety data from this trial in the NDA submission. As we anticipated at the beginning of the trial, based on the prior Phase 2b data, the results of the trial showed no statistical significant efficacy in men and the safety profile for Gimoti was favorable compared to placebo with good tolerability.

In December 2016, we had another pre-new drug application, or pre-NDA, meeting with FDA, in which FDA agreed that a comparative exposure PK trial was acceptable as a basis for submission of a Gimoti NDA. In March 2017, we had a type A meeting with FDA to finalize the design of the comparative exposure PK trial and reach agreement on certain other chemistry, manufacturing and controls-related items associated with the proposed NDA submission.

In October 2017, we announced positive topline results from the comparative exposure PK trial. The objective of the trial was to identify a dose of Gimoti that met the criteria for bioequivalence compared to the Reglan Tablets after nasal and oral administration to healthy volunteers under fasted conditions.

The comparative exposure PK trial was an open label, 4-way crossover and enrolled 108 healthy male and female volunteers who each received one Reglan Tablet dose and three different doses of Gimoti in a random sequence. Following discussions at pre-NDA meetings with FDA, we planned to select a Gimoti dose based on criteria that includes a 90% confidence interval for the ratio of area under the plasma concentration curve, or AUC, falling within the exposure equivalence range of 80-125% of Reglan Tablets. Though only one dose was needed to meet the dose selection criteria, the comparative exposure PK trial was designed to test three different strengths of Gimoti. Based on results of the study, two of the three doses tested met the dose selection criteria for the pooled data in women and men. The maximum observed plasma concentration, or C_{max}, for Gimoti was slightly lower than the equivalence range, but was anticipated and had been previously discussed with FDA as a likely outcome given the different route of administration and prior Gimoti PK trial results. Additionally, data showed the AUC and C_{max} increased in a dose related manner across all three strengths tested. Relative to safety, all Gimoti doses were well tolerated with no clinically significant adverse events reported following any of the doses.

Additional analysis of the PK data by sex revealed statistically significant differences in exposure between women and men given the same metoclopramide dose (nasal and oral). Based on this further analysis of results from the comparative exposure PK trial, statistically significantly lower AUC's were found in men compared to women. The findings were not explicitly attributable to differences in body mass index, or BMI, or weight. Similarly sex-based differences were observed in a previous healthy volunteer study we conducted, irrespective of the route of metoclopramide administration (nasal, oral and IV).

In the most recent comparative exposure PK trial, results for women independently met equivalence criteria for $AUC_{0\text{-}inf}$ and $AUC_{0\text{-}t}$ at the tested Gimoti dose to be proposed in the NDA. We plan to submit our NDA for a female-only indication based on a dose in women with equivalent exposure to Reglan Tablets and will submit supporting efficacy and safety data from our Phase 2b and Phase 3 trials, specifically for women, at doses similar or lower than the dose to be proposed in the NDA.

In parallel, we recently held a pre-NDA meeting with FDA to discuss and clarify its expectations of items being prepared for inclusion in the NDA for Gimoti. The planned NDA will include our proposal for a risk management strategy and a post-approval safety study that will be designed to confirm prior safety findings and rule-out possible differences in side effects compared to the Reglan Tablet over 8 weeks. We expect to discuss the details of the post-marketing safety trial with FDA during the NDA review process. With the new sex-based PK findings, and to incorporate the feedback received by FDA at the most recent pre-NDA meeting, we expect to file the Gimoti NDA in the second quarter of 2018.

In March 2018, we announced that FDA granted the Company's request for a small business waiver of the Prescription Drug User Fee Act, or PDUFA, fee of approximately $2.4 million for its 505(b)(2) NDA for Gimoti.

We have no products approved for sale, and we have not generated any revenue from product sales or other arrangements. We have primarily funded our operations through the sale of our convertible preferred stock prior to our initial public offering in September 2013, borrowings under our bank loans and the sale of shares of our common stock on the Nasdaq Capital Market. We have incurred losses in each year since our inception. Substantially all of our operating losses resulted from expenses incurred in connection with advancing Gimoti through development activities and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We may never become profitable, or if we do, we may not be able to sustain profitability on a recurring basis.

As of December 31, 2017 we had cash and cash equivalents of approximately $7.7 million. We believe our existing cash and cash equivalents will be sufficient to fund our operations into October 2018. Current funds on hand are intended to fund pre-approval and pre-commercialization activities for Gimoti, including the planned NDA submission, and for working capital and general corporate purposes.

Technology Acquisition Agreement

In June 2007, we acquired all worldwide rights, data, patents and other related assets associated with Gimoti from Questcor Pharmaceuticals, Inc., or Questcor, pursuant to an asset purchase agreement. We paid Questcor $650,000 in the form of an upfront payment and $500,000 in May 2014 as a milestone payment based upon the initiation of the first patient dosing in our Phase 3 clinical trial for Gimoti. In August 2014, Mallinckrodt, plc, acquired Questcor. As a result of that acquisition, Questcor transferred its rights included in the asset purchase agreement with us to Mallinckrodt. In addition to the payments we made to Questcor, we may also be required to make additional milestone payments to Mallinckrodt totaling up to $51.5 million. These milestones include up to $4.5 million in payments if Gimoti achieves the following development targets:

- $1.5 million upon FDA's acceptance for review of an NDA for Gimoti; and
- $3 million upon FDA's approval of Gimoti.

The remaining $47 million in milestone payments depend on Gimoti's commercial success and will only apply if Gimoti receives regulatory approval. In addition, we will be required to pay to Mallinckrodt a low single digit royalty on net sales of Gimoti. Our

obligation to pay such royalties will terminate upon the expiration of the last patent right covering Gimoti, which is expected to occur in 2030.

Financial Operations Overview

Research and Development Expenses

We expense all research and development expenses as they are incurred. Research and development expenses primarily include:

- clinical trial and regulatory-related costs;
- expenses incurred under agreements with CROs, investigative sites and consultants that conduct our clinical trials;
- manufacturing and stability testing costs and related supplies and materials; and
- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense.

All of our research and development expenses to date have been incurred in connection with Gimoti. The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We are unable to estimate with any certainty the costs we will incur in the continued development of Gimoti. Clinical development timelines, the probability of success and development costs can differ materially from expectations. We may never succeed in achieving marketing approval for our product candidate.

The costs of clinical trials may vary significantly over the life of a project owing to, but not limited to, the following:

- per patient trial costs;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible subjects;
- the number of subjects that participate in the trials;
- the number of doses that subjects receive;
- the cost of comparative agents used in trials;
- the drop-out or discontinuation rates of subjects;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profile of the product candidate.

We do not yet know when Gimoti may be commercially available, if at all.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation. Other general and administrative expenses include professional fees for accounting, tax, patent costs, legal services, insurance, facility costs and costs associated with being a publicly-traded company, including fees associated with investor relations and directors and officers liability insurance premiums. We expect that general and administrative expenses will increase in the future as we expand our operating activities, prepare for the growth needs associated with commercialization and continue to incur additional costs associated with being a publicly-traded company and maintaining compliance with exchange listing and Securities and Exchange Commission requirements. These increases will likely include higher consulting costs, legal fees, accounting fees, directors' and officers' liability insurance premiums and fees associated with investor relations.

Other Expenses

Other expenses consist of changes in the fair value of the warrant liability, which represents the change in the fair value of common stock warrants from the date of issuance to the end of the reporting period. The warrant liability will be revalued each reporting period until the liability is settled. We use the Black Scholes valuation model to value the related warrant liability. In addition, costs associated with the issuance of common stock warrants were recorded as other expense upon issuance. Other expense also consists of interest expense incurred on our former outstanding debt.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing financial statements, we are required to estimate and accrue expenses, the largest of which are research and development expenses. This process involves the following:

- communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in our financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to CMOs in connection with the production of clinical study materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of subjects, site initiation and the completion of clinical study milestones. Our service providers invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ materially from our estimates. To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

Warrant Accounting

Certain of the warrants to purchase shares of our common stock, issued as a part of our registered direct offerings in July and August 2016, are classified as warrant liability and recorded at fair value. These warrants contain a feature that could require the transfer of cash in the event a change of control occurs without the authorization of our Board of Directors, and therefore, are classified as a liability in accordance with the Financial Accounting Standards Board Accounting Standards Codification 480.

The fair value of each warrant is estimated on the date of issuance, and each subsequent balance sheet date, using the Black-Scholes valuation model using the appropriate risk-free interest rate, expected term and volatility assumptions. The expected life of the warrants were calculated using the remaining life of the warrant. Due to our limited historical data as a public company, the estimated volatility is calculated based upon our historical volatility and comparable companies whose share prices are publicly available for a sufficient period of time. The risk-free rate is based upon U.S. Treasury securities with remaining terms similar to the expected term of the stock award being valued.

This warrant liability is subject to remeasurement at each balance sheet date and we recognize any change in the fair value of the warrant liability in the statement of operations. We will continue to adjust the carrying value of the warrants for changes in the estimated fair value until the earlier of the modification, exercise or expiration of the warrants. At that time, the liabilities will be reclassified to additional paid-in capital, a component of stockholders' equity. We anticipate that the value of the warrants could fluctuate from quarter to quarter and that such fluctuation could have a material impact on our financial statements from quarter to quarter and year to year.

Stock-Based Compensation

Stock-based compensation expense is recorded at the estimated fair value of the award as of the grant date and is recognized as expense on a straight-line basis over the employee's requisite service period, which is generally the vesting period of the award. Stock-based compensation expense is based on awards ultimately expected to vest, and therefore, the recorded expense includes an estimate of future forfeitures. Forfeitures are to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Prior to our initial public offering, or IPO, in September 2013, we granted stock options to purchase common stock to employees with exercise prices equal to the value of the underlying stock, as determined by the board of directors on the date the equity award was granted. The board of directors determined the fair value of the underlying common stock by considering a number of factors, including historical and projected financial results, the risks we faced at the time, the preferences of our preferred stockholders and the lack of liquidity of our common stock. Subsequent to the IPO, the exercise price of the stock options granted to our employees and members of our board of directors was determined by the closing market price of our stock on the date the stock options were granted.

The fair value of each option award is estimated on the date of grant using the Black-Scholes valuation model using the appropriate risk-free interest rate, expected term and volatility assumptions. The expected life of options was calculated using the simplified method, which calculates the life as the average of the contractual term of the stock option and the vesting period of the option. Due to our limited historical data as a public company, the estimated volatility is calculated based upon our historical volatility and comparable companies whose share prices are publicly available for a sufficient period of time. The risk-free interest rate is based upon U.S. Treasury securities with remaining terms similar to the expected term of the stock award being valued. We granted options to purchase 856,000 and 414,000 shares of common stock in 2017 and 2016, respectively.

In February 2016, we effected a one-time option exchange, wherein employees were offered the opportunity to exchange certain outstanding stock options for the grant of a lesser number of replacement stock options. The participants received three new stock options for every four stock options tendered for exchange. As a result, 703,500 stock options were exchanged for 527,625 replacement stock options. The replacement stock options have a three-year vesting schedule and an exercise price of $3.04 per share, which was the closing price of our common stock on the date of the option exchange. All other terms of the replacement stock options remain the same as the original stock options that were exchanged.

Other Information

Tax Cuts and Jobs Act

On December 22, 2017, President Trump signed into law the tax legislation commonly known as the Tax Cuts and Jobs Act, or the Act. The effects of the new federal legislation are recognized upon enactment, which is the date the president signs a bill into law. The Act includes numerous changes in existing tax law, including a permanent reduction in the federal corporate income tax rate from 35% to 21%. The rate reduction takes effect on January 1, 2018. As a result of this rate change, we have revalued our deferred tax assets at December 31, 2017. Deferred income taxes result from temporary differences between the tax basis of assets and liabilities and their reported amounts in the financial statements that will result in taxable or deductible amounts in future years. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in years in which those temporary differences are expected to be recovered or settled. As changes in tax laws or rates are enacted, deferred tax assets and liabilities are adjusted through income tax expense. Based on currently available information, we recorded a reduction of approximately $7.9 million in the fourth quarter of 2017 related to the revaluation of our deferred tax assets, which did not result in additional tax expense in the quarter as our deferred tax assets have a full valuation allowance. This amount may be subject to further adjustment in subsequent periods throughout 2018 in accordance with subsequent interpretive guidance issued by the SEC or the IRS. Further, there may be other material adverse effects resulting from the legislation that we have not yet identified.

Net Operating Loss Carryforwards

As of December 31, 2017, we had federal and California tax net operating loss carryforwards of approximately $61.9 million and $41.7 million, respectively. The federal and California net loss carryforwards will begin to expire in 2027 and 2017, respectively, unless previously utilized. As of December 31, 2017, we also had federal and California research and development tax credit carryforwards of $2.0 million and $1.2 million, respectively. The federal research and development tax credit carryforwards will begin to expire in 2027 unless previously utilized. The California research and development tax credit will carry forward indefinitely.

Furthermore, under recently enacted U.S. tax legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond may only offset 80% of our taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not completed our analysis to determine what, if any, impact any prior ownership change has had on our ability to utilize our net operating loss carryforwards.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company," we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an "emerging growth company" until the earliest of (a) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (b) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering, or IPO, (c) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years or (d) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. Unless we lose our status as an emerging growth company earlier, we will cease being an emerging growth company on December 31, 2018.

Results of Operations

Comparison of Years Ended December 31, 2017 and 2016

The following table summarizes the results of our operations for the fiscal years ended December 31, 2017 and 2016:

	Year Ended December 31,		Increase/
	2017	2016	(Decrease)
Research and development	$ 7,137,493	$ 6,951,600	$ 185,893
General and administrative	$ 4,093,189	$ 3,592,825	$ 500,364
Other expense	$ 998,830	$ 204,106	$ 794,724

Research and Development Expenses. Research and development expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 increased by approximately $186,000. During 2017, we prepared for and conducted our comparative exposure PK trial, which included product development activities and manufacturing Gimoti for such trial. In addition, we continued our work related to the preparation of an NDA. Costs incurred in 2017 included approximately $2.5 million for wages, taxes and employee insurance, including approximately $820,000 of stock-based compensation expense, approximately $2.2 million of clinical trial costs, approximately $1.4 million related to manufacturing costs and approximately $1 million related to costs associated with the preparation of the NDA. Costs incurred in 2016 included approximately $3.7 million related to conducting and analyzing data related to the Phase 3 clinical trials, approximately $2.3 million for wages, taxes and employee insurance, including approximately $698,000 of stock-based compensation expense, and approximately $860,000 related to costs associated with the preparation of an NDA.

General and Administrative Expenses. General and administrative expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 increased by approximately $500,000. Costs incurred in 2017 primarily included approximately $2.0 million for wages, taxes and employee insurance, including approximately $1.0 million of stock-based compensation expense, and approximately $1.6 million for legal, accounting, directors and officers liability insurance and other costs associated with being a public company. Costs incurred in 2016 primarily included approximately $1.9 million for wages, taxes and employee insurance, including approximately $1.0 million of stock-based compensation expense, and approximately $1.4 million for legal, accounting, directors and officers liability insurance and other costs associated with being a public company.

Other Expenses. Other expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 increased by approximately $795,000. In 2017, the change in fair value of warrant liability resulted in an expense of approximately $1 million. The warrant liability is subject to remeasurement at each reporting period and we recognize any change in the fair value of the warrant liability in the statement of operations. We anticipate that the value of the warrants could fluctuate from quarter to quarter and that such fluctuation could have a material impact on our financial statements from quarter to quarter and year to year. Other expenses for the year ended December 31, 2016, included an expense of approximately $534,000 related to equity financings and approximately $268,000 of interest expense incurred on our former outstanding debt with Square 1. These expenses were offset by approximately $598,000 in income from the change in the fair value of the warrant liability.

Liquidity and Capital Resources

Since our inception in 2007, we have funded our operations primarily from the sale of equity securities and borrowings under loan and security agreements. Prior to our IPO, we received $17.7 million in net proceeds from the sale of our Series A convertible preferred stock and advances of $5.5 million under the loan and security agreements. During 2013, we completed our IPO and raised approximately $25.1 million, net of offering costs and commissions.

In April 2016, we entered into an At Market Issuance Sales Agreement, or the FBR Sales Agreement, with B. Riley FBR, Inc. (as successor by merger to FBR Capital Markets & Co.), or FBR, and filed a prospectus supplement, pursuant to which we may sell from time to time, at our option up to an aggregate of 649,074 shares of our common stock through FBR as the sales agent. Through December 31, 2016, we sold 56,000 shares of common stock and received net proceeds of approximately $296,000 under the FBR Sales Agreement.

In November 2017, we filed a new shelf registration statement with the SEC on Form S-3, or the replacement shelf registration statement. The replacement shelf registration statement replaced the registration statement on Form S-3 we originally filed with the SEC on November 13, 2014, which registration statement expired in November, 2017. The replacement shelf registration was declared effective by the SEC in December 2017. In November 2017, we also entered into an amendment, or the Amendment, to the FBR Sales Agreement, pursuant to which we may sell from time to time, at our option, up to an aggregate of $16 million worth of shares of our common stock through FBR, as sales agent. The Amendment provides, among other things, that sales under the FBR Sales Agreement will be made pursuant to the replacement registration statement, including the base prospectus filed as part of such registration statement. The SEC declared this registration statement effective on December 28, 2017.

Future sales under the FBR Sales Agreement will depend on a variety of factors including, but not limited to, market conditions, the trading price of our common stock and our capital needs. There can be no assurance that FBR will be successful in consummating future sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate.

We will not be able to make future sales of our common stock pursuant to the FBR Sales Agreement unless certain conditions are met, which include the accuracy of representations and warranties made to FBR under the FBR Sales Agreement. Furthermore, FBR is permitted to terminate the FBR Sales Agreement in its sole discretion upon ten days' notice, or at any time in certain circumstances, including the occurrence of an event that would be reasonably likely to have a material adverse effect on our assets, business, operations, earnings, properties, condition (financial or otherwise), prospects, stockholders' equity or results of operations. We have no obligation to sell the remaining shares available for sale pursuant to the FBR Sales Agreement. However, under current SEC regulations, at any time during which the aggregate market value of our common stock held by non-affiliates, or public float, is less than $75 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements, including sales under the FBR Sales Agreement, is limited to an aggregate of one-third of our public float. As of February 28, 2018, our public float was approximately $36.1 million, which means we may only sell approximately $12.0 million of securities using shelf registration statements. We have sold 79,758 shares of common stock at a weighted average price of $2.08 per share under the baby shelf rules in the twelve-month period ended February 28, 2018 and have received approximately $160,000, net of commissions and fees. The Company currently has the capacity to issue up to approximately $11.9 million worth of additional shares of common stock pursuant to the FBR Sales Agreement. If our public float decreases, the amount of securities we may sell under our Form S-3 shelf registration statements will also decrease.

In July 2016, we completed an at-the-market offering of 1,804,512 shares of common stock at a purchase price of $2.49375 per share, or the July 2016 Financing. Concurrently in a private placement, for each share of common stock purchased by an investor, such investor received an unregistered warrant to purchase three-quarters of a share of our common stock, for a total of 1,353,384 shares, or the July Warrants. The July Warrants have an exercise price of $2.41 per share, are immediately exercisable and will expire on January 25, 2022. The aggregate gross proceeds from the sale of the common stock and warrants were $4.5 million, and the net proceeds after deduction of commissions and fees were approximately $4.0 million.

In connection with the July 2016 Financing, we issued to our placement agent, Rodman & Renshaw, a unit of H.C. Wainwright & Co. LLC, or Wainwright, and its designees unregistered warrants to purchase an aggregate of 90,226 share of our common stock, or the

July Wainwright Warrants. The July Wainwright Warrants have substantially the same terms as the July Warrants, except that the July Wainwright Warrants will expire on July 21, 2021 and have an exercise price equal to $3.1172 per share of common stock.

In August 2016, we completed an at-the-market offering of 3,244,120 shares of common stock at a purchase price of $3.0825 per share, the August 2016 Financing. Concurrently in a private placement, for each share of common stock purchased by an investor, such investor received from an unregistered warrant to purchase one half of a share of our common stock, for a total of 1,622,060 shares, or August Warrants. The August Warrants have an exercise price of $3.03 per share, are immediately exercisable and will expire on February 3, 2022. The aggregate gross proceeds from the sale of the common stock and warrants were $10.0 million, and the net proceeds after deduction of commissions and fees were approximately $9.2 million.

In connection with the August 2016 Financing, we issued to our placement agent, Wainwright, and its designees unregistered warrants to purchase an aggregate of 162,206 shares of our common stock, or the August Wainwright Warrants. The August Wainwright Warrants have substantially the same terms as the August Warrants, except that the August Wainwright Warrants will expire on July 29, 2021 and have an exercise price equal to $3.853125 per share of common stock.

In February 2017, an institutional investor from our July 2016 financing converted its warrant to purchase 526,315 shares of our common stock by a "cashless" exercise and received 211,860 shares of our common stock. The warrant had an exercise price of $2.41 per share. The shares were issued, and the warrants were sold, in reliance upon the registration exemption set forth in Section 4(a)(2) of the Securities Act of 1933, as amended. The value of the exercised warrants were adjusted to their fair value immediately prior to the exercise and approximately $1.4 million was reclassified from warrant liability to Additional Paid-in Capital. Subsequent to this transaction, warrants to purchase 2,449,129 shares of our common stock remain classified as a liability.

In February and March 2017, we completed the sale of 2,775,861 shares of our common stock in an underwritten public offering led by Laidlaw & Company (UK) Ltd. The price to the public in this offering was $2.90 per share resulting in gross proceeds to us of approximately $8.0 million. After deducting underwriting discounts and commissions, and offering expenses paid by us, the net proceeds to us from this offering was approximately $7.3 million.

In August 2016, we repaid in full the entire $4.5 million of outstanding principal and interest under the Loan and Security Agreement, dated as of May 28, 2014, as amended, or the Loan Agreement, between us and Square 1. In connection with such repayment, the Loan Agreement was terminated, and all security, liens or other encumbrances on assets of ours were released.

We incurred $82,685 of loan origination costs related to this credit facility. The remaining unamortized costs of approximately $38,000 were charged to interest expense upon the payment of the loan in August 2016.

In connection with the funding of the term loan, we issued to Square 1 a warrant to purchase 22,881 shares of our common stock at an exercise price of $5.90 per share, the closing price of our common stock on the day of funding of the credit facility. During July 2016, Square 1 converted its warrant by a "cashless" conversion and received 9,887 shares of our common stock. The value determined for the warrant at the time of the grant of $108,122 was recorded as a debt discount, as well as to stockholders' equity. The remaining unamortized debt discount associated with the warrant of approximately $59,000 was charged to interest expense upon the payment of the loan in August 2016.

Our independent registered public accounting firm included an explanatory paragraph in their report on our financial statements as of and for the year ended December 31, 2017 with respect to our ability to continue as a going concern. This doubt about our ability to continue as a going concern could materially limit our ability to raise additional funds through the issuance of new debt or equity securities or otherwise. Future reports on our financial statements may also include an explanatory paragraph with respect to our ability to continue as a going concern. We have incurred significant losses since our inception and have never been profitable, and it is possible we will never achieve profitability. We have devoted our resources to developing Gimoti, but it cannot be marketed until regulatory approvals have been obtained. Based upon our currently expected level of operating expenditures, we expect to be able to fund our operations into October 2018. This period could be shortened if there are any significant increases in planned spending on our Gimoti development program, pre-approval and pre-commercialization activities, including marketing and manufacturing of Gimoti, completion of a planned NDA submission, and our general and administrative costs to support operations. There is no assurance that other financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

We expect to continue to incur expenses and increase operating losses for at least the next several years. In the near-term, we anticipate incurring costs as we:

- continue the pre-approval and pre-commercialization activities for Gimoti, including the preparation of the NDA;
- prepare for and complete further clinical development, if necessary;

- continue the preparation of the commercial manufacturing process;
- maintain, expand and protect our intellectual property portfolio; and
- continue to fund the additional accounting, legal, insurance and other costs associated with being a public company.

Although our current cash and cash equivalents are expected to be sufficient to fund our operations into October 2018, it may not be sufficient to complete any additional development requirements requested by FDA. Accordingly, we will continue to require substantial additional capital beyond our current cash and cash equivalents to continue our clinical and regulatory development and potential commercialization activities. The amount and timing of our future funding requirements will depend on many factors further described below, including the costs associated with completing and submitting the Gimoti NDA and the extent of any additional clinical development required by FDA. We anticipate that we will seek to fund our operations through public or private equity, debt financings or other sources, such as potential collaboration arrangements. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategies.

The following table summarizes our cash flows for the year ended December 31, 2017 and 2016:

	Year Ended December 31,	
	2017	2016
Net cash used in operating activities	$ (8,716,905)	$ (8,707,742)
Net cash provided by financing activities	$ 7,389,101	$ 9,023,658
Net increase (decrease) in cash and cash equivalents	$ (1,327,804)	$ 315,916

Operating Activities. The primary use of our cash has been to fund our clinical research and other general operations. The cash used in operating activities during 2017 was primarily related to preparing for and conducting our comparative exposure PK clinical trial, analyzing the data from that trial, the manufacture of Gimoti for such trial, and the preparation of our NDA. We expect that cash used in operating activities will continue in 2018 related to the completion and filing of the NDA, as well as to pre-approval and pre-commercialization activities.

Financing Activities. During the year ended December 31, 2017, we received net proceeds of approximately $7.3 million from the sale of 2,775,861 shares of common stock in an underwritten public offering. In addition, we received proceeds of approximately $135,000 from the sale of 75,529 shares of common stock through our employee stock purchase plan, or ESPP. During the year ended December 31, 2016, we received net proceeds of approximately $13.2 million from the sale of 5,048,632 shares of common stock and 2,975,444 warrants to purchase our common stock. In addition, we received net proceeds of approximately $355,000 from the sale of 56,000 shares of common stock pursuant to the FBR Sales Agreement and the sale of 34,067 shares of common stock through our ESPP. These net proceeds from the sales of common stock were offset by the repayment of the $4.5 million Square 1 loan.

We believe that our existing cash and cash equivalents as of December 31, 2017, together with interest thereon, will be sufficient to meet our anticipated cash requirements into October 2018. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

The amount and timing of our future funding requirements will depend on many factors, including but not limited to:

- we may not have sufficient financial and other resources to complete clinical development for Gimoti;
- we may not be able to provide acceptable evidence of safety and efficacy for Gimoti;
- FDA may disagree with the design of our future clinical trials, if any are necessary;
- variability in subjects, adjustments to clinical trial procedures and inclusion of additional clinical trial sites;
- FDA may not agree with the analysis of our clinical trial results;
- the results of our clinical trials may not meet the level of statistical or clinical significance or other bioequivalence parameters required by FDA for marketing approval;
- we may be required to undertake additional clinical trials and other studies of Gimoti before we can submit an NDA, to FDA or receive approval of the NDA;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to Gimoti, such as dysgeusia, headache, diarrhea, nasal discomfort, tremor, myoclonus, somnolence, rhinorrhea, throat irritation, and fatigue;
- if approved, Gimoti will compete with well-established products already approved for marketing by FDA, including oral and intravenous forms of metoclopramide, the same active ingredient in the nasal spray for Gimoti;

- we may not be able to obtain, maintain and enforce our patents and other intellectual property rights; and
- we may not be able to establish commercial-scale manufacturing capabilities.

Off-Balance Sheet Arrangements

Through December 31, 2017, we have not entered into and did not have any relationships with unconsolidated entities or financial collaborations, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purpose.

Contractual Obligations and Commitments

In December 2016, we entered into an operating lease for office space in Solana Beach, California. The lease commenced on January 1, 2017 with an expiration date of December 31, 2018. We also pay pass through costs and utility costs, which are expensed as incurred.

As of December 31, 2017, future minimum lease payments for our facility lease are approximately $139,000 for the year ending December 31, 2018.

Item 7A. Quantitative and Qualitative Disclosure about Market Risk

Interest Rate Fluctuation Risk

Our cash and cash equivalents as of December 31, 2017 consisted of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of our cash and cash equivalents, a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operations.

Foreign Currency Exchange Risk

We contract with organizations to manufacture drug product, active pharmaceutical ingredient, and container closure system materials, and in the future may contract with CROs and investigational sites in foreign countries. We may become subject to fluctuations in foreign currency rates in connection with these agreements, though we do not believe such fluctuations will have a material impact to our operations.

Inflation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our business, financial condition or results of operations during the years ended December 31, 2017 and 2016.

Item 8. Financial Statements and Supplementary Data

Our financial statements and the report of our independent registered public accounting firm are included in this report on the pages indicated in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Business Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential

future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As required by Securities and Exchange Commission Rule 13a-15(b), as of December 31, 2017 we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Business Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Business Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2017.

Management's Report on Internal Control Over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Business Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that: (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Business Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled "Internal Control — Integrated Framework (2013 Framework)" published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2017, the end of our most recent fiscal year.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the quarter ended December 31, 2017 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2018 Annual Meeting of Stockholders, or the Definitive Proxy Statement, and which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2017, under the headings "Election of Directors," "Corporate Governance and Other Matters," "Executive Officers," and "Section 16(a) Beneficial Ownership Reporting Compliance," and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our internet website at www.evokepharma.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a "code of ethics" within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation

Information required by this item will be contained in our Definitive Proxy Statement under the heading "Executive Compensation and Other Information" and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Information required by this item will be contained in our Definitive Proxy Statement under the headings "Security Ownership of Certain Beneficial Owners and Management" and is incorporated herein by reference.

Item 13. Certain Relationships, Related Transactions and Director Independence

Information required by this item will be contained in our Definitive Proxy Statement under the headings "Certain Relationships and Related Party Transactions" and "Independence of the Board of Directors" and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Information required by this item will be contained in our Definitive Proxy Statement under the heading "Independent Registered Public Accounting Firm's Fees" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) *Documents filed as part of this report.*

1. *Financial Statements.* The following financial statements of Evoke Pharma, Inc., together with the report thereon of BDO USA, LLP, an independent registered public accounting firm, are included in this Annual Report on Form 10-K:

2. *Financial Statement Schedules.*

None.

3. *Exhibits.*

A list of exhibits to this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding the signature page and is incorporated herein by reference.

(b) See Exhibit Index.

(c) See Item 15(a)(2) above.

Item 16. Form 10-K Summary

None.

Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Evoke Pharma, Inc.
Solana Beach, CA

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Evoke Pharma, Inc. (the "Company") as of December 31, 2017 and 2016, the related statements of operations, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

Going Concern Uncertainty

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2014.

San Diego, California

March 7, 2018

Evoke Pharma, Inc.

Balance Sheets

	December 31,	
	2017	**2016**
Assets		
Current Assets:		
Cash and cash equivalents	$ 7,679,267	$ 9,007,071
Prepaid expenses	251,046	267,711
Other current assets	—	7,997
Total current assets	7,930,313	9,282,779
Other assets	11,551	11,551
Total assets	$ 7,941,864	$ 9,294,330
Liabilities and stockholders' equity		
Current Liabilities:		
Accounts payable and accrued expenses	$ 1,048,927	$ 478,223
Accrued compensation	1,025,911	933,450
Total current liabilities	2,074,838	1,411,673
Warrant liability	3,701,277	4,095,019
Total liabilities	5,776,115	5,506,692
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; authorized shares — 5,000,000 at December 31, 2017 and 2016; issued and outstanding shares — 0 at December 31, 2017 and 2016	—	—
Common stock, $0.0001 par value; authorized shares — 50,000,000 at December 31, 2017 and 2016; issued and outstanding shares — 15,413,610 and 12,350,360 at December 31, 2017 and 2016, respectively	1,541	1,235
Additional paid-in capital	73,202,863	62,595,546
Accumulated deficit	(71,038,655)	(58,809,143)
Total stockholders' equity	2,165,749	3,787,638
Total liabilities and stockholders' equity	$ 7,941,864	$ 9,294,330

See accompanying notes.

Evoke Pharma, Inc.

Statements of Operations

	Year Ended December 31,	
	2017	**2016**
Operating expenses:		
Research and development	$ 7,137,493	$ 6,951,600
General and administrative	4,093,189	3,592,825
Total operating expenses	11,230,682	10,544,425
Loss from operations	(11,230,682)	(10,544,425)
Other income (expense):		
Interest income (expense), net	6,519	(268,029)
Financing costs related to warrant liability	—	(533,692)
Change in fair value of warrant liability	(1,005,349)	597,615
Total other expense, net	(998,830)	(204,106)
Net loss	$ (12,229,512)	$ (10,748,531)
Net loss per share of common stock, basic	$ (0.82)	$ (1.15)
Net loss per share of common stock, diluted	$ (0.90)	$ (1.15)
Weighted-average shares used to compute basic net loss per share	14,897,885	9,338,068
Weighted-average shares used to compute diluted net loss per share	14,951,036	9,338,068

See accompanying notes.

Evoke Pharma, Inc.

Statements of Stockholders' Equity

	Common Stock		Additional Paid-In	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Deficit	Equity
Balance at December 31, 2015	7,201,774	$ 720	$ 51,524,821	$ (48,060,612)	$ 3,464,929
Stock-based compensation expense	—	—	1,706,524	—	1,706,524
Issuance of common stock from At-The-Market offering, net	56,000	6	256,107	—	256,113
Issuance of common stock from employee stock purchase plan	34,067	3	98,739	—	98,742
Issuance of common stock from warrant exercise	9,887	1	(1)	—	—
Issuance of common stock and warrants, net	5,048,632	505	8,802,531	—	8,803,036
Reclassification of warrant liability due to warrant amendment	—	—	206,825	—	206,825
Net loss	—	—	—	(10,748,531)	(10,748,531)
Balance at December 31, 2016	12,350,360	1,235	62,595,546	(58,809,143)	3,787,638
Stock-based compensation expense	—	—	1,819,431	—	1,819,431
Issuance of common stock from employee stock purchase plan	75,529	7	134,746	—	134,753
Issuance of common stock from warrant exercise	211,860	21	(21)	—	—
Issuance of common stock, net	2,775,861	278	7,254,070	—	7,254,348
Reclassification of warrant liability due to warrant exercise	—	—	1,399,091	—	1,399,091
Net loss	—	—	—	(12,229,512)	(12,229,512)
Balance at December 31, 2017	15,413,610	$ 1,541	$ 73,202,863	$ (71,038,655)	$ 2,165,749

See accompanying notes.

Evoke Pharma, Inc.

Statements of Cash Flows

	Year Ended December 31,	
	2017	**2016**
Operating activities		
Net loss	$ (12,229,512)	$ (10,748,531)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	1,819,431	1,706,524
Non-cash interest	—	120,889
Financing costs allocated to warrant liability	—	533,692
Change in fair value of warrant liability	1,005,349	(597,615)
Change in operating assets and liabilities:		
Prepaid expenses and other assets	24,662	554,014
Accounts payable and accrued expenses	663,165	(276,715)
Net cash used in operating activities	(8,716,905)	(8,707,742)
Financing activities		
Payment on bank loan	—	(4,500,000)
Proceeds from issuance of common stock, net	7,389,101	354,855
Proceeds from issuance of common stock and warrants, net	—	13,168,803
Net cash provided by financing activities	7,389,101	9,023,658
Net increase (decrease) in cash and cash equivalents	(1,327,804)	315,916
Cash and cash equivalents at beginning of period	9,007,071	8,691,155
Cash and cash equivalents at end of period	$ 7,679,267	$ 9,007,071
Supplemental disclosure of cash flow information		
Interest paid	—	$ 169,813
Non-cash financing activities		
Fair value of warrants issued to placement agent	—	$ 369,863
Reclassification of warrant liability to equity due to exercise of warrants	$ 1,399,091	—

See accompanying notes.

1. Organization and Basis of Presentation

Evoke Pharma, Inc. (the "Company") was incorporated in the state of Delaware in January 2007. The Company is a publicly-held specialty pharmaceutical company focused primarily on the development of drugs to treat gastroenterological disorders and disease.

Since its inception, the Company has devoted substantially all of its efforts to product development, raising capital and building infrastructure, and has not realized revenues from its planned principal operations. The Company does not anticipate realizing revenues for the foreseeable future. The Company's activities are subject to the significant risks and uncertainties associated with any specialty pharmaceutical company that has substantial expenditures for research and development, including funding its operations.

Clinical Trial Results

In July 2016, the Company announced topline results from its Phase 3 clinical trial that evaluated the efficacy and safety of Gimoti™ (formerly known as EVK-001) in women with symptoms associated with diabetic gastroparesis. In this study, Gimoti did not achieve its primary endpoint of symptom improvement at Week 4.

In December 2016, the Company had a pre-New Drug Application ("pre-NDA") meeting with the U.S. Food and Drug Administration ("FDA"), in which FDA agreed that a comparative exposure pharmacokinetic ("PK") trial was acceptable as a basis for submission of a Gimoti new drug application ("NDA"). The comparative exposure PK trial will serve as a portion of the full 505(b)(2) data package to include prior efficacy and safety data developed by the Company and FDA's prior findings of safety and efficacy for the Listed Drug, Reglan Tablets.

In March 2017, the Company met with FDA to discuss the design of the comparative exposure PK trial and certain other chemistry, manufacturing and controls related items associated with the proposed NDA submission. In October 2017, the Company announced positive topline results from the comparative exposure PK trial. The objective of the trial was to identify a dose of Gimoti that met the criteria for bioequivalence compared to the Reglan Tablets after nasal and oral administration to healthy volunteers under fasted conditions. Based on these results, the Company expects to submit the Gimoti NDA to FDA in the second quarter of 2018.

Going Concern

The Company has incurred recurring losses and negative cash flows from operations since inception and expects to continue to incur net losses for the foreseeable future until such time, if ever, that it can generate significant revenues from the sale of its sole product, Gimoti. The Company ended 2017 with approximately $7.7 million in cash and cash equivalents, and the Company anticipates that it will continue to incur losses from operations due to a planned NDA submission for Gimoti, pre-approval and pre-commercialization activities, including marketing and manufacturing of Gimoti, and general and administrative costs to support operations. As a result, the Company believes that there is substantial doubt about its ability to continue as a going concern for one year after the date these financial statements are issued.

The determination as to whether the Company can continue as a going concern contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. In its report on the Company's financial statements for the year ended December 31, 2017, the Company's independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding the Company's ability to continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business.

The Company's net losses may fluctuate significantly from quarter to quarter and year to year. The Company believes that its current cash and cash equivalents will be sufficient to meet estimated working capital requirements and fund operations into October 2018. The Company will need to raise additional debt or equity financing to fund future operations. There can be no assurance that additional financing will be available when needed or on acceptable terms. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, and/or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations, financial condition and future prospects.

2. Summary of Significant Accounting Policies

Use of Estimates

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of financial statements in conformity with GAAP requires management to make estimates and

assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ materially from those estimates.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment operating in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents include cash in readily available checking and savings accounts.

Fair Value of Financial Instruments

The carrying amounts of all financial instruments, including accounts payable and accrued expenses, and employee-related liabilities, are considered to be representative of their respective fair values because of the short-term nature of those instruments. Based on the borrowing rates currently available to the Company for loans with similar terms, the Company believes that the fair value of long-term debt approximates its carrying value.

Concentrations of Risk

Financial instruments that potentially subject the Company to significant credit risk consist primarily of cash and cash equivalents. The Company maintains deposits in a federally insured financial institution in excess of federally insured limits. The Company has established guidelines designed to maintain safety and liquidity, has not experienced any losses in such accounts and believes the exposure to significant risk to the cash balance is minimal.

The Company relies on a contract research organization ("CRO") to manage the preparation and submission of the planned NDA. If this CRO is unable to continue the management of the NDA preparation, the delays could adversely affect the timing of the Company's NDA submission with FDA.

In addition, the Company relies on third-party manufacturers for the production of its drug candidate. If the third-party manufacturers are unable to continue manufacturing the Company's drug candidate, or if the Company loses one of its sole source suppliers used in its manufacturing processes, the Company may not be able to meet any development needs or commercial supply demand for Gimoti, if approved by FDA, and the development and/or commercialization of Gimoti could be materially and adversely affected.

Warrant Accounting

Certain of the warrants to purchase shares of the Company's common stock, issued as a part of the at-the-market registered direct offerings in July and August 2016, are classified as warrant liability and recorded at fair value. These warrants contain a feature that could require the transfer of cash in the event a change of control occurs without the authorization of our Board of Directors, and therefore, are classified as a liability in accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 480.

The fair value of each warrant is estimated on the date of issuance, and each subsequent balance sheet date, using the Black-Scholes valuation model using the appropriate risk-free interest rate, expected term and volatility assumptions. The expected life of the warrant was calculated using the remaining life of the warrant. Due to our limited historical data as a public company, the estimated volatility is calculated based upon the Company's historical volatility, supplemented, as necessary, with historical volatility of comparable companies in the biotechnology industry whose share prices are publicly available for a sufficient period of time. The risk-free rate is based upon U.S. Treasury securities with remaining terms similar to the expected term of the stock award being valued.

This warrant liability is subject to remeasurement at each balance sheet date and the Company recognizes any change in the fair value of the warrant liability in the statement of operations. The Company will continue to adjust the carrying value of the warrants for changes in the estimated fair value until the earlier of the modification, exercise or expiration of the warrants. At that time, the liabilities will be reclassified to additional paid-in capital, a component of stockholders' equity. The Company anticipates that the value of the warrants could fluctuate from quarter to quarter and that such fluctuation could have a material impact on the Company's financial statements.

Stock-Based Compensation

Stock-based compensation expense for stock option grants and employee stock purchases under the Company's Employee Stock Purchase Plan (the "ESPP") is recorded at the estimated fair value of the award as of the grant date and is recognized as expense on a straight-line basis over the employee's requisite service period. The estimation of stock option and ESPP fair value requires management to make estimates and judgments about, among other things, employee exercise behavior, forfeiture rates and volatility of the Company's common stock. The judgments directly affect the amount of compensation expense that will be recognized.

The Company grants stock options to purchase common stock to employees and members of the board of directors with exercise prices equal to the Company's closing market price on the date the stock options are granted. The risk-free interest rate assumption was based on the yield of an applicable rate for U.S. Treasury instruments with maturities similar to those of the expected term of the award being valued. The weighted average expected term of options and employee stock purchases was calculated using the simplified method as prescribed by accounting guidance for stock-based compensation. This decision was based on the lack of relevant historical data due to the Company's limited historical experience. In addition, due to the Company's limited historical data, the estimated volatility was calculated based upon the Company's historical volatility, supplemented, as necessary, with historical volatility of comparable companies in the biotechnology industry whose share prices are publicly available for a sufficient period of time. The assumed dividend yield was based on the Company never paying cash dividends and having no expectation of paying cash dividends in the foreseeable future.

Research and Development Expenses

Research and development costs are expensed as incurred and primarily include compensation and related benefits, stock-based compensation expense and costs paid to third-party contractors to perform research, conduct clinical trials and develop drug materials and delivery devices. The Company expenses costs relating to the purchase and production of pre-approval inventories as research and development expense in the period incurred until FDA approval is received.

The Company bases its expense accruals related to clinical studies on estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on its behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients, site initiation and the completion of clinical study milestones. Service providers typically invoice the Company monthly in arrears for services performed. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the Company does not identify costs that have begun to be incurred, or if the Company underestimates or overestimates the level of services performed or the costs of these services, actual expenses could differ materially from estimates. To date, the Company has not experienced significant changes in estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, no assurance can be made that changes to the estimates will not be made in the future as the Company becomes aware of additional information about the status or conduct of clinical studies and other research activities.

The Company does not own or operate manufacturing facilities for the production of Gimoti, nor does it plan to develop its own manufacturing operations in the foreseeable future. The Company currently depends on third-party contract manufacturers for all of its required raw materials, drug substance and finished product for its preclinical research, product development and clinical trials. The Company has agreements with Cosma S.p.A. to supply metoclopramide for the manufacture of Gimoti, and with Thermo Fisher Scientific Inc., who recently acquired Patheon UK Limited, for product development and manufacturing of Gimoti. The Company currently utilizes a third-party consultant, which it engages on an as-needed, hourly basis, to manage product development and manufacturing contractors.

Income Taxes

The Company accounts for income taxes in accordance with ASC 740, *Income Taxes*. Under ASC 740, deferred tax assets and liabilities reflect the future tax consequences of the differences between the financial reporting and tax basis of assets and liabilities using current enacted tax rates. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized.

The Company's policy related to accounting for uncertainty in income taxes prescribes a recognition threshold and measurement attributed criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common stock outstanding for the period, without consideration for common stock equivalents and adjusted for the weighted-average number of common shares outstanding that are subject to repurchase. The Company has excluded 45,000 shares of common stock subject to repurchase from the weighted-average number of common shares outstanding for the years ended December 31, 2017 and 2016. Diluted net loss per share is calculated by dividing the net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of shares subject to repurchase, warrants for the purchase of common stock, options outstanding under the Company's equity incentive plans and potential shares to be purchased under the ESPP. For the periods, the following table sets forth the outstanding potentially dilutive securities that have been excluded from the calculation of diluted net loss per share because to do so would be anti-dilutive:

	Year Ended December 31,	
	2017	2016
Common stock subject to repurchase	45,000	45,000
Warrants to purchase common stock	2,744,500	3,323,876
Common stock options	2,131,624	1,275,624
Employee stock purchase plan	27,785	43,752
Total excluded securities	4,948,909	4,688,252

For the years ended December 31, 2017 and 2016, dilutive shares of 53,061 and 0, respectively, related to the outstanding warrants, were included in the diluted net loss per share of common stock calculation.

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases*. The new standard establishes a right-of-use ("ROU") model that requires a lessee to record a ROU asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. The new standard is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. A modified retrospective transition approach is required for lessees for capital and operating leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements, with certain practical expedients available. As discussed in Note 4, the Company's only significant lease is its facility lease, which expires on December 31, 2018. Until the current lease is extended, or a new lease is entered into, the Company is uncertain as to the impact of its pending adoption of the new standard on the Company's financial statements.

3. Debt

On August 4, 2016, the Company repaid in full the $4.5 million of outstanding principal and interest under the Loan and Security Agreement, dated as of May 28, 2014, as amended (the "Loan Agreement"), between the Company and Square 1 Bank, a division of Pacific Western Bank ("Square 1"). In connection with such repayment, the Loan Agreement was terminated, and all security, liens or other encumbrances on assets of the Company were released.

The Company incurred $82,685 of loan origination costs related to this credit facility. The remaining unamortized costs of approximately $38,000 were charged to interest expense upon the payment of the loan in August 2016.

In connection with the funding of the term loan, the Company issued to Square 1 a warrant to purchase 22,881 shares of the Company's common stock at an exercise price of $5.90 per share, the closing price of the Company's common stock on the day of funding of the credit facility. During July 2016, Square 1 converted its warrant by a "cashless" conversion and received 9,887 shares of the Company's common stock. The value determined for the warrant at the time of the grant of $108,122 was recorded as a debt discount, as well as to stockholders' equity. The remaining unamortized debt discount associated with the warrant of approximately $59,000 was charged to interest expense upon the payment of the loan in August 2016.

Total interest incurred under the loan and security agreements for the years ended December 31, 2017 and 2016 was $0 and $148,500, respectively.

4. Commitments

In December 2016, the Company entered into an operating lease for office space in Solana Beach, California. The lease commenced on January 1, 2017 with an expiration date of December 31, 2018. The Company has an option to extend the lease for an additional two years subject to specified prior written notice. The lease contains annual rent increases.

Rent expense for 2017 and 2016 was approximately $135,000 and $116,000, respectively. The Company also pays pass through costs and utility costs, which are expensed as incurred.

As of December 31, 2017, the Company has future minimum lease payments under its facility lease in 2018 of approximately $139,000.

5. Technology Acquisition Agreement

In June 2007, the Company acquired all worldwide rights, data, patents and other related assets associated with Gimoti from Questcor Pharmaceuticals, Inc. ("Questcor") pursuant to an Asset Purchase Agreement. The Company paid Questcor $650,000 in the form of an upfront payment and $500,000 in May 2014 as a milestone payment based upon the initiation of the first patient dosing in the Company's Phase 3 clinical trial for Gimoti. In August 2014, Mallinckrodt, plc, ("Mallinckrodt") acquired Questcor. As a result of that acquisition, Questcor transferred its rights included in the Asset Purchase Agreement with the Company to Mallinckrodt. In addition to the payments made to Questcor, the Company may also be required to make additional milestone payments to Mallinckrodt totaling up to $51.5 million. These milestones include up to $4.5 million in payments if Gimoti achieves the following development targets:

- $1.5 million upon FDA acceptance for review of an NDA for Gimoti; and
- $3 million upon FDA approval of Gimoti.

The remaining $47 million in milestone payments depend on Gimoti's commercial success and will only apply if Gimoti receives regulatory approval. In addition, the Company will be required to pay to Mallinckrodt a low single digit royalty on net sales of Gimoti. The Company's obligation to pay such royalties will terminate upon the expiration of the last patent right covering Gimoti, which is expected to occur in 2030.

6. Preferred Stock, Common Stock and Stockholders' Equity

Preferred Stock

Under the Company's amended and restated certificate of incorporation, the Company is authorized to issue 5,000,000 shares of preferred stock with a $0.0001 par value. No shares of preferred stock were outstanding as of December 31, 2017 or 2016.

Common Stock

As of December 31, 2017, there were 15,413,610 shares of common stock outstanding. Each share of common stock is entitled to one vote. The holders of the common stock are also entitled to receive dividends whenever funds are legally available and when declared by the board of directors of the Company. To date, no dividends have been declared.

Sale of Common Stock and Warrants

On July 25, 2016, the Company completed a registered direct offering of 1,804,512 shares of common stock at a purchase price of $2.49375 per share (the "July 2016 Financing"). Concurrently in a private placement, for each share of common stock purchased by an investor, such investor received from the Company an unregistered warrant to purchase three-quarters of a share of common stock, for a total of 1,353,384 shares (the "July Warrants"). The July Warrants have an exercise price of $2.41 per share, are immediately exercisable and will expire on January 25, 2022. The aggregate gross proceeds from the sale of the common stock and warrants were $4.5 million, and the net proceeds after deduction of commissions and fees were $4.0 million.

In connection with the July 2016 Financing, the Company issued to its placement agent, Rodman & Renshaw, a unit of H.C. Wainwright & Co. LLC ("Wainwright"), and its designees unregistered warrants to purchase an aggregate of 90,226 shares of the Company's common stock (the "July Wainwright Warrants"). The July Wainwright Warrants have substantially the same terms as the July Warrants, except that the July Wainwright Warrants will expire on July 21, 2021 and have an exercise price equal to $3.1172 per share of common stock.

On August 3, 2016, the Company completed a registered direct offering of 3,244,120 shares of common stock at a purchase price of $3.0825 per share (the "August 2016 Financing") and together with the July 2016 Financing (the "2016 Financings"). Concurrently in a private placement, for each share of common stock purchased by an investor, such investor received from the Company an unregistered warrant to purchase one half of a share of common stock, for a total of 1,622,060 shares (the "August Warrants"). The August Warrants have an exercise price of $3.03 per share, are immediately exercisable and will expire on February 3, 2022. The aggregate gross proceeds from the sale of the common stock and warrants were $10 million, and the net proceeds after deduction of commissions and fees was approximately $9.2 million.

In connection with the August 2016 financing, the Company issued to its placement agent, Wainwright, and its designees unregistered warrants to purchase an aggregate of 162,206 shares of the Company's common stock (the "August Wainwright Warrants"). The August Wainwright Warrants have substantially the same terms as the August Warrants, except that the August Wainwright Warrants will expire on July 29, 2021 and have an exercise price equal to $3.853125 per share of common stock.

The warrants issued in connection with the 2016 Financings had a total initial fair value of $4,899,459 on their respective closing dates as determined using the Black Scholes valuation model and such value was recorded as the initial carrying value of the warrant liability. The fair value of the warrants is remeasured at each financial reporting period with any change in fair value recognized as a change in fair value of the warrant liability in the Statement of Operations.

On December 15, 2016, the Company entered into amendments (the "Warrant Amendments") with certain of the holders (the "Holders") of the Company's outstanding warrants to purchase common stock issued on July 25, 2016 and August 3, 2016. Pursuant to the Warrant Amendments, the Holders' right to require the Company to purchase the outstanding warrants upon the occurrence of certain fundamental transactions will not apply if the fundamental transaction is a result of a transaction that has not been approved by the Company's board of directors. As a result of this amendment, warrants to purchase 252,432 shares of the Company's common stock were no longer required to be classified as liabilities. The value of amended warrants were adjusted to their fair value immediately prior to the amendment and approximately $207,000 was reclassified from warrant liability to Additional Paid-in Capital.

On February 16, 2017, an institutional investor from the Company's financing which closed in July 2016 converted its warrant to purchase 526,315 shares of our common stock by a "cashless" exercise and received 211,860 shares of the Company's common stock. The warrant had an exercise price of $2.41 per share. The shares were issued, and the warrants were sold, in reliance upon the registration exemption set forth in Section 4(a)(2) of the Securities Act of 1933, as amended. The value of the exercised warrants were adjusted to their fair value immediately prior to the exercise and approximately $1.4 million was reclassified from warrant liability to Additional Paid-in Capital. Subsequent to this transaction, warrants to purchase 2,449,129 shares of the Company's common stock remain classified as a liability.

Sale of Common Stock in Public Offering

In February and March 2017, the Company completed the sale of 2,775,861 shares of its common stock in an underwritten public offering led by Laidlaw & Company (UK) Ltd. The price to the public in this offering was $2.90 per share resulting in gross proceeds to the Company of approximately $8.0 million. After deducting underwriting discounts and commissions and offering expenses paid by the Company, the net proceeds to the Company from this offering was approximately $7.3 million.

At the Market Equity Offering Program

On April 15, 2016, the Company terminated its At Market Sales Agreement with MLV & Co. LLC and entered into a new At Market Issuance Sales Agreement with B. Riley FBR, Inc. (as successor by merger to FBR Capital Markets & Co., "FBR") ("FBR Sales Agreement"), and filed a prospectus supplement, pursuant to which the Company may sell from time to time, at its option, up to an aggregate of 649,074 shares of the Company's common stock through FBR as the sales agent. The sales of shares made through this equity program are made in "at-the-market" offerings as defined in Rule 415 of the Securities Act. Through December 31, 2016, the Company sold 56,000 shares of common stock at a weighted average price per share of $5.45 and received proceeds of approximately $296,000, net of commissions and fees.

In November 2017, the Company filed a new shelf registration with the SEC on Form S-3 to replace a prior Form S-3 shelf registration which was set to expire on November 25, 2017. This new shelf registration was declared effective by the SEC on December 28, 2017. The new shelf registration statement includes a prospectus for the at-the-market offering to sell up to an aggregate of $16.0 million of shares of the Company's common stock through FBR as a sales agent. The Company did not sell any shares of common stock through the FBR Sales Agreement during 2017. Through February 28, 2018, the Company sold 79,758 shares of common stock at a weighted average price per share of $2.08 pursuant to the FBR Sales Agreement and received net proceeds of approximately $160,000, net of commissions and fees. The Company currently has the capacity to issue up to approximately $11.9 million worth of additional shares of common stock pursuant to the FBR Sales Agreement.

Under current SEC regulations, if at the time the Company files its Annual Report on Form 10-K, or Form 10-K, the Company's public float is less than $75 million, and for so long as its public float remains less than $75 million, the amount the Company can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is limited to an aggregate of one-third of the Company's public float, which is referred to as the baby shelf rules. As of February 28, 2018, the Company's public float was approximately $36.1 million, based on 12,938,176 shares of outstanding common stock held by non-affiliates and at a price of $2.79 per share, which was the last reported sale price of the Company's common stock on The Nasdaq Capital Market on January 29, 2018. As a result of the Company's public float being below $75 million, the Company will be limited by the baby shelf rules until such time as the Company's public float exceeds $75 million, which means the Company only has the capacity to sell shares up to one-third of its public float under shelf registration statements in any twelve-month period. If the

Company's public float decreases, the amount of securities we may sell under our Form S-3 shelf registration statement will also decrease.

Future sales will depend on a variety of factors including, but not limited to, market conditions, the trading price of the Company's common stock and the Company's capital needs. There can be no assurance that FBR will be successful in consummating future sales based on prevailing market conditions or in the quantities or at the prices that the Company deems appropriate.

In addition, the Company will not be able to make future sales of common stock pursuant to the FBR Sales Agreement unless certain conditions are met, which include the accuracy of representations and warranties made to FBR under the FBR Sales Agreement. Furthermore, FBR is permitted to terminate the FBR Sales Agreement in its sole discretion upon ten days' notice, or at any time in certain circumstances, including the occurrence of an event that would be reasonably likely to have a material adverse effect on the Company's assets, business, operations, earnings, properties, condition (financial or otherwise), prospects, stockholders' equity or results of operations. The Company has no obligation to sell the remaining shares available for sale pursuant to the FBR Sales Agreement.

Warrants

The Company has issued warrants to purchase common stock to banks that have loaned funds to the Company, as well as to representatives of the underwriters of the Company's initial public offering and certain of its affiliates. A summary of the Company's warrant activity is as follows:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)
Outstanding at December 31, 2016	3,323,876	$ 3.29	4.96
Issued	—	—	—
Exercised	(526,315)	$ 2.41	4.07
Expired/Forfeited	—	—	—
Outstanding at December 31, 2017	2,797,561	$ 3.46	3.94

Equity Incentive Award Plans

The Company adopted the 2007 Equity Incentive Plan (the "2007 Plan") in May 2007 under which 450,000 shares of common stock were reserved for issuance to employees, nonemployee directors and consultants of the Company. As of December 31, 2016, no options were available for future grant under this plan.

In August 2013, the Company adopted the 2013 Equity Incentive Award Plan (the "2013 Plan") as a successor to the 2007 Plan. Under the 2013 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units and other awards to individuals who are then employees, officers, non-employee directors or consultants of the Company. A total of 510,000 shares of common stock were initially reserved for issuance under the 2013 Plan. In addition, the number of shares of common stock available for issuance under the 2013 Plan will be annually increased on the first day of each fiscal year during the term of the 2013 Plan, beginning with the 2014 fiscal year, by an amount equal to the least of: (i) 300,000 shares; (ii) four percent of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine.

In February 2016, the Company effected a one-time option exchange, wherein employees were offered the opportunity to exchange certain outstanding stock options for the grant of a lesser number of replacement stock options. The participants received three new stock options for every four stock options tendered for exchange. As a result, 703,500 stock options were exchanged for 527,624 replacement stock options. The replacement stock options have a three-year vesting schedule and an exercise price of $3.04 per share, which was the closing price of the Company's common stock on the date of the option exchange. All other terms of the replacement stock options remain the same as the original stock options that were exchanged. As a result of this transaction, the Company recognized an incremental stock-based compensation expense of approximately $4,700 at the time of the transaction and will recognize an additional approximately $141,000 of stock-based compensation expense over the three-year vesting term of the exchanged options.

On April 27, 2016, the Company's stockholders approved an amendment and restatement of the Company's 2013 Equity Incentive Award Plan (the "Restated Plan") to increase the number of shares of common stock reserved under the Restated Plan by 500,000 shares, to an aggregate of 4,786,425 shares, and to extend the term of the Restated Plan into 2026.

As a result of the annual increases since the 2013 Plan originated, and the increase of stock options reserved under the Restated Plan approved by the Company's stockholders in April 2016, the Company has increased the number shares reserved for issuance under the 2013 Plan by 1,276,425 shares. As of December 31, 2017, 72,801 options remain available for future grant under the 2013 Plan. On January 1, 2018, the Company further increased the number of shares reserved for issuance under the 2013 Plan by 300,000 shares, making 372,801 options available for future grant under the 2013 Plan.

Options granted under the 2007 Plan and 2013 Plan have ten year terms from the date of grant and generally vest over a one to four year period. The Company granted options to purchase 856,000 and 414,000 shares of common stock in 2017 and 2016, respectively. The exercise price of all options granted during the years ended December 31, 2017 and 2016 was equal to the market value per share of the Company's common stock on the date of grant.

A summary of the Company's stock option activity under the 2007 Plan and 2013 Plan is as follows:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2016	1,275,624	$ 4.04	8.34	$ 191,160
Granted	856,000	$ 2.45	9.13	—
Exercised	—	—	—	—
Expired/Forfeited/Exchanged	—	—	—	—
Outstanding at December 31, 2017	2,131,624	$ 3.40	8.06	$ 219,480
Vested and expected to vest at December 31, 2017	2,131,624	$ 3.40	8.06	$ 219,480
Exercisable at December 31, 2017	1,111,270	$ 4.08	7.38	$ 219,480

The intrinsic values above represent the aggregate value of the total pre-tax intrinsic value based upon a common stock price of $2.26 and $2.02 at December 31, 2017 and 2016, respectively, and the contractual exercise price.

The weighted average grant date fair value per share of employee stock options granted during the years ended December 31, 2017 and 2016, was $1.87 and $2.04, respectively.

The 2007 Plan permits the early exercise of options, but the Company has the option to repurchase any unvested shares at the original purchase price (the exercise price paid by the purchaser) upon any voluntary or involuntary termination. The shares of common stock issued from the exercise of stock options are restricted and vest over time or on the achievement of certain milestones. Any unvested shares immediately vest in the event of termination for reasons other than cause, and vesting accelerates in the event of a merger, sale, or other change in control of the Company. Of the total 332,000 stock options exercised, 287,000 were vested as of December 31, 2017 and 2016. The remaining 45,000 exercised stock options vest upon the submission of the NDA for Gimoti.

There were no options exercised in 2017 and 2016.

The Company had the following nonvested options under the 2007 Plan and 2013 Plan:

	Shares	Weighted Average Grant Date Fair Value Per Share
Nonvested at December 31, 2016	690,961	$ 3.34
Granted	856,000	$ 2.45
Vested	(526,607)	$ 3.22
Expired/Forfeited/Exchanged	—	—
Nonvested at December 31, 2017	1,020,354	$ 2.65

Employee Stock Purchase Plan

On June 13, 2013, the Company's board of directors adopted the ESPP, and the Company's stockholders approved the ESPP on August 29, 2013. The ESPP became effective on the day prior to the effectiveness of the IPO. The ESPP permits participants to purchase the Company's common stock at 85% of the fair market value through payroll deductions of up to 20% of their eligible compensation. A total of 30,000 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP has been annually increased on the first day of each fiscal year during the term of the ESPP by an amount equal to the lesser of: (i) 30,000 shares; (ii) one percent of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine.

On May 3, 2017, the Company's stockholders approved an amendment and restatement of the Company's ESPP to increase the number of shares of common stock reserved under the ESPP by 100,000 shares (to an aggregate of 1,250,000 shares), to increase the annual evergreen provision from 30,000 shares to 100,000 shares, and to extend the term of the ESPP into 2027. As a result, the Company increased the number shares reserved for issuance under the ESPP by 220,000 shares since the inception of the ESPP. As of December 31, 2017, 91,934 shares remain available for future issuance under the ESPP. On January 1, 2018, the Company further increased the number of shares reserved for future issuance under the ESPP by 100,000 shares, making 191,934 shares available for future issuance under the ESPP after that increase.

Payroll withholdings from the Company's employees of approximately $135,000 and $99,000 resulted in the issuance of 75,529 and 34,067 shares of common stock through its ESPP during the years ended December 31, 2017 and 2016, respectively.

The estimated fair value of the shares to be acquired under the ESPP was determined on the initiation date of each six month purchase period using the Black-Scholes option-pricing valuation model with the following weighted-average assumptions for ESPP shares to be purchased during the year ended December 31, 2017 and 2016:

	Year Ended December 31,	
	2017	2016
Risk free interest rate	0.79% - 1.10%	0.47% - 0.50%
Expected term	6 months	6 months
Expected volatility of common stock	37.60% - 99.23%	83.83% - 212.80%
Expected dividend yield	0.0%	0.0%

Stock-Based Compensation

Stock-based compensation expense includes charges related to stock option grants and employee stock purchases under the Company's ESPP. The Company measures stock-based compensation expense based on the grant-date fair value of any awards granted to its employees. Such expense is recognized over the period of time that employees provide service and earn rights to the awards.

The estimated fair value of each option award granted was determined on the date of grant using the Black-Scholes option-pricing valuation model with the following weighted-average assumptions for options grants during the two years ended December 31, 2017:

	Year Ended December 31,	
	2017	2016
Risk free interest rate	1.93% - 2.16%	1.25% - 1.58%
Expected option term	5.5 - 6.0 years	5.3 - 6.0 years
Expected volatility of common stock	94.05% - 98.23%	74.44 - 75.91%
Expected dividend yield	0.0%	0.0%

The Company recognized non-cash stock-based compensation expense to employees and directors in its research and development and its general and administrative functions as follows:

	Year Ended December 31,	
	2017	2016
Research and development	$ 819,815	$ 698,032
General and administrative	999,616	1,008,492
Total stock-based compensation expense	$ 1,819,431	$ 1,706,524

As of December 31, 2017, there was approximately $1.7 million of unrecognized compensation costs related to outstanding employee and board of director options, which is expected to be recognized over a weighted average period of 1.13 years.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consists of the following at December 31, 2017 and 2016:

	December 31,	
	2017	2016
Stock options issued and outstanding	2,131,624	1,275,624
Authorized for future option grants	72,801	628,801
Warrants to purchase common stock	2,797,561	3,323,876
Authorized for employee stock purchase plan	91,934	37,463
Total common stock reserved for future issuance	5,093,920	5,265,764

7. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

As noted in Note 6, during the third quarter of 2016 the Company entered into the 2016 Financings with an institutional investor providing for the issuance and sale by the Company of 5,048,632 shares of the Company's common stock and warrants to purchase up to 2,975,444 shares of the Company's common stock for aggregate gross proceeds of $14.5 million. In addition, as partial payment for services, the Company issued to the underwriters warrants to purchase up to 252,432 shares of the Company's common stock.

The Company utilizes a valuation hierarchy for disclosure of the inputs to the valuations used to measure fair value. This hierarchy prioritizes the inputs into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs are quoted prices for similar assets and liabilities in active markets or inputs that are observable for the asset or liability, either directly or indirectly through market corroboration, for substantially the full term of the financial instrument. Level 3 inputs are unobservable inputs based on the Company's own assumptions used to measure assets and liabilities at fair value. A financial asset or liability's classification within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement.

The Company had no assets or liabilities classified as Level 1 or Level 2. The warrant liability is classified as Level 3.

The Company has classified the warrants as a liability and has remeasured the liability to estimated fair value at December 31, 2017 and 2016, using the Black Scholes option valuation model with the following assumptions:

	December 31,	
	2017	2016
Risk-free interest rate	2.09%	1.93%
Expected volatility	100.39%	94.19%
Expected term	4.08 years	5.08 years
Expected dividend yield	0.0%	0.0%

The following fair value hierarchy table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis as of December 31, 2017:

	Fair Value Measurement as of December 31, 2017			
	Level 1	Level 2	Level 3	Balance
Warrant liability	$ -	$ -	$ 3,701,277	$ 3,701,277
Total	$ -	$ -	$ 3,701,277	$ 3,701,277

The following table presents a reconciliation of the Company's warrant liability measured at fair value on a recurring basis using significant unobservable inputs (Level 3) for the years ended December 31, 2017 and 2016:

	December 31,	
	2017	2016
Beginning balance of warrant liability	$ 4,095,019	$ -
Issuance of warrants	-	4,899,459
Change in fair value upon re-measurement	1,005,349	(597,615)
Reclassification to Additional Paid-in Capital due to warrant amendment	-	(206,825)
Reclassification to Additional Paid-in Capital due to warrant exercise	(1,399,091)	-
Ending balance of warrant liability	$ 3,701,277	$ 4,095,019

There were no transfers between Level 1 and Level 2 in any of the periods reported.

8. Employee Benefit Plan

The Company has established a defined contribution 401(k) plan (the "Plan") for all employees who are at least 21 years of age. Employees are eligible to participate in the Plan beginning on the date of employment. Under the terms of the Plan, employees may make voluntary contributions as a percentage of compensation. The Company's contributions to the Plan are discretionary, and no contributions have been made by the Company to date. For the years ended December 31, 2017 and 2016, the Company adopted Safe Harbor 401(k) provisions. In order to maintain the Plan's compliance with Internal Revenue Service regulations, approximately $3,700 was contributed to the accounts of certain employees for the year ended December 31, 2016 and approximately $3,500 will be contributed to the accounts of certain employees for the year ended December 31, 2017.

9. Income Taxes

The Company accounts for uncertain tax positions in accordance with Accounting Standards Codification Topic 740, *Income Taxes* ("ASC 740"). The application of income tax law and regulations is inherently complex. Interpretations and guidance surrounding income tax laws and regulations change over time. As such, changes in the Company's subjective assumptions and judgments can materially affect amounts recognized in its financial statements.

The Company's policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had no accrual for interest and penalties on the balance sheet at December 31, 2017. The Company has an uncertain tax position of $1.9 million related to California net operating losses at December 31, 2017. The Company is subject to taxation in the United States and state jurisdictions, and the Company's tax years beginning 2007 to date are subject to examination by taxing authorities.

On December 22, 2017, President Trump signed into law the tax legislation commonly known as the Tax Cuts and Jobs Act (the "Act"). The effects of the new federal legislation are recognized upon enactment, which is the date the president signs a bill into law. The Act includes numerous changes in existing tax law, including a permanent reduction in the federal corporate income tax rate from 35% to 21%. The rate reduction takes effect on January 1, 2018. As a result of this rate change, the Company has revalued its deferred tax assets at December 31, 2017. Deferred income taxes result from temporary differences between the tax basis of assets and liabilities and their reported amounts in the financial statements that will result in taxable or deductible amounts in future years.

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to faxable income in years in which those temporary differences are expected to be recovered or settled. As changes in tax laws or rates are enacted, deferred tax assets and liabilities are adjusted through income tax expense. Based on currently available information, the Company recorded a reduction of approximately $7.9 million in the fourth quarter of 2017 related to the revaluation of its deferred tax assets, which did not result in additional tax expense in the quarter as the Company's deferred tax assets have a full valuation allowance. This amount may be subject to further adjustment in subsequent periods throughout 2018 in accordance with subsequent interpretive guidance issued by the SEC or the IRS. Further, there may be other material adverse effects resulting from the legislation that we have not yet identified.

A reconciliation of the federal statutory income tax rate and the effective income tax rate is as follows for the years ended December 31, 2017 and 2016:

	December 31,	
	2017 (%)	2016 (%)
Federal statutory rate	34	34
Warrant liability FMV adjustment	(8)	6
Stock issuance costs	—	(5)
Research and development credits	3	3
Removal of net operating loss and other credits	33	(33)
Impact of federal tax rate change	(65)	—
Stock compensation and other permanent items	3	(5)
Effective income tax rate	—	—

Pursuant to Internal Revenue Code ("IRC") Sections 382 and 383, annual use of the Company's net operating loss and research and development credit carryforwards may be limited in the event a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not completed an IRC Section 382/383 analysis regarding the limitation of net operating loss and research and development credit carryforwards. Until this analysis has been completed, the Company has removed the deferred tax assets for net operating losses of approximately $15.9 million and a research and development credit of approximately $3.0 million generated through December 31, 2017 from its deferred tax asset schedule, and has recorded a corresponding decrease to its valuation allowance. When this analysis is finalized, the Company plans to update its unrecognized tax benefits accordingly. The Company does not expect this analysis to be completed within the next twelve months and, as a result, the Company does not expect that the unrecognized tax benefits will change within twelve months of this reporting date. Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact the Company's effective tax rate.

Significant components of the Company's deferred tax assets at December 31, 2017 and 2016 are as follows:

	December 31,	
	2017	2016
Acquired technology	$ 103,000	$ 201,000
Stock compensation expense	490,000	539,000
Accruals and other	216,000	130,000
Total deferred tax assets	809,000	870,000
Less valuation allowance	(809,000)	(870,000)
Net deferred tax assets	$ —	$ —

At December 31, 2017, the Company has federal and California net operating loss carryforwards of approximately $61.9 million and $41.7 million, respectively. The federal and California loss carryforwards begin to expire in 2027 and 2017, respectively, unless previously utilized. The Company also has federal and California research tax credit carryforwards of approximately $2.0 million and $1.2 million, respectively. The federal research credit carryforwards will begin expiring in 2027 unless previously utilized. The California research credit will carry forward indefinitely. Furthermore, under recently enacted U.S. tax legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond may only offset 80% of our taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

A summary of the changes in the amount of unrecognized tax benefits (excluding interest and penalties) for 2017 and 2016 are as follows:

	2017	2016
Beginning balance of unrecognized tax benefits	$ 1,961,595	—
Additions based on tax positions of prior years	—	$ 1,961,595
Ending balance of unrecognized tax benefits	$ 1,961,595	$ 1,961,595

Due to the full valuation allowance that the Company has on the deferred tax assets, there are no unrecognized tax benefits that would impact the effective tax rate, if recognized.

The Company recognizes interest and penalties related to unrecognized tax benefits in income tax expense. To date, as no benefit has been taken related to the uncertain tax position, there have been no interest and penalties recognized.

10. Subsequent Events

For the purposes of the financial statements as of December 31, 2017 and the year then ended, the Company has evaluated subsequent events through the date the audited annual financial statements were issued. The Company has concluded that no subsequent event has occurred other than what has been disclosed.

11. Summarized Quarterly Data (Unaudited)

The following financial information reflects all adjustments, which include only normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the financial results of the interim periods. Summarized quarterly data for the years ended December 31, 2017 and 2016 are as follows:

	For the Quarters Ended			
	March 31,	June 30,	September 30,	December 31,
2017				
Research and development expense	$ 770,686	$ 2,017,569	$ 2,717,698	$ 1,631,540
General and administrative expense	$ 1,209,570	$ 871,979	$ 984,047	$ 1,027,594
Change in fair value of warrant liability	$ 3,072,747	$ (1,261,912)	$ 1,544,138	$ (2,349,624)
Net loss	$ (5,052,039)	$ (1,625,969)	$ (5,243,061)	$ (308,443)
Net loss per common share, basic (1)	$ (0.37)	$ (0.11)	$ (0.34)	$ (0.02)
Net loss per common share, diluted (1)	$ (0.37)	$ (0.13) (2)	$ (0.34)	$ (0.07)
Weighted average shares outstanding, basic	13,528,311	15,343,325	15,351,295	15,368,610
Weighted average shares outstanding, diluted	13,528,311	15,420,954	15,351,295	15,503,583
2016				
Research and development expense	$ 2,015,076	$ 2,095,149	$ 1,339,343	$ 1,502,032
General and administrative expense	$ 1,137,753	$ 802,655	$ 830,092	$ 822,325
Change in fair value of warrant liability	—	—	$ 198,945	$ (796,560)
Net loss	$ (3,225,409)	$ (2,970,498)	$ (3,025,281)	$ (1,527,343)
Net loss per common share, basic and diluted (1)	$ (0.45)	$ (0.41)	$ (0.29)	$ (0.12)
Weighted average shares outstanding, basic and diluted	7,168,005	7,217,577	10,614,692	12,305,360

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per-share calculations will not necessarily equal the annual per share calculation.

(2) Net loss per common share, diluted, for the quarter ended June 30, 2017 was revised from ($0.19) to ($0.13) to correct the computation of diluted loss per share under the treasury stock method. No adjustments were made to any other quarters.

Exhibit Index

Exhibit Number	Description of Exhibit
3.1(2)	Amended and Restated Certificate of Incorporation of the Company
3.2(2)	Amended and Restated Bylaws of the Company
4.1(3)	Form of the Company's Common Stock Certificate
4.2(4)	Investor Rights Agreement dated as of June 1, 2007
4.3(4)	Warrant dated June 1, 2012 issued by the Company to Silicon Valley Bank
4.4(3)	Form of Warrant Agreement dated September 30, 2013 issued by the Company to the representative of the underwriters and certain of its affiliates in connection with the closing of the Company's initial public offering.
4.5(10)	Form of Warrant issued by the Company to certain investors under the Securities Purchase Agreement between the Company and such investors dated July 25, 2016
4.6(11)	Form of Warrant issued by the Company to certain investors under the Securities Purchase Agreement between the Company and such investors dated August 3, 2016
4.7 (12)	Form of Amendment to Common Stock Purchase Warrant, amending certain of the warrants dated July 25, 2016 and August 3, 2016
10.1(4)	Form of Indemnity Agreement for Directors and Officers
10.2(5)#	Amended and Restated Employment Agreement, effective as of June 7, 2013, between the Company and David A. Gonyer
10.3(4)#	2007 Equity Incentive Plan, as amended, and form of option agreement thereunder
10.4(1)#	2013 Equity Incentive Award Plan and form of option agreement thereunder
10.5(5)#	2013 Employee Stock Purchase Plan
10.6(5)#	Amended and Restated Retention Letter, dated May 22, 2013, between the Company and David A. Gonyer
10.7(5)#	Amended and Restated Retention Letter, dated May 22, 2013, between the Company and Matthew D'Onofrio
10.8†(6)	Asset Purchase Agreement, dated as of June 1, 2007, between the Company and Questcor Pharmaceuticals, Inc.
10.9(7)#	Employment Agreement, effective as of December 1, 2013, between the Company and Marilyn R. Carlson
10.10(8)#	Non-Employee Director Compensation Policy, as Amended and Restated Effective January 28, 2016
10.11(9)	2013 Equity Incentive Award Plan, as amended and restated, effective April 27, 2016
10.12(10)	Form of Securities Purchase Agreement dated as of July 20, 2016 by and between the Company and certain investors party thereto
10.13(10)	Engagement Letter dated as of July 19, 2016 by and between the Company and Rodman & Renshaw, a unit of H.C. Wainwright & Co., LLC
10.14(11)	Form of Securities Purchase Agreement dated as of July 29, 2016 by and between the Company and certain investors party thereto
10.15(11)	Engagement Letter dated as of July 29, 2016 by and between the Company and Rodman & Renshaw, a unit of H.C. Wainwright & Co., LLC
10.16(13)	Standard Office Lease, dated as of December 19, 2016, between the Company and SB Corporate Centre III-IV, LLC
10.17(13)#	Amendment to Amended and Restated Employment Agreement, effective as of January 25, 2017 between the Company and Matthew D'Onofrio
10.18(13)#	Amendment to Employment Agreement, effective as of January 25, 2017, between the Company and Marilyn R. Carlson

Exhibit Number	Description of Exhibit
10.19(14)	Non-Employee Director Compensation Policy, as Amended and Restated Effective January 25, 2017
10.20(15)†	Master Services Agreement made as of January 27, 2014, between the Company and Spaulding Clinical Research, LLC and Work Order dated as of April 17, 2017 thereunder
10.21†	Manufacturing Services Agreement dated November 7, 2017, between the Company and Patheon UK Limited
10.22(16)	Amendment No. 1 to At Market Issuance Sales Agreement, effective as of November 14, 2017, between the Company and B. Riley FBR, Inc.
10.23†(17)	Master Supply Agreement dated as of May 11, 2016 by and between the Company and Cosma S.p.A.
23.1	Consent of BDO USA, LLP, Independent Registered Public Accounting Firm
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
32.1*	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2*	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

(1) Incorporated by reference to the Company's Amendment No. 4 to Registration Statement on Form S-1 filed with the SEC on August 30, 2013.
(2) Incorporated by reference to the Company's Current Report on Form 8-K filed with the SEC on September 30, 2013.
(3) Incorporated by reference to the Company's Amendment No. 3 to Registration Statement on Form S-1 filed with the SEC on August 16, 2013.
(4) Incorporated by reference to the Company's Registration Statement on Form S-1 filed with the SEC on May 24, 2013.
(5) Incorporated by reference to the Company's Amendment No. 1 to Registration Statement on Form S-1 filed with the SEC on June 14, 2013.
(6) Incorporated by reference to the Company's Amendment No. 2 to Registration Statement on Form S-1 filed with the SEC on July 3, 2013.
(7) Incorporated by reference to the Company's Current Report on Form 8-K filed on December 2, 2013.
(8) Incorporated by reference to the Company's Annual Report on Form 10-K filed on March 10, 2016.
(9) Incorporated by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A filed with the SEC on March 15, 2016.
(10) Incorporated by reference to the Company's Current Report on Form 8-K filed on July 20, 2016.
(11) Incorporated by reference to the Company's Current Report on Form 8-K filed with the SEC on August 1, 2016.
(12) Incorporated by reference to the Company's Current Report on Form 8-K filed with the SEC on December 16, 2016.
(13) Incorporated by reference to the Company's Annual Report on Form 10-K filed on March 15, 2017.
(14) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 15, 2017.
(15) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 14, 2017.
(16) Incorporated by reference to Company's Registration Statement on Form S-3 filed with the SEC on November 14, 2017
(17) Incorporated by reference to Company's Quarterly Report on Form 10-Q filed with the SEC on August 15, 2016
† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 406 under the Securities Act of 1933.
# Management contract or compensatory plan or arrangement.
* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

EVOKE PHARMA, INC.

Date: March 7, 2018

By: /s/ David A. Gonyer
David A. Gonyer
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ David A. Gonyer David A. Gonyer, R.Ph.	President, Chief Executive Officer and Director (principal executive officer)	March 7, 2018
/s/ Matthew J. D'Onofrio Matthew J. D'Onofrio	Executive Vice President, Chief Business Officer, Treasurer and Secretary (principal financial and accounting officer)	March 7, 2018
/s/ Cam L. Garner Cam L. Garner	Chairman of the Board of Directors	March 7, 2018
/s/ Todd C. Brady, M.D., Ph.D. Todd C. Brady, M.D., Ph.D.	Director	March 7, 2018
/s/ Scott L. Glenn Scott L. Glenn	Director	March 7, 2018
/s/ Malcolm R. Hill, Pharm. D. Malcolm R. Hill, Pharm. D.	Director	March 7, 2018
/s/ Ann D. Rhoads Ann D. Rhoads	Director	March 7, 2018
/s/ Kenneth J. Widder, M.D. Kenneth J. Widder, M.D.	Director	March 7, 2018

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

Manufacturing Services Agreement

7 November 2017

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MANUFACTURING SERVICES AGREEMENT

THIS MANUFACTURING SERVICES AGREEMENT (the "Agreement") is made as of October 31, 2017 (the "**Effective Date**")

B E T W E E N:

PATHEON UK LIMITED of Kingfisher Drive, Covingham, Swindon Wiltshire, SN23 5BZ, UK
a corporation existing under the laws of England

("**Patheon**"),

- and -

EVOKE PHARMA, INC. of 420 Stevens Ave, Suite 370, Solana Beach, California 92075, USA
a corporation existing under the laws of California

("**Client**").

THIS AGREEMENT WITNESSES THAT in consideration of the rights conferred and the obligations assumed herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each party), and intending to be legally bound the parties agree as follows:

ARTICLE 1

STRUCTURE OF AGREEMENT AND INTERPRETATION

1.1

The following terms will, unless the context otherwise requires, have the respective meanings set out below and grammatical variations of these terms will have corresponding meanings:

"**Active Materials**", **"Active Pharmaceutical Ingredients" or "API"** means the materials listed in Schedule D;

"**Active Materials Credit Value**" means the value of the Active Materials for certain purposes of this Agreement, as set forth in Schedule D;

"**Actual Annual Yield**" or "**AAY**" has the meaning specified in Section 2.2(a);

"**Actual Yearly Volume**" or "**AYV**" has the meaning specified in Section 4.2.1;

"**Affiliate**" means:

(a) a business entity which owns, directly or indirectly, a controlling interest in a party to this Agreement, by stock ownership or otherwise; or

(b) a business entity which is controlled by a party to this Agreement, either directly or indirectly, by stock ownership or otherwise; or

(c) a business entity, the controlling interest of which is directly or indirectly common to the majority ownership of a party to this Agreement;

For this definition, "control" means the ownership of shares carrying at least a majority of the votes for the election of the directors of a corporation;

"Annual Product Review Report" means the annual product review report prepared by Patheon or an Affiliate of Patheon as described in Title 21 of the United States Code of Federal Regulations, Section 211.180(e);

"**Annual Report"** means the annual report to the FDA prepared by Client regarding the Product as described in Title 21 of the United States Code of Federal Regulations, Section 314.81(b)(2);

"**Annual Volume**" means the minimum volume of Product to be manufactured in any Year of this Agreement as set forth in Schedule B;

"**Applicable Laws**" means (i) for Patheon, the Laws of the jurisdiction where the Manufacturing Site is located; and (ii) for Client and the Products, the Laws of all jurisdictions where the Products are manufactured, distributed, and marketed as these are agreed and understood by the parties in this Agreement;

"**Authority**" means any governmental or regulatory authority, department, body or agency or any court, tribunal, bureau, commission or other similar body, whether federal, state, provincial, county or municipal;

"Bill Back Items" means the expenses for all third party supplier fees for the purchase or use of columns, standards, tooling, non-standard pallets, PAPR or PPE suits (where applicable) and other project-specific items necessary for Patheon to perform the Manufacturing Services, and which are not included as Components;

"**Business Day**" means a day other than a Saturday, Sunday or a day that is a statutory holiday in the United Kingdom or the jurisdiction where the Manufacturing Site is located, namely France, and the USA;

"**Capital Equipment Agreement**" means a separate agreement that the parties may enter into that will address responsibility for the purchase of capital equipment and facility modifications that may be required to perform the Manufacturing Services;

"**cGMPs**" means, as applicable, current good manufacturing practices as described in:

(a) Parts 210 and 211 of Title 21 of the United States' Code of Federal Regulations;

(b) EC Directive 2003/94/EC; and

(c) Division 2 of Part C of the *Food and Drug Regulations* (Canada);

together with the latest Health Canada, FDA and EMA guidance documents pertaining to manufacturing and quality control practice, all as updated, amended and revised from time to time;

"Client Intellectual Property" means Intellectual Property generated or derived by Client before entering into this Agreement, or by Patheon while performing any Manufacturing Services or otherwise generated or derived by Patheon in its business which Intellectual Property is specific to the development, manufacture, use, and/or sale of Client's Product or Active Materials that are the subject of the Manufacturing Services (including, but not limited to, any new use, new formulation or any change in the method of producing, testing or storing Product in each case that are specific to the Product), including but not limited to (i) any regulatory filings made by Client, formulations, chemical compositions, or Specifications of the Product, and (ii) any and all Confidential Information of Client, including any chemical structures, composition of matter rights, process technology and other Inventions owned or controlled by Client at the Effective Date;

"**Client Property**" has the meaning specified in Section 8.3(v);

"**Client-Supplied Components**" means those Components to be supplied by Client or that have been supplied by Client;

"**CMC**" has the meaning specified in Section 7.8(c);

"**Commencement Date**" means the date on which any Regulatory Authority first approves Client's Product for commercial manufacture as notified by Client to Patheon;

"**Components**" means, collectively, all packaging components, raw materials, ingredients, excipients, containers, and other materials (including labels, product inserts and other labelling for the Products) required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Confidential Information**" has the meaning specified in Section 11.1;

"**Conversion Fee**" means the Price for performing the Manufacturing Services excluding the cost of Components;

"C-TPAT" has the meaning specified in Section 2.1(f);

"**Deficiencies**" have the meaning specified in Section 7.8(d);

"**Deficiency Notice**" has the meaning specified in Section 6.1(a);

"Delivery Date" means the date scheduled for shipment of Product under a Firm Order as set forth in Section 5.1(d);

"Disclosing Party" has the meaning specified in Section 11.1;

"**EMA**" means the European Medicines Agency;

"**FDA**" means the United States Food and Drug Administration;

"**Firm Orders**" have the meaning specified in Section 5.1(c);

"**Force Majeure Event**" has the meaning specified in Section 13.7;

"**GST**" has the meaning specified in Section 13.16(a)(iii);

"**Health Canada**" means the section of the Canadian Government known as Health Canada and includes, among other departments, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate;

"**Importer of Record**" has the meaning specified in Section 3.2(a);

"**Initial Term**" has the meaning specified in Section 8.1;

"**Intellectual Property**" includes, without limitation, rights in patents, patent applications, formulae, trademarks, trademark applications, trade-names, Inventions, copyrights, industrial designs, trade secrets, and know how;

"**Invention**" means information about any innovation, improvement, development, discovery, computer program, device, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which it is contained and whether or not patentable or copyrightable;

"**Inventory**" means all inventories of Components and work-in-process produced or held by Patheon for the manufacture of the Products but, for greater certainty, does not include the Active Materials;

"**Laws**" means all laws, statutes, ordinances, regulations, rules, by-laws, judgments, decrees or orders of any Authority;

"Long Term Forecast" has the meaning specified in Section 5.1(a);

"**Manufacturing Services**" means the manufacturing, quality control, quality assurance, stability testing, packaging, and related services, as set forth in this Agreement, required to manufacture Product or Products using the Active Materials, Components, and Bill Back Items;

"**Manufacturing Site**" means the applicable facility where the Manufacturing Services are performed that is owned and operated by Patheon France S.A.S that is located at located at 40, boulevard de Champaret - BP 448 38317 Bourgoin-Jallieu Cedex (France);

"Materials" means all Components and Bill Back Items required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Maximum Credit Value**" means the maximum value of Active Materials that may be credited by Patheon under this Agreement, as set forth on Schedule D;

"**Minimum Order Quantity**" means the minimum number of batches of the Product to be produced during the same cycle of manufacturing as set forth on Schedule B;

"**Obsolete Stock**" has the meaning specified in Section 5.2(b);

"**Patheon Competitor**" means a business that derives greater than [***] of its revenues from performing contract pharmaceutical development or commercial manufacturing services for third parties;

"Patheon Intellectual Property" means Intellectual Property generated or derived by Patheon before performing any Manufacturing Services, or Intellectual Property that is otherwise generated or derived by Patheon in its business which Intellectual Property is not specific to, or dependent upon, Client's Active Material or Product including, without limitation, Inventions and Intellectual Property which may apply to manufacturing processes or the formulation or development of drug products, drug product dosage forms or drug delivery systems unrelated to the specific requirements of the Product(s); provided that Patheon Intellectual Property shall not include Product Inventions;

"Price" means the price measured in EUROS to be charged by Patheon for performing the Manufacturing Services, and includes the cost of Components (other than Client-Supplied Components), certain cost items as set forth on Schedule B, and annual stability testing costs as set forth on Schedule C (as defined in Section 13.1);

"**Product(s)**" means the product(s) listed on Schedule A;

"**Product Claims**" have the meaning specified in Section 6.3(c);

"**Quality Agreement**" means the separate and binding agreement between Client and Patheon France S.A.S setting out the quality assurance standards for the Manufacturing Services to be performed by Patheon for Client for this Agreement;

"**Recall**" has the meaning specified in Section 6.2(a);

"**Recipient**" has the meaning specified in Section 11.1;

"**Regulatory Authority**" means the FDA, EMA, and Health Canada and any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products including the Products in the Territory;

"**Regulatory Approval**" has the meaning specified in Section 7.8(a);

"**Representatives**" means a party's directors, officers, employees, advisers, agents, consultants, subcontractors, service partners, professional advisors, or representatives;

"Resident Jurisdiction" has the meaning specified in Section 13.16(a)(i);

"**Shortfall**" has the meaning specified in Section 2.2(b);

"**Specifications**" means the file for the Product, which is given by Client to Patheon in accordance with the procedures listed on Schedule A and which contains documents relating to the Product, including, without limitation:

(a) specifications for Active Materials and Components;

(b) manufacturing specifications, directions, and processes;

(c) storage requirements;

(d) all environmental, health and safety information for the Product including material safety data sheets; and

(e) the finished Product specifications, packaging specifications and shipping requirements for the Product;

all as updated, amended and revised from time to time by Client in accordance with the terms of this Agreement;

"Surplus" has the meaning specified in Section 2.2(c);

"**Target Yield**" has the meaning specified in Section 2.2(a);

"**Target Yield Determination Batches**" has the meaning specified in Section 2.2(a);

"**Tax**" or "**Taxes**" have the meaning specified in Section 13.16(a);

"**Technical Dispute**" has the meaning specified in Section 12.2;

"**Territory**" means world-wide;

"**Third Party Rights**" means the Intellectual Property of any third party;

"**VAT**" has the meaning specified in Section 13.16(d);

"**Year**" means in the first year of this Agreement, the period from the Effective Date up to and including December 31 of the same calendar year, and thereafter will mean a calendar year.

"**Yearly Forecast Volume**" or "**YFV**" has the meaning specified in Section 4.2.1; and

"**Zero Forecast Period**" has the meaning specified in Section 5.1(f).

1.2

Unless otherwise agreed in writing, all monetary amounts expressed in this Agreement are in EUROS.

1.3 Headings.

The division of this Agreement into Articles, Sections, Subsections, and Schedules and the insertion of headings are for convenience of reference only and will not affect the interpretation of this Agreement. Unless otherwise indicated, any reference in this Agreement to a Section or Schedule refers to the specified Section, or Schedule to this Agreement. In this Agreement, the terms "**this Agreement**",

"**hereof**", "**herein**", "**hereunder**" and similar expressions refer to this Agreement as a whole and not to any particular part, Section, or Schedule of this Agreement.

1.4

Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa.

1.5

The following Schedules are attached to, incorporated in, and form part of this Agreement:

Schedule A	-Product List and Specifications
Schedule B	- Minimum Order Quantity, Annual Volume, and Price
Schedule C	-Annual Stability Testing [and Validation Activities (if applicable)]
Schedule D	-Active Materials, Active Materials Credit Value, and Maximum Credit Value
Schedule E	-Technical Dispute Resolution
Schedule F	-Quarterly Active Materials Inventory Report
Schedule G	-Report of Annual Active Materials Inventory Reconciliation and Calculation of Actual Annual Yield

ARTICLE 2

PATHEON'S MANUFACTURING SERVICES

2.1 Manufacturing Services.

2.1.1 **Appointment**. Subject to the terms of this Agreement, Client hereby appoints Patheon to perform the Manufacturing Services for the "**Territory**" and to supply "**Product**" to Client for its commercial purposes, and Patheon hereby agrees to perform the Manufacturing Services and supply the Product to Client for its commercial purposes in accordance with the Specifications, cGMPs and all Applicable Laws for the Product Price set forth in Schedule B. Except as otherwise set forth in this Section 2.1, Client will have the right to purchase Product from Patheon during the term of this Agreement by placing Firm Orders for its Product requirements in accordance with Section 5.1. Notwithstanding the foregoing, during the Initial Term, Client agrees to purchase from Patheon [***] of its Product requirements based on total number of bottles ordered (the "**Exclusivity Obligation**"). Any Product produced with respect to qualifying such alternative Product manufacturers shall not count towards Client's Exclusivity Obligation hereunder. Patheon will be obligated to manufacture and supply all such Product ordered pursuant to Section 5. But the Exclusivity Obligation will cease to be binding on Client and will be permanently converted into a non-exclusive right to purchase Product from Patheon for the remaining portion of the Initial Term (i) in the event of a material breach by Patheon of any of the terms of this Agreement, which breach is not cured within the period set forth in Section 8.2(a), or (ii) under the circumstances set forth in Section 2.2(f). In the event that Client's requirements for Product exceed those identified in Schedule B and such required increase in production by Patheon needs additional capital investment, then the parties shall discuss in good faith the allocation of cost and timelines associated therewith. In the absence of any good faith agreement, Client shall be entitled to obtain the additional product above Patheon's existing

capacity from a third party without any obligation to Patheon. In the event that Patheon enters into any other agreements, including licensing or manufacturing agreements, with any third parties in relation to the manufacture of any product(s) for intranasal administration of metoclopramide, Client's Exclusivity Obligation under this Section 2.1.1 shall immediately terminate.

Client will be entitled to take such steps as are necessary to qualify one or more alternative Product manufacturers at any time during the term of this Agreement. Patheon agrees to cooperate with Client and provide all assistance, at Client's expense, as may reasonably be requested by Client to qualify an alternate manufacturer. Patheon will not have to give an alternative manufacturer access to the Manufacturing Site.

2.1.2 **Performance of Manufacturing Services**. In performing the Manufacturing Services, Patheon and Client agree that:

(a) Conversion of Active Materials and Components. Patheon will convert Active Materials and Components into Products.

(b) Quality Control and Quality Assurance. Patheon will perform the quality control and quality assurance testing specified in the Quality Agreement. Batch review and release to Client will be the responsibility of Patheon's quality assurance group. Patheon will perform its batch review and release responsibilities in accordance with Patheon's standard operating procedures. Each time Patheon ships Products to Client, it will give Client a certificate of analysis and certificate of compliance including a statement that the batch has been manufactured and tested in accordance with Specifications and cGMPs. Client will have sole responsibility for the release of Products to the market. The form and style of batch documents, including, but not limited to, batch production records, lot packaging records, equipment set up control, operating parameters, and data printouts, raw material data, and laboratory notebooks are the exclusive property of Patheon. Specific Product related information contained in those batch documents is Client property.

(c) Components. Patheon will purchase all Components (with the exception of Client-Supplied Components) and test all Components (including Client-Supplied Components if required by the specifications) at Patheon's expense as required by the Specifications.

(d) Stability Testing. Patheon will conduct stability testing on the Products in accordance with the protocols set out in the Specifications for the separate fees and during the time periods set out in Schedule C. Patheon will not make any changes to these testing protocols without prior written approval from Client. If a confirmed stability test failure occurs, Patheon will notify Client within [***], after which Patheon and Client will jointly determine the proceedings and methods to be undertaken to investigate the cause of the failure, including which party will bear the cost of the investigation. Patheon will not be liable for these costs unless it has failed to perform the Manufacturing Services in accordance with the Specifications and cGMPs. Patheon will give Client all stability test data and results at Client's request.

(e) Packaging and Artwork. Patheon will package the Products in accordance with the Specifications. Client will be responsible for the cost of artwork development. Patheon with consent of Client, will determine and imprint the batch numbers and expiration dates for each Product shipped. The batch numbers, the serialization numbers and expiration dates will be affixed on the Products and on the shipping carton of each Product as outlined in the Specifications and as required by cGMPs. Client may, in its sole discretion, make changes to labels, product inserts, and other packaging for the Products. Those changes will be submitted by Client to all applicable Regulatory Authorities and other third parties responsible for the approval of the Products. Client will be responsible for the cost of labelling obsolescence when changes occur, as contemplated in Section 4.4. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Laws; or (ii) Patheon consents in writing to the use of its name. At least [***] prior to the Delivery Date of Product for which new or modified artwork is required, Client will provide at no cost to Patheon, final camera ready artwork for all packaging Components to be used in the manufacture of the Product that meet the Specifications. For the avoidance of doubt, the parties acknowledge and agree that Client will be responsible for complying with any and all regulatory requirements for the labeling of the Product.

(f) Active Materials and Client-Supplied Components. As soon as possible and at least [***] before the scheduled production date, Client will deliver the Active Materials and any Client-Supplied Components to the Manufacturing Site DDP (Incoterms 2010), at no cost to Patheon, with any VAT paid by Client, in sufficient quantity to enable Patheon to manufacture the desired quantities of Product and to ship Product on the Delivery Date. If the Active Materials and/or Client-Supplied Components are not received [***] before the scheduled production date, Patheon may delay the shipment of Product by the same number of days as the delay in receipt of the Active Materials and/or Client-Supplied Components. But if Patheon is unable to manufacture Product to meet this new shipment date due to prior third party production commitments, Patheon may delay the shipment until a later date as agreed to by the parties. All shipments of Active Material will be accompanied by certificate(s) of analysis from the Active Material manufacturer and the Client, confirming the identity and purity of the Active Materials and its compliance with the Active Material specifications. For Active Materials or Client-Supplied Components which may be subject to import or export, Client agrees that its vendors and carriers will comply with applicable requirements of the U.S. Customs and Border Protection Service and the Customs Trade Partnership Against Terrorism ("**C-TPAT**").

(g) Bill Back Items. Bill Back Items will be charged to Client, with prior written approval, at Patheon's cost plus an [***] handling fee, with a maximum handling fee of [***] per item acquired. Patheon will use commercially reasonable efforts to obtain the best available pricing for all Bill Back Items, and will provide Client with an estimate for the actual costs of Bill Back.

(h) Validation Activities (if applicable). At the Client's request, Patheon will (i) assist in the development and approval of the validation protocols for analytical methods and manufacturing procedures (including packaging procedures) for the Products and (ii) validate all applicable processes, methods, equipment, utilities, facilities and computers

used in the manufacture, packaging, storage, testing and release of Products in conformance with all Applicable Laws, including, but not limited to, cGMPs. Upon request, Patheon will provide to Client a copy of the results of Product specific validation when such results are available. The fees for this service are not included in the Price and will be mutually agreed from time to time.

(i) Product Rejection for Finished Product Specification Failure. If a batch or a portion of a batch is rejected (outside of typical batch yield variations) and the deviation does not determine that Patheon has failed to provide the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws ("**Rejected Properly Manufactured Product"**), Client will pay Patheon the applicable fee per unit for the Rejected Properly Manufactured Product. For greater certainty, Client will pay Patheon the applicable fee per unit for the Rejected Properly Manufactured Product under the circumstances described in Section 6.3(c). The API in the Rejected Properly Manufactured Product will be included in the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a).

(j) Storage. Until finished Products have been issued a Certificate of Analysis and Compliance or unless otherwise directly requested by Client, Patheon shall store all such Products in preparation for shipment to Client's destination of choice identifiably distinct from any other raw material and finished or filled product stocks and shall comply with all storage requirements set forth in the Specifications and all Applicable Laws, including, but not limited to, cGMPs. Patheon shall assume responsibility for any loss or damage to such finished Product while stored by Patheon.

(k) Additional Services. If Client requests services other than those expressly set forth herein (such as qualification of a new packaging configuration or shipping studies, or validation of alternative batch sizes), Patheon will provide a good faith and reasonable written quote of the fee for the additional services and Client will advise Patheon whether it wishes to have the additional services performed by Patheon. The scope of work and fees will be set forth in a separate agreement signed by the parties. The terms and conditions of this Agreement will apply to these services.

2.2 Active Material Yield.

(a) Reporting. Patheon will give Client a quarterly inventory report of the Active Materials held by Patheon using the inventory report form set out in Schedule F, which will contain the following information for the quarter:

Quantity Received: The total quantity of Active Materials that complies with the Specifications and is received at the Manufacturing Site during the applicable period.

Quantity Dispensed: The total quantity of Active Materials dispensed at the Manufacturing Site during the applicable period. The Quantity Dispensed is calculated by adding the Quantity Received to the inventory of Active Materials that complies with the Specifications held at the beginning of the applicable period, less the inventory of Active Materials that complies with the Specifications held at the end of the period. The Quantity Dispensed will only include Active Materials received and dispensed in commercial manufacturing of Products and, for certainty, will not include any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv)

Active Materials received or dispensed in technical transfer activities or development activities during the applicable period, including without limitation, any regulatory, stability, validation or test batches manufactured during the applicable period.

(b) **Quantity Converted:** The total amount of Active Materials contained in the Products manufactured with the Quantity Dispensed (including any additional Products produced in accordance with Section 6.3(a) or 6.3(b)), delivered by Patheon, and not rejected, recalled or returned in accordance with Section 6.1 or 6.2 because of Patheon's failure to perform the Manufacturing Services in accordance with Specifications, cGMPs, and Applicable Laws.

(c) Within [***] after the end of each Year, Patheon will prepare an annual reconciliation of Active Materials on the reconciliation report form set forth in Schedule G including the calculation of the "**Actual Annual Yield**" or "**AAY**" for the Product at the Manufacturing Site during the Year. AAY is the percentage of the Quantity Dispensed that was converted to Products and is calculated as follows:

$$\frac{\text{Quantity Converted during the Year}}{\text{Quantity Dispensed during the Year}} \times [***]$$

After Patheon has produced a minimum of 25 successful commercial production batches of Product (for clarity, including batches for marketing product, prescription product or a combination thereof) and has produced commercial production batches for at least [***] at the Manufacturing Site (collectively, the "**Target Yield Determination Batches**"), the parties will agree on the target yield for the Product at the Manufacturing Site (each, a "**Target Yield**"). The Target Yield will be revised annually to reflect the actual manufacturing experience as agreed to by the parties.

(b) Shortfall Credit Calculation. Patheon will use commercially reasonable efforts to maintain AAY levels for the Product above the applicable Target Yield. If the Actual Annual Yield falls more than [***] for less than [***] batch [***] for [***] batches, or [***] for greater than [***] batches below the respective Target Yield in a Year, then the shortfall for the Year (the " **Shortfall**") will be calculated as follows:

Shortfall = [***]

(c) Surplus Calculation. If the Actual Annual Yield is more than the respective Target Yield in a Year, then the surplus for that Year (the "**Surplus**") will be determined based on the following calculation:

Surplus = [***]

(c) Credit for Shortfall. If there is a Shortfall for the Product in a Year, then Patheon will credit Client's account for the amount of the Shortfall not later than [***] after the end of the Year. If there is a Surplus for a Product in a Year, then Patheon will be entitled to apply the amount of the Surplus as a credit against any Shortfall for that Product which may occur in the next Year. If there is no Shortfall in the next Year t he Surplus credit will expire. Each credit under this Section 2.2(c) will be summarized on the reconciliation report form set forth in Schedule G. Upon expiration or termination of this Agreement, any remaining credit owing under this Section will be paid to Client. The Annual Shortfall, if any, will be disclosed by Patheon on the reconciliation report form.

(d) Casualty Losses. Patheon shall notify Client in writing in the event that an amount of API with a value greater than or equal to [***] of API is damaged, lost or otherwise rendered unusable at any one time as soon as practicable following such incident. In addition, and notwithstanding any provision in this Section 2.2 to the contrary, [***] involving Patheon's Manufacturing Site (a "**Casualty Loss**") within [***] after Patheon receives the proceeds of insurance from its insurance provider in cleared funds and an appropriate invoice from Client. Patheon's liability for a Casualty Loss will not exceed the lesser of [***] USD or [***]. Patheon shall only insure Active Materials up to the values recommended and provided to Patheon by Client. If any such losses are unrecoverable due to the under-estimation of such values, then Patheon shall not be liable for such unrecoverable losses. Said insurance shall be on an "all risks of physical damage" form, subject to the policy's terms and conditions with exclusions such as: Delay, Deterioration, Inherent Vice, Nuclear Hazards, Loss of Market, Wear and Tear, Error or Deficiency in Design, Mechanical or Electrical Malfunction, Infidelity of the Assured or its Employees, Radioactive Contamination, Losses caused by Process, Mysterious Disappearance, Taking of Inventory, Biological, Biochemical or Electromagnetic Contamination. For purposes of calculating the AAY above, all Active Materials reimbursed to Client as a Casualty Loss shall be removed from the Quantity Received and Quantity Dispensed totals.

(e) Maximum Credit. Excluding liability for Casualty Losses, Patheon's liability for Active Material calculated in accordance with this Section 2.2 the Product in a Year will not exceed, in the aggregate, the Maximum Credit Value set forth in Schedule D.

(f) No Material Breach. It will not be a material breach of this Agreement by Patheon under Section 8.2(a) if the Actual Annual Yield is less than the Target Yield. But Client will be released from the Exclusivity Obligation set forth in Section 2.1.1 if the Actual Annual Yield falls more than [***] below the Target Yield in any Year.

ARTICLE 3

CLIENT'S OBLIGATIONS

3.1

Upon receipt of a properly rendered invoice in accordance with Section 5.5, Client will pay Patheon for performing the Manufacturing Services according to the Prices specified in Schedules B and

C. These Prices may be subject to adjustment under other parts of this Agreement. Client will also pay Patheon for any Bill Back Items.

6.2 Qualification of Additional Sources of Supply.

(a) Client will at its sole cost and expense deliver the Active Materials to Patheon in accordance with Section 2.1(f). If applicable, Patheon and the Client will reasonably cooperate to permit the import of the Active Materials to the Manufacturing Site. Client's obligation will include obtaining the proper release of the Active Materials from the applicable Customs Agency and Regulatory Authority. Client or Client's designated broker will be the "**Importer of Record**" for Active Materials imported to the Manufacturing Site. The Active Materials will be held by Patheon on behalf of Client as set forth in this Agreement. Title to the Active Materials will at all times remain the property of Client. Any Active Materials received by Patheon will only be used by Patheon to perform the Manufacturing Services. Client will be responsible for paying for all rejected Product that arises from defects in the Active Materials which could not be reasonably discoverable by Patheon using the test methods set forth in the Specifications. Client's failure to supply Patheon with Active Materials in accordance with the timeframes set forth in Section 2.1(f) will not be deemed a breach of this Agreement.

(b) If Client asks Patheon to qualify an additional source for the Active Material or any Component, Patheon may agree to evaluate the Active Material or Component to be supplied by the additional source to determine if it is suitable for use in the Product. The parties will agree on the scope of work to be performed by Patheon at Client's cost. For an Active Material, this work at a minimum will include: (i) laboratory testing to confirm the Active Material meets existing specifications; (ii) manufacture of an experimental batch of Product that will be placed on [***] accelerated stability; and (iii) manufacture of [***] validation batches that will be placed on concurrent stability (one batch may be the registration batch if manufactured at full scale).

(d) Patheon will promptly advise Client if it encounters supply problems, including delays and/or delivery of non-conforming Active Material or Components from a Client designated additional source; and Patheon and Client will cooperate to reduce or eliminate any supply problems from these additional sources of supply. Client will be obligated to certify all Client designated sources of supply on an annual basis at its expense and will provide Patheon with copies of these annual certifications as specified in the Quality Agreement. If Patheon agrees to certify a Client designated additional sources of supply on behalf of Client, it will do so at Client's expense.

ARTICLE 4

CONVERSION FEES AND COMPONENT COSTS

4.1

The Price for the first Year will be listed in Schedules B and C and will be subject to the adjustments set forth in Sections 4.2 and 4.3. The Price may also be [***] by Patheon at any time upon

written notice to Client if there are changes to the underlying manufacturing, packaging or testing assumptions set forth in Schedule B that result in an increase or decrease in the cost of performing the Manufacturing Services.

4.2 Subsequent Years' Pricing.

After the first Year, Patheon may adjust the Price effective January 1st of each Year as follows:

(a) Manufacturing and Stability Testing Costs. Patheon may adjust the conversion component of the Price and the annual stability testing costs for inflation, based upon the preliminary number for any increase in the "Indices de salaires mensuels de base des salaries de l'industrie pharmaceutique", published by Les Entreprises du médicament (LEEM) during the prior Contractual Year (For illustration: http://www.leem.org/article/les-indices-des-salaires-de-lindustrie-pharmaceutique) in August of the preceding Year compared to the final number for the same month of the Year prior to that, unless the parties otherwise agree in writing. On or about [***] of each Year, Patheon will give Client a statement setting forth the calculation for the inflation adjustment to be applied in calculating the Price for the next Year.

(b) Component Costs. If Patheon incurs an increase in Component costs during the Year (for clarity, this excludes Client-Supplied Components), it may increase the Price for the next Year to pass through the additional Component costs at Patheon's cost; provided, however, that in the event any proposed increase in the cost of a Component exceeds [***] of the cost for that Component upon which the most recent fee quote was based, and that a change of supplier is mutually agreed between Patheon and Client pursuant to Section 4.2(e), Patheon and Client will use commercially reasonable efforts to locate an equivalent alternative lower cost supplier for the applicable Component. If as a result of both parties' efforts pursuant to Section 4.2(e) (but not if Patheon is acting alone) Patheon incurs a net decrease (including any rebates or discounts) in Component costs during the Year, the net cost savings will be [***] in accordance with Section 4.2(e) and it will decrease the Price for the next Year to pass through the additional Component cost savings allocated to Client (but not those allocated to Patheon). On or about [***] of each Year, Patheon will give Client information about the increase or decrease in Component costs which will be applied to the calculation of the Price for the next Year to reasonably demonstrate that any Price increase or decrease is in compliance with this Section 4.2(b). But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(c) Pricing Basis. Client acknowledges that the Price in any Year is quoted based upon the Minimum Order Quantity and the Annual Volume specified in Schedule B. The Price is subject to change if the specified Minimum Order Quantity changes or if the Annual Volume is not ordered in a Year. For greater certainty, if Patheon and Client agree that the Minimum Order Quantity will be reduced or the Annual Volume in the lowest tier will not be ordered in a Year whether as a result of a decrease in estimated Annual Volume or otherwise and, as a result of the reduction, Patheon demonstrates to Client that its costs to perform the Manufacturing Services or to acquire the Components for the Product

will increase on a per unit basis (including the amount of the increase), then Patheon may increase the Price by an amount sufficient to absorb the documented increased costs. On or before November 30 of each Year, Patheon will give Client a statement setting forth the information to be applied in calculating those cost increases for the next Year. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(d) Tier Pricing (if applicable). The pricing in Schedule B is set forth in Annual Volume tiers based upon the Client's volume forecasts under Section 5.1. The Client will be invoiced during the Year for the unit price set forth in the Annual Volume tier based on the [***] forecast provided in September of the previous Year. Within [***] after the end of each Year or of the termination of the Agreement, Patheon will send Client a reconciliation of the actual volume of Product ordered by the Client during the Year with the pricing tiers. If Client has overpaid during the Year, Patheon will issue a credit to the Client for the amount of the overpayment within [***] after the end of the Year or will issue payment to the Client for the overpayment within [***] after the termination of the Agreement. If Client has underpaid during the Year, Patheon will issue an invoice to the Client under Section 5.5 for the amount of the underpayment within [***] after the end of the Year or termination of the Agreement. If Client disagrees with the reconciliation, the parties will work in good faith to resolve the disagreement amicably. If the parties are unable to resolve the disagreement within [***], the matter will be handled under Section 12.1.

(e) Cost Improvement Program. Patheon and Client agree to work together to develop cost reduction initiatives as part of an overall cost improvement program, provided such program does not involve additional capital or extraordinary costs unless otherwise agreed to by parties in writing. All net cost savings (net of implementation costs) realized from the cost improvement program [***], unless otherwise agreed to by the parties in writing. A "Cost Reduction Initiative" for the purpose of this Agreement will be an initiative that reduces the internal or out-of-pocket costs incurred by a party in connection with the performance of its obligations under this Agreement. It is further agreed by the parties that on-going method improvements developed or adopted by either Client or Patheon independently of the other party(ies), will not be a cost reduction initiative under this section, and there will be no obligation on such party to share the net cost savings realized from such improvement with the other party(ies) to this Agreement.

(f) For all Price adjustments under this Section 4.2, Patheon will deliver to Client on or before [***] of each Year a revised Schedule B to be effective for Product delivered on or after the first day of the next Year. If in any Year Patheon would have been entitled to increase the Price based on any of the provisions of this Section 4.2 but Patheon did not exercise its right to do so, then at the expiry of any subsequent Year, Patheon will be entitled to make cumulative adjustments as set out in Section 4.2 based on changes during all of the preceding Years since Patheon last adjusted the Price.

4.3 Next Year Pricing.

During any Year, the Prices set out in Schedule B will be adjusted as follows:

Extraordinary Increases in Component Costs. If, at any time, market conditions result in Patheon's cost of Components being materially greater than normal forecasted increases, then Patheon will be entitled to adjust the Price for any affected Product to compensate it for the increased Component costs. Changes materially greater than normal forecasted increases will have occurred if: (i) the cost of a Component increases by [***] of the cost for that Component upon which the most recent Price or fee quote was based; or (ii) the aggregate cost for all Components required to manufacture the Product increases by [***] of the total Component costs for the Product upon which the most recent fee quote was based. If Component costs have been previously adjusted to reflect an increase in the cost of one or more Components, the adjustments set out in (i) and (ii) above will operate based on the last cost adjustment for the Components.

For a Price adjustment under this Section 4.3, Patheon will deliver to Client a revised Schedule B and budgetary pricing information, adjusted Component costs, and other documents reasonably sufficient to demonstrate that a Price adjustment is justified. Upon request of Client, Patheon will share the standard prices to be paid by Patheon to its supplier for the Components as stipulated in Patheon's SAP system, it being understood and agreed that Patheon will have no obligation to deliver any supporting documents that are subject to obligations of confidentiality between Patheon and its suppliers, but Patheon shall use commercially reasonable efforts to minimize the restrictions imposed by such confidentiality obligations on disclosure of supporting documents to Client. The revised Price will be effective for any Product delivered on or after the first day of the month following Client's receipt of the revised Schedule B.

4.4 Changes or Regulatory Authority Requirements.

Amendments to the Specifications or the Quality Agreement requested by Client will be implemented only following a technical and cost review that Patheon will perform at Client's cost and are subject to Client and Patheon reaching agreement on Price changes required because of the amendment. Amendments to the Specifications, the Quality Agreement, or the Manufacturing Site requested by Patheon will only be implemented following the written approval of Client, the approval not to be unreasonably withheld, conditioned or delayed. If Client accepts a proposed Price change, the proposed change in the Specifications or the Quality Agreement and the associated scope of work will be implemented at Client's cost, and the Price change will become effective, only for those orders of Product that are manufactured under the revised Specifications. In addition, Client agrees to purchase, at the price paid by Patheon (including all costs incurred by Patheon for the purchase, handling and transport of the Inventory), all Inventory held under the "old" Specifications and purchased or maintained by Patheon in order to fill Firm Orders or under Section 5.2, if the Inventory can no longer be used under the revised Specifications. Patheon will use commercially reasonable efforts to cancel any open purchase orders for Components no longer required under any revised Specifications that were placed by Patheon with suppliers in order to fill Firm Orders or under Section 5.2 and if the orders may not be cancelled without penalty, will be assigned to and paid for by Client. Additional payments or price increases may also be required to compensate Patheon for fees and other expenses incurred by Patheon to comply with additional Regulatory Authority requirements which apply to the Manufacturing Services.

4.5 Multi-Country Packaging Requirements.

If Client decides to have Patheon perform Manufacturing Services for the Product for more than one country inside the Territory, then Client will inform Patheon of the packaging requirements for each such country and Patheon will prepare a quotation for consideration by Client of any additional costs for Components (other than Client-Supplied Components) and the changeover fees for the Product destined for each new country. The agreed additional packaging requirements and related packaging costs and change over fees will be set out in a written amendment to this Agreement.

ARTICLE 5

ORDERS, SHIPMENT, INVOICING, PAYMENT

5.1 Orders and Forecasts.

(a) Long Term Forecast. As soon as reasonably practicable following the Effective Date, Client will give Patheon a non-binding [***] forecast of Client's volume requirements for the Product for each Year during the term of the Agreement (the "**Long Term Forecast**"). The Long Term Forecast will thereafter be updated [***] during the Initial Term. If Patheon is unable to accommodate any portion of the Long Term Forecast, it will notify Client and the parties will agree on any revisions to the forecast.

(b) Rolling [***] Forecast. As soon as reasonably practicable following the Effective Date, Client will give Patheon a non-binding [***] forecast of the volume of Product that Client expects to order in the first [***] of commercial manufacture of the Product. This forecast will then be updated by Client on or before the tenth day of each month on a rolling forward basis. Client will update the forecast forthwith if it determines that the volumes estimated in the most recent forecast have changed by more than [***]. The most recent [***] forecast will prevail.

(c) Firm Orders. On a rolling basis during the term of this Agreement, Client will issue an updated [***] forecast on or before the [***] of each month. This forecast will start on the first day of the next month. The first [***] of this updated forecast will be considered binding firm orders. Concurrent with the [***] forecast, Client will issue a new firm written order in the form of a purchase order or otherwise ("**Firm Order**") by Client to purchase and, when accepted by Patheon, for Patheon to manufacture and deliver the agreed quantity of the Products. The Delivery Date will not be less than [***] following the date that the Firm Order is submitted. Firm Orders submitted to Patheon will specify Client's purchase order number, quantities by Product type, monthly delivery schedule, and any other elements necessary to ensure the timely manufacture and shipment of the Products. The quantities of Products ordered in those written orders will be firm and binding on Client and may not be reduced by Client. Expedited Firm Orders will be subject to additional fees.

(d) Acceptance of Firm Order. Patheon will accept Firm Orders by sending an acknowledgement to Client within [***] of its receipt of the Firm Order. The acknowledgement will include, subject to confirmation from the Client, the Delivery Date

for the Product ordered. The Delivery Date may be amended by agreement of the parties or as set forth in Section 2.1(f). If Patheon fails to acknowledge receipt of a Firm Order within the [***] period, the Firm Order will be deemed to have been accepted by Patheon.

(e) Cancellation of a Firm Order. If Client cancels a Firm Order, Client will pay Patheon [***] of the Conversion Fee for the Firm Order.

5.2

If Client forecasts zero volume for [***] period during the term of this Agreement (the "**Zero Forecast Period**"), then Patheon will have the option, at its sole discretion, to provide a [***] notice to Client of Patheon's intention to terminate this Agreement on a stated day within the Zero Forecast Period. Client thereafter will have [***] to either (i) withdraw the zero forecast and re-submit a reasonable volume forecast, or (ii) negotiate other terms and conditions on which this Agreement will remain in effect. Otherwise, Patheon will have the right to terminate this Agreement at the end of the [***] notice period.

5.3

(a) Client understands and acknowledges that Patheon will rely on the Firm Orders and rolling forecasts submitted under Section 5.1(b) in ordering the Components (other than Client-Supplied Components) required to meet the Firm Orders. In addition, Client understands that to ensure an orderly supply of the Components**,** Patheon may want to purchase the Components in sufficient volumes to meet the production requirements for Products during part or all of the forecasted periods referred to in Section 5.1(b) or to meet the production requirements of any longer period agreed to by Patheon and Client. Accordingly, Client authorizes Patheon to purchase Components to satisfy the Manufacturing Services requirements for Products for the first [***] contemplated in the most recent forecast given by Client under Section 5.1(b). Patheon may make other purchases of Components to meet Manufacturing Services requirements for longer periods if agreed to in writing by the parties. Client will give Patheon written authorization to order Components for any launch quantities of Product requested by Client which will be considered a Firm Order when accepted by Patheon.

(b) Client will reimburse Patheon for the cost of Components ordered by Patheon under Firm Orders or under Section 5.2(a) that are not included in finished Products manufactured for Client within six months after the forecasted month for which the purchases have been made (or for a longer period as the parties may agree) or if the Components have expired or are rendered obsolete due to changes in artwork or applicable regulations during the period (collectively, "**Obsolete Stock**"). This reimbursement will include Patheon's cost to purchase (plus a [***] handling fee up to [***] per line item) and destroy the Obsolete Stock; provided, however, that the client will have the option but not the obligation to take title to and possession of all or any portion of such Components by written notice to Patheon, in which case Patheon will cooperate with the Client in the surrender, delivery and transfer of such Components as promptly as is commercially reasonable, with any shipping and related expenses to be borne by the Client. If any non-expired Components are used in Products subsequently manufactured for Client or in third party products manufactured by Patheon, Client will receive credit for any costs of those Components previously paid to Patheon by Client.

(c) If Client fails to take possession or arrange for the destruction of non-expired Components within [***] of purchase or, in the case of the delivery of conforming finished Product not accepted by Client within [***] of manufacture, Client will pay Patheon [***] per pallet per month thereafter for storing the Components or finished Product. Storage fees for Components or Product which contain controlled substances or require refrigeration will be charged at [***] per pallet per month. Storage fees are subject to a one pallet minimum charge per month. Patheon may ship finished Product held by it longer than one month to the Client at Client's expense on [***] written notice to the Client.

5.4

Client may order Manufacturing Services for batches of Products only in multiples of the Minimum Order Quantities as set out in Schedule B.

5.5

The Product will be delivered to Client only after it has been manufactured and packaged in accordance with the Specifications. Unless agreed in advance by the Parties in writing, Patheon shall not deliver any Products prior to approval by Patheon's Quality Assurance department in accordance with the applicable Quality Agreement and Applicable Law. Shipments of Products will be made EXW (INCOTERMS 2010) Patheon's shipping point unless otherwise mutually agreed. Risk of loss or of damage to Products will remain with Patheon until Patheon loads the Products onto the carrier's vehicle for shipment at the shipping point at which time risk of loss or damage will transfer to Client. Patheon will, in accordance with Client's instructions and as agent for Client, at Client's risk (i) arrange for shipping, including preparing and executing a packing list, so that the Product will be delivered to the delivery address on the delivery date set forth in the applicable Firm Order, with such shipping to be paid by Client and (ii) at Client's risk and expense, obtain any export license or other official authorization necessary to export the Products. For clarity, the export of a drug product to non-EU countries which do not have a marketing authorization in France is subject to an export declaration to the French Health Authorities (ANSM). The export declaration can be handled by Patheon, this activity is charged [***] per export declaration that is actually shipped (as requested by Client). Client will arrange for insurance (including transit insurance) for the Product at all times from delivery and will select the freight carrier used by Patheon to ship Products and may monitor Patheon's shipping and freight practices as they pertain to this Agreement. Shipment charges will either be paid by Client directly to the shipping company or by Patheon to the shipping company on Client's behalf, in which case Client will pay Patheon the cost of shipment together with a handling fee of [***] up to [***] per shipment. Client will be responsible for complying with all applicable export laws and regulations and will pay any applicable export fees or taxes. Products will be packed and transported in accordance with the Specifications. Patheon will use commercially reasonable efforts to ensure that the date that Product is QP batch certified by Patheon will not be more than three months after the date of manufacture (excluding any Product that is the subject of a deviation or any event not solely within Patheon's control).

5.6

Invoices will be sent by email to the email address given by Client to Patheon in writing. Invoices will be issued when the Product is manufactured and released by Patheon to the Client. Patheon will also submit to Client, with each shipment of Products, a duplicate copy of the invoice covering the shipment. Patheon will also give Client an invoice covering any Inventory, Bill Back Items or Components

which are to be purchased by Client under Section 5.2 of this Agreement. Each invoice will, to the extent applicable, identify Client's Manufacturing Services purchase order number, Product numbers, names and quantities, unit price, freight charges, and the total amount to be paid by Client. Client will pay all invoices within [***] of the date of confirmed delivery email transmission of the invoice, i.e. confirmed by delivery receipt of the email transmission. If any portion of an invoice is disputed, the Client will pay Patheon for the undisputed amount and the parties will use good faith efforts to reconcile the disputed amount as soon as practicable. Interest on undisputed past due accounts will accrue at [***] per month which is equal to an annual rate of [***].

5.7

Claims for late delivery of Products will be dealt with by reasonable agreement of the parties, it being understood and agreed that Patheon, upon Client's request, will in any case use all reasonable efforts to remedy any late delivery of Products to be delivered under this Agreement. It is understood and agreed that if the Firm Order is more than [***] late Client may cancel any Firm Order for Products that are not delivered by Patheon in accordance with the agreed timelines, without any payment for such Firm Order being due by Client to Patheon provided that a Firm Order may not be cancelled (i) if any delay is caused by a late or incomplete delivery of Active Material or any related documentation or (ii) if Patheon has commenced performance of the Manufacturing Services relating to the Firm Order. Patheon shall be entitled to invoice any part of a Firm Order that has been delivered in accordance with Section 5.5. Any claim for a late delivery by Patheon will be deemed waived if it has not been presented within [***] of the date of receipt of invoice by Client. Any Firm Orders for Products cancelled pursuant to this Section 5.7 shall count towards Client's Exclusivity Obligation.

ARTICLE 6

PRODUCT CLAIMS AND RECALLS

6.1

(a) Product Claims. Client has the right to reject and return, at Patheon's expense for any Products for which Patheon has responsibility under Section 6.3 (and otherwise at Client's expense), any portion of any shipment of Products that deviate from the Specifications, cGMPs, or Applicable Laws, without invalidating any remainder of the shipment. Client will visually inspect the Products manufactured by Patheon upon receipt thereof and will give Patheon written notice (a "**Deficiency Notice**") of all claims for Products that deviate from the Specifications, cGMPs, or Applicable Laws, within [***] after Client's receipt thereof (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, within [***] after discovery by Client, but not after the expiration date of the Product). Should Client fail to give Patheon the Deficiency Notice within the applicable [***] period, then the delivery will be deemed to have been accepted by Client on the [***] after delivery or discovery, as applicable.

(b) Determination of Deficiency. Upon receipt of a Deficiency Notice, Patheon will have [***] to advise Client by notice in writing that it disagrees with the contents of the Deficiency Notice, if applicable. If Client and Patheon fail to agree within [***] after Patheon's notice to Client as to whether any Products identified in the Deficiency Notice deviate from the Specifications, cGMPs, or Applicable Laws, then the parties will mutually select an independent laboratory to evaluate if the Products deviate from the Specifications, cGMPs, or Applicable Laws. The parties will cause the independent laboratory to conduct

its evaluation as promptly as reasonably practicable. This evaluation will be binding on the parties. If the evaluation certifies that any Products deviate from the Specifications, cGMPs, or Applicable Laws, Client may reject those Products in the manner contemplated in this Section 6.1 and Patheon will be responsible for the cost of the evaluation. If the evaluation does not so certify for any of the Products, then Client will be deemed to have accepted delivery of the Products which are deemed to be conforming on the date the evaluation is delivered by the independent laboratory to the parties and Client will be responsible for the cost of the evaluation. With respect to any Products which Patheon agrees are deficient in accordance with the Deficiency Notice, or which are otherwise found to be deficient by the independent laboratory, Client will be entitled to the remedies set forth in Section 6.3(a).

(c) Shortages. Claims for shortages in the amount of Products shipped by Patheon will be dealt with by reasonable agreement of the parties.

6.2

(a) Records and Notice. Patheon and Client will each maintain records necessary to permit a Recall of any Products delivered to Client or customers of Client. Each party will promptly notify the other by telephone (to be confirmed in writing) of any information which might affect the marketability, safety or effectiveness of the Products or which might result in the Recall or seizure of the Products. Upon receiving this notice or upon this discovery, each party will stop making any further shipments of any Products in its possession or control until a decision has been made whether a Recall or some other corrective action is necessary. The decision to initiate a Recall or to take some other corrective action, if any, will be made and implemented by Client. "**Recall**" will mean any action (i) by Client to recover title to or possession of quantities of the Products sold or shipped to third parties (including, without limitation, the voluntary withdrawal of Products from the market); or (ii) by any regulatory authorities to detain or destroy any of the Products. Recall will also include any action by either party to refrain from selling or shipping quantities of the Products to third parties which would be subject to a Recall if sold or shipped.

(b) Recalls. If (i) any Regulatory Authority issues a directive, order or, following the issuance of a safety warning or alert about the Product, a written request that any Product be Recalled, (ii) a court of competent jurisdiction orders a Recall, or (iii) Client determines that any Product should be Recalled or that a "Dear Doctor" letter is required relating the restrictions on the use of any Product, Patheon will co-operate as reasonably required by Client, having regard to all applicable laws and regulations.

(c) Product Returns. Client will have the responsibility for handling customer returns of the Products. Patheon will give Client any assistance that Client may reasonably require to handle the returns.

6.3 Rejected Products.

(a) Defective Product. If Client rejects Products under Section 6.1 and the deviation is determined to have arisen from Patheon's failure to provide the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will credit Client's account for Patheon's invoice price for the defective Products. If Client previously paid for the defective Products, Patheon will promptly, at Client's election, either: (i) refund the invoice price for the defective Products; (ii) offset the amount paid against other amounts due to Patheon hereunder; or (iii) replace the Products with conforming Products, (provided that Patheon is able to manufacture replacement Product at the same Manufacturing Site as that of the rejected Products),without Client being liable for payment therefor under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. Patheon's responsibility for any loss of Active Materials in defective Product will be captured and calculated in the Active Materials Yield under Section 2.2.

(b) Recalled Product. If a Recall or return results from, or arises out of, a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will be responsible for the documented out-of-pocket expenses of the Recall or return and will promptly, at Client's election, either: (i) refund the invoice price for such Recalled or returned Products; (ii) offset such Recalled Product Credit Amount against other amounts due to Patheon hereunder; or (iii) use its commercially reasonable efforts to replace such Recalled or returned Products with conforming Products using the next available manufacturing slot without the Client being liable for payment therefore, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's direction, cost and expense. Patheon's responsibility for any loss of Active Materials in Recalled Product will be captured and calculated in the Active Materials Yield under Section 2.2.

(c) Except as set forth in Sections 6.3(a) and (b) above and for breaches of its representations and warranties set forth in Section 9.3 below, Patheon will not be liable to Client nor have any responsibility to Client for any deficiencies in, or other liabilities associated with, any Product manufactured by it, (collectively, "**Product Claims**"). For greater certainty, Patheon will have no obligation for any Product Claims to the extent the Product Claim (i) is caused by deficiencies in the Specifications, the safety, efficacy, or marketability of the Products or any distribution thereof, (ii) results from a defect in a Component that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications, (iii) results from a defect in the Active Materials, Client-Supplied Components or Components supplied by a Client designated additional source that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications, (iv) is caused by actions of Client or third parties occurring after the Product is shipped by Patheon under Section 5.5, (v) is due to packaging design or labelling defects or omissions for which Patheon has no responsibility, (vi) is due to any unascertainable reason despite Patheon having performed the Manufacturing Services in accordance with the Specifications, cGMP's, and Applicable Laws, or (vii) is due to any other breach by Client of its obligations under this Agreement.

6.4

Client will not dispose of any damaged, defective, returned, or Recalled Products for which it intends to assert a claim against Patheon without Patheon's prior written authorization to do so. Alternatively, Patheon may instruct Client to return the Products to Patheon. Patheon will bear the cost of disposition for any damaged, defective, returned or Recalled Products for which it bears responsibility under Section 6.3, and will promptly reimburse Client for any such costs which may be incurred by Client. In all other circumstances, Client will bear the cost of disposition, including all applicable fees for Manufacturing Services, for any damaged, defective, returned, or Recalled Products. Notwithstanding the foregoing, the Client will have the right at all times to retain a reasonable sample of such Products for its own archival purposes.

6.5 Complaints.

Client will have the sole responsibility for responding to questions and complaints from its customers. Questions or complaints received by Patheon from Client's customers, healthcare providers or patients will be promptly referred to Client. Patheon will co-operate as reasonably required to allow Client to determine the cause of and resolve any questions and complaints. This assistance will include follow-up investigations, including testing. In addition, Patheon will give Client all agreed upon information that will enable Client to respond properly to questions or complaints about the Products as set forth in the Quality Agreement. Patheon will notify Client promptly and in any event not later than specified in the Quality Agreement after it becomes aware of any adverse event associated with the use of the Products, whether or not determined to be attributable to the Products, and whether or not deemed to be serious or

non-serious. Such information will be sent to the Client as set forth in the Quality Agreement. If it is determined that the cause of the complaint or adverse event resulted from a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, Patheon will bear all costs incurred under this Section 6.5. In all other circumstances, such costs will be borne by Client.

6.6

Except for the indemnity set forth in Section 10.3 and subject to the limitations set forth in Sections 10.1 and 10.2, the remedies described in this Article 6 will be Client's sole remedy for any failure by Patheon to provide the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws or for any breach by Patheon of its representations and warranties set forth in Section 9.3.

ARTICLE 7

CO-OPERATION

7.1

Each party will forthwith upon execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the parties. The relationship managers will meet not less than quarterly to review the current status of the business relationship and manage any issues that have arisen.

7.2

Subject to Section 7.8, each party may communicate with any governmental agency, including but not limited to governmental agencies responsible for granting Regulatory Approval for the Products, regarding the Products if, in the opinion of that party's counsel, the communication is necessary to comply with the terms of this Agreement or the requirements of any law, governmental order or regulation. Unless, in the reasonable opinion of its counsel, there is a legal prohibition against doing so, a party will permit the other party to accompany and take part in any communications with the agency, and to receive copies of all communications from the agency.

7.3

Patheon will keep records of the manufacture, testing, and shipping of the Products, Active Materials, and Components and retain samples of the Products, Active Materials, and Components as are necessary to comply with all Applicable Laws, including manufacturing regulatory requirements applicable to Patheon, the Manufacturing Site, the Products, the Active Materials and/or Components (provided that the requirements applicable to the Products, Active Materials and Components are notified and agreed with Patheon in advance), as well as to assist with resolving Product complaints and other similar investigations. Copies of the records and samples will be retained for one year following the date of Product expiry, or longer if required by law or regulation, following which time Client will be contacted concerning the delivery and destruction of the documents and/or samples of Products. Patheon reserves the right to destroy or return to Client, at Client's sole expense, any document or samples for which the retention period has expired if Client fails to arrange for destruction or return within [***] of receipt of notice from Patheon. Client

is responsible for retaining samples of the Products necessary to comply with the legal/regulatory requirements applicable to Client.

7.4 Inspection.

Client may inspect Patheon reports and records relating to this Agreement during normal business hours and with reasonable advance notice, but a Patheon representative must be present during the inspection.

7.5 Access.

Patheon will give Client reasonable access at agreed times to the areas of the Manufacturing Site in which the Products are manufactured, stored, handled, or shipped to permit Client to verify that the Manufacturing Services are being performed in accordance with the Specifications, cGMPs, and Applicable Laws. But, with the exception of "for-cause" audits, Client will be limited each Year to one cGMP-type audit, lasting no more than [***] days, and involving no more than two auditors. Client may request additional cGMP-type audits, additional audit days, or the participation of additional auditors subject to payment to Patheon of a fee of [***] for each additional audit day and [***] per audit day for each additional auditor. The right of access set forth in Sections 7.4 and 7.5 will not include a right to access or inspect Patheon's financial records. Patheon will support the Pre-Approval Inspection of the FDA ("PAI") and equivalent regulatory inspection for other jurisdictions (where applicable) and provide a copy of the resulting report. The first PAI is at no cost to Client. Additional PAI or equivalent support will be subject to additional fees.

7.6 Regulatory Inspections.

Patheon will make its internal practices, books and records relating to the manufacture of the Products available and allow access to all facilities used for manufacturing the Products to any Authority having jurisdiction over the manufacture of the Products for the purposes of determining Patheon's compliance with Applicable Laws, including, but not limited to, cGMPs. Patheon will notify Client by telephone and e-mail within [***] of any proposed or announced inspections, and as soon as possible (but in any case within [***]) after any unannounced inspection, by any Authority relating to the Products. Patheon will provide the Client with a reasonable description in writing of each such inspection promptly (but in no event later than specified in the Quality Agreement) thereafter, and with copies of any Authority-issued inspection observation reports (including, without limitation, form 483s and equivalent forms from other regulatory bodies) and Authority correspondence, purged only of confidential information that is unrelated to the Products. Patheon will also notify Client of receipt of any other form 483's or warning letters or any other significant regulatory action which Patheon's quality assurance group determines could impact the regulatory status of the Products. Patheon and Client will cooperate in resolving any concerns with any Authority, and the Client may review Patheon's responses to any such reports and communications, and Patheon will in its reasonable discretion incorporate into such responses any comments received from the Client. Patheon will also inform the Client of any action taken by any Authority against Patheon or any of its officers or employees which may be reasonably expected to adversely affect the Products or Patheon's ability to supply the Products hereunder within a time period specified in the Quality Agreement.

7.7 Reports.

Patheon will supply on an annual basis all Product data in its control, including release test results, complaint test results, and all investigations (in manufacturing, testing, and storage), that Client reasonably requires in order to complete any filing under any applicable regulatory regime, including any Annual Report that Client is required to file with the FDA. At the Client's request, Patheon will provide a copy of the Patheon standard Annual Product Review Report to the Client at no additional cost unless otherwise specified in Schedule B. Any additional data or report requested by Client beyond the scope of cGMPs and customary FDA requirements, including Continuous Process Verification data, will be subject to an additional fee to be agreed upon between Patheon and the Client.

7.8 Regulatory Filings.

(a) Regulatory Authority. Client will have the sole responsibility at Client's expense for filing all documents with all Regulatory Authorities and taking any other actions that may be required for the receipt and/or maintenance of Regulatory Authority approval for the commercial manufacture, distribution and sale of the Products ("**Regulatory Approval**") and will provide copies thereof to Patheon on request. Patheon will assist Client, to the extent consistent with Patheon's obligations under this Agreement, to obtain Regulatory Authority approval for the commercial manufacture, distribution and sale of the Products as quickly as reasonably possible.

(b) Verification of Data. At least [***] prior to filing any documents with any Regulatory Authority that incorporate data generated by Patheon, Client will give Patheon a copy of the documents incorporating this data to give Patheon the opportunity to verify the accuracy and regulatory validity of those documents as they relate to Patheon generated data; provided, however, that the parties may agree to a shorter time for the review as needed.

(c) Verification of CMC. At least [***] prior to filing with any Regulatory Authority any documentation which is, or is equivalent to, the FDA's Chemistry and Manufacturing Controls ("**CMC**") related to any Marketing Authorization, such as a US New Drug Application, US Abbreviated New Drug Application, US Biologics Licence Application, or EU Marketing Authorisation Application, Client will give Patheon a copy of the CMC as well as all supporting documents which have been relied upon to prepare the CMC. This disclosure will permit Patheon to verify that the CMC accurately describes the validation or scale-up work that Patheon has performed and the manufacturing processes that Patheon will perform under this Agreement. Client will give Patheon copies of all regulatory filings at the time of submission which contain CMC information regarding the Product. Notwithstanding the foregoing, Client may omit from the materials provided to Patheon any CMC documentation and supporting documents which have been previously provided to Patheon by Client and which have not been modified or edited by Client.

(d) Deficiencies. If, in Patheon's sole discretion, acting reasonably, Patheon determines that any of the information given by Client under clauses (b) and (c) above is inaccurate or deficient in any manner whatsoever (the "**Deficiencies**"), Patheon will notify Client in writing of the Deficiencies. The parties will work together to have the Deficiencies resolved prior to the date of filing of the relevant application and in any event before any pre-approval inspection or before the Product is placed on the market if a pre-approval inspection is not performed, provided that to the extent of any disagreement

concerning the form or content any information or submissions covered by subsections (b) and (c) above, Client will have the final decision-making authority.

(e)Client Responsibility. For clarity, the parties agree that in reviewing the documents referred to in subsections (b) and (c) above, Patheon's role will be limited to verifying the accuracy of the description of the work undertaken or to be undertaken by Patheon. Subject to the foregoing, Patheon will not assume any responsibility for the accuracy of any application for receipt of an approval by a Regulatory Authority. The Client is solely responsible for the preparation and filing of the application for approval by the Regulatory Authority and any relevant costs will be borne by the Client, excepts as otherwise provided in this Section 7.8.

(f) Inspection by Regulatory Authorities. If Client does not give Patheon the documents requested under subsection (b) and (c) above within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be jeopardized, Patheon may, in its sole discretion, delay or postpone any inspection by the Regulatory Authority until Patheon has reviewed the requested documents and is satisfied with their contents.

(g) Pharmacovigilance. Client will be responsible, at its expense, for all pharmacovigilance obligations for the Products pursuant to Applicable Laws. Patheon will promptly provide to Client any information or data which it compiles pursuant to pharmacovigilance obligations or activities as specified in the Quality Agreement.

(h)No Patheon Responsibility. Patheon will not assume any responsibility for the accuracy or cost of any application for Regulatory Approval. If a Regulatory Authority, or other governmental body, requires Patheon to incur fees, costs or activities in relation to the Products which Patheon considers unexpected and extraordinary, then Patheon will notify Client in writing and the parties will discuss in good faith appropriate mutually acceptable actions, including fee/cost sharing, or termination of all or any part of this Agreement. Patheon will not be obliged to undertake these activities or to pay for the fees or costs if, in Patheon's sole discretion, doing so is commercially inadvisable for Patheon.

ARTICLE 8

TERM AND TERMINATION

8.1 Initial Term.

This Agreement will become effective as of the Effective Date and will continue until December 31 of the Year that is five full Years after the Commencement Date (the "**Initial Term**"), unless terminated earlier by one of the parties in accordance herewith. This Agreement will automatically renew after the Initial Term for successive terms of one Year each (each a "**Renewal Term**"), unless either party gives written notice to the other party of its intention to terminate this Agreement at least 18 months prior to the end of the Initial Term or 18 months prior to the end of any Renewal Term.

8.2

(a) Either party at its sole option may terminate this Agreement upon written notice where the other party has failed to remedy a material breach of any of its representations, warranties, or other

obligations under this Agreement within [***] following receipt of a written notice of the breach from the aggrieved party that expressly states that it is a notice under this Section 8.2(a).

(b) Either party at its sole option may immediately terminate this Agreement upon written notice, but without prior advance notice, to the other party if: (i) the other party is declared insolvent or bankrupt by a court of competent jurisdiction; (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by the other party; or (iii) this Agreement is assigned by the other party for the benefit of creditors.

(c) Client may terminate this Agreement upon [***] prior written notice if any Authority takes any action, or raises any objection, that prevents Client from importing, exporting, purchasing, or selling the Product. But if this occurs, Patheon and Client must still fulfill all of its obligations under Section 8.3 and 8.4 below and under any Capital Equipment Agreement regarding the Product.

(d) Patheon or Client may terminate this Agreement upon [***] prior written notice if Client or Patheon assigns under Section 13.6 any of its rights under this Agreement to an assignee that is: (i) in the opinion of the non-assigning Party acting reasonably, not a credit worthy substitute for the assigning Party; or (ii) a Patheon or Client Competitor.

8.3

(a) If this Agreement is completed, expires, or is terminated in whole or in part for any reason, then:

(i) Patheon will cease the manufacture of Products and will terminate any unfilled orders with third parties that Patheon may have previously submitted with respect to Components, to the extent such orders may be terminated or revoked;

(ii) Client will take delivery of and pay for all undelivered Products that are manufactured and/or packaged under a Firm Order, at the Price in effect at the time the Firm Order was placed;

(iii) Client will purchase, at Patheon's out-of-pocket cost (including all costs incurred by Patheon for the purchase and handling of the Inventory), the Inventory applicable to the Products which was purchased, produced or maintained by Patheon in contemplation of filling Firm Orders or in accordance with Section 5.3 prior to expiration or notice of termination being given;

(iv) Client will satisfy the purchase price payable under Patheon's non-cancellable orders with suppliers of Components, if the orders were made by Patheon in reliance on Firm Orders or in accordance with Section 5.3 and prior to expiration or notice of termination being given; and

(v) Client acknowledges that no Patheon Competitor will be permitted access to the Manufacturing Site; and Client will make commercially reasonable efforts, at its own expense, to remove from Patheon site(s), within [***], all unused Active

Material and Client-Supplied Components, all applicable Inventory and Materials (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at a Patheon site or that is otherwise under Patheon's care and control ("**Client Property**"). If Client fails to remove the Client Property within [***] following the completion, termination, or expiration of the Agreement, Client will pay Patheon [***] per pallet, per month, one pallet minimum (except that Client will pay [***] per pallet, per month, one pallet minimum, for any of the Client Property that contains controlled substances, requires refrigeration or other special storage requirements) thereafter for storing the Client Property and will assume any third party storage charges invoiced to Patheon regarding the Client Property. Patheon will invoice Client for the storage charges as set forth in Section 5.6 of this Agreement.

(b) Any completion, termination or expiration of this Agreement will not affect any outstanding obligations or payments due prior to the completion, termination or expiration, nor will it prejudice any other remedies that the parties may have under this Agreement or any related Capital Equipment Agreement. For greater certainty, completion, termination or expiration of this Agreement for any reason will not affect the obligations and responsibilities of the parties under Articles 10 and 11 and Sections 5.5, 5.6, 8.3, 13.1, 13.2, 13.3 and 13.16, all of which survive any completion, termination or expiration.

8.4

Following termination of this Agreement for any reason, or at Client's request during a period beginning at least [***] before the end of the term of this Agreement following the Parties' reasonable conclusion that this Agreement will not be extended after the term of this Agreement, Patheon shall provide assistance to transfer part or all of the Client's manufacturing process, know-how and analytical testing methodology for the Product to Client or Client's designee ("**Technology Transfer**") to assist Client or its designee to manufacture the Product. Patheon shall also disclose to Client or its designee any Patheon Intellectual Property that has been used by Patheon to perform the Manufacturing Services. For the purposes of such assistance, Patheon shall, upon request of Client prepare a written proposal to implement the Technology Transfer, including fees therefore. Client shall pay the agreed fees for any of such Technology Transfer provided by Patheon. No Patheon Competitor will be permitted access to the Manufacturing Site pursuant to this Section.

ARTICLE 9

REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1

Each party covenants, represents, and warrants that:

(a) it has the full right and authority to enter into this Agreement and that it is not aware of any impediment that would inhibit its ability to perform its obligations hereunder;

(b) this Agreement has been duly executed and delivered by, and is a legal and valid obligation binding upon such party, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights and judicial principles affecting the availability of specific performance and general principles of equity, whether enforceability is considered a proceeding at law or equity; and

(c) the entry into, the execution and delivery of, and the carrying out and other performance of its obligations under this Agreement by such party (i) does not conflict with, or contravene or constitute any default under, any agreement, instrument or understanding, oral or written, to which it is a party, including, but not limited to, its certificate of incorporation or by-laws, and (ii) does not violate Applicable Laws or any judgment, injunction, order or decree of any Authority having jurisdiction over it.

9.2

Client covenants, represents, and warrants that:

(a) Non-Infringement.

(i) the Specifications for each of the Products are its or its Affiliate's property and that Client may lawfully disclose the Specifications to Patheon;

(ii) any Client Intellectual Property, used by Patheon in performing the Manufacturing Services according to the Specifications (A) is owned or controlled by Client or its Affiliate, (B) may be lawfully used as directed by Client, and (C) to its knowledge does not infringe and will not infringe any Third Party Rights;

(iii) to the knowledge of Client, the performance of the Manufacturing Services by Patheon for the Product under this Agreement or the use or other disposition of the Product by Patheon as may be required to perform its obligations under this Agreement does not and will not infringe any Third Party Rights;

(iv) to the knowledge of Client, there are no actions or other legal proceedings involving the Client that concerns the infringement of Third Party Rights related to any of the Specifications, or any of the Active Materials and the Components, or the sale, use, or other disposition of any Product made in accordance with the Specifications;

(b) Quality and Compliance.

(i) the Specifications for the Product conforms to all applicable cGMPs and Applicable Laws;

(ii) the Products, if labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws (i) may be lawfully sold and distributed in every jurisdiction in which Client markets the Products, (ii) will be fit for the purpose intended, and (iii) will be safe for human consumption;

(iii) on the date of shipment, the API will conform to the specifications for the API that Client has given to Patheon and that the API will be adequately contained, packaged, and labelled and will conform to the affirmations of fact on the container.

9.3

Patheon covenants, represents, and warrants that:

(a) it will perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws;

(b) any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's unencumbered property, (ii) may be lawfully used by Patheon, and (iii) does not infringe and will not infringe any Third Party Rights;

(c) it will not in the performance of its obligations under this Agreement use the services of any person it knows is debarred or suspended under 21 U.S.C. §335(a) or (b);

(d) it does not currently have, and it will not hire, as an officer or an employee any person whom it knows has been convicted of a felony under the laws of the United States for conduct relating to the regulation of any drug product under the United States *Federal Food, Drug, and Cosmetic Act*;

(e) it has and will maintain throughout the term of this Agreement, the expertise, with respect to personnel and equipment, to fulfill the obligations established hereunder, and has obtained all requisite material licenses, authorizations and approvals required by all Authorities to manufacture the Products (excluding the Regulatory Approval);

(f) the Manufacturing Site, all other facilities, all equipment and all personnel to be employed by Patheon in rendering the Manufacturing Services are currently, and will be at the time each batch of Products is produced, qualified in accordance with all Applicable Laws, including, but not limited to, cGMPs;

(g) there are no pending or uncorrected citations or adverse conditions noted in any inspection of the Manufacturing Site or any other facilities to be employed by Patheon in rendering the Manufacturing Services which would cause the Products to be misbranded or adulterated within the meaning of the Act, including, but not limited to, all cGMPs;

(h) to the knowledge of Patheon, the Patheon Intellectual Property used by Patheon to manufacture the finished Product in accordance with this Agreement does not and will not infringe any Third Party Rights, except to the extent caused or contributed to by any breach of Client's warranties under Section 9.2(a);

(i) to the knowledge of Patheon, there are no claims against Patheon asserting that any Patheon Intellectual Property to be used for the Manufacturing Services infringes, misappropriates, or violates any Third Party Rights;

(j) all employees, consultants, subcontractors and agents performing services for Patheon hereunder have assigned, or will assign, in writing to Patheon all of their right, title and interest in, to and under any and all Inventions directly relating to the Product; and

(k) all Product manufactured and supplied to the Client under this Agreement will not be, as a result of any failure by Patheon to provide the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, adulterated or misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act or other Applicable Laws as of the time that the finished Product is transferred to the carrier at Patheon's shipping point.

9.4

(a) Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products or the Specifications, including, without limitation, all marketing and post-marketing approvals.

(b) Patheon will maintain at all relevant times all governmental permits, licenses, approval, and authorities required to enable it to lawfully and properly perform the Manufacturing Services.

9.5 No Warranty.

EXCEPT AS SET FORTH IN THIS SECTION 9, NEITHER PARTY MAKES ANY WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET FORTH IN THIS AGREEMENT. PATHEON MAKES NO WARRANTY OR CONDITION OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY WARRANTY OR CONDITION OF MERCHANTABILITY FOR THE PRODUCTS.

ARTICLE 10

REMEDIES AND INDEMNITIES

10.1 Limitation of Liabilities.

Under no circumstances whatsoever will either party be liable to the other in contract, tort, negligence, breach of statutory duty, or otherwise for (i) any (direct or indirect) loss of profits, of production, of anticipated savings, of business, or goodwill or (ii) for any other liability, damage, costs, or expense of any kind incurred by the other party of an indirect or consequential nature, regardless of any notice of the possibility of these damages.

10.2

(a) Active Materials. Except as expressly set forth in Section 2.2 and Article 6, under no circumstances will Patheon be responsible for any loss or damage to the Active Materials. Patheon's maximum responsibility for loss or damage to the Active Materials will not exceed the Maximum Credit Value set forth in Schedule D.

(b) Maximum Liability. Except for any liability arising (i) [***], or (ii) under [***], or (iii) in connection with Section 10.2(c), and subject to Section 10.2(d), Patheon's maximum aggregate liability to Client in any Year under this Agreement, including, without limitation, any liability arising under Section

6.3(b) relating to the expenses of a Recall or Product return, Sections 2.2 or 10.3 (except as stated above) hereof or resulting from any and all breaches of its representations, warranties, or any other obligations under this Agreement will not exceed [***] of revenues (being payments of the Price) received from Client and its Affiliates or properly invoiced under this Agreement by Patheon during the 12-month period prior to the event giving rise to the applicable claim or set of related claim(s) arising out of the same facts or circumstances.

(c) Defective or Recalled Product. Patheon's maximum aggregate liability to Client for any obligation to (i) refund, offset or replace any defective Product under Section 6.3(a) or (ii) replace any recalled Product under Section 6.3(b), will not exceed [***] of the Price for the defective or recalled Product as applicable. This Section 10.2(c) will not be subject to Section 10.2(b).

(d) Death, Personal Injury and Fraudulent Misrepresentation. Nothing contained in this Agreement shall act to exclude or limit either party's liability for (i) personal injury or death caused by the negligence of either party; (ii) fraudulent misrepresentation; or (iii) any acts or omissions for which the governing law prohibits the exclusion or limitation of liability.

10.3

Patheon agrees to defend and indemnify Client, its officers, employees, and agents against all losses, damages, costs, claims, demands, judgments and liability to, from and in favour of third parties (other than Affiliates) resulting from, or relating to any claim of personal injury or property damage to the extent that the injury or damage is the result of (i) a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, or (ii) any other breach of the Agreement by Patheon, including, without limitation, any representation, warranty or covenant contained herein, except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence or wrongful act(s) of Client, its officers, employees, agents, or Affiliates.

10.4

Client agrees to defend and indemnify Patheon, its officers, employees, and agents against all losses, damages, costs, claims, demands, judgments and liability to, from and in favour of third parties (other than Affiliates) resulting from, or relating to any claim of infringement or alleged infringement of any Third Party Rights in the Products, or any portion thereof, or any claim of personal injury or property damage to the extent that the injury or damage is arises other than from (i) a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, or (ii) any other breach of this Agreement by Patheon, including, without limitation, any representation, warranty or covenant contained herein, except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence or wrongful act(s) of Patheon, its officers, employees, agents, or Affiliates.

10.5

If a claim occurs for which a party has an indemnification obligation under Section 10.3 or 10.4, the indemnified party (the "**Indemnitee**") will: (a) promptly notify the indemnifying party (the "**Indemnitor**") in writing of the claim; (b) use commercially reasonable efforts to mitigate the effects of the claim; (c) reasonably cooperate with the Indemnitor in the defense of the claim; and (d) permit the

Indemnitor to control the defense and settlement of the claim, with counsel reasonably satisfactory to the Indemnitee, all at the Indemnitor 's cost and expense. If the Indemnitor assumes the defense of the claim, the Indemnitee may participate in such defense with the Indemnitee's own counsel who will be retained, at the Indemnitee's sole cost and expense; provided, however, that neither the Indemnitor nor the Indemnitee will consent to the entry of any judgment or enter into any settlement with respect to the claim without the prior written consent of the other party, which consent will not be unreasonably withheld or delayed. If the Indemnitee withholds consent in respect of a judgment or settlement involving only the payment of money by the Indemnitor and which would not involve any stipulation or admission of liability or result in the Indemnitee becoming subject to injunctive relief or other relief, the Indemnitor will have the right, upon written notice to the Indemnitee within five days after receipt of the Indemnitee's written denial of consent, to pay to the Indemnitee, or to a trust for its or the applicable third party's benefit, such amount established by such judgment or settlement in addition to all interest, costs or other charges relating thereto, together with all attorneys' fees and expenses incurred to such date for which the Indemnitor is obligated under this Agreement, if any, at which time the Indemnitor's rights and obligations with respect to such claim will cease. The Indemnitor will not be liable for any settlement or other disposition of a claim by the Indemnitee which is reached without the written consent of the Indemnitor.

10.6

This Agreement (including, without limitation, this Article 10) is reasonable and creates a reasonable allocation of risk for the relative profits the parties each expect to derive from the Products. Patheon assumes only a limited degree of risk arising from the manufacture, distribution, and use of the Products because Client has developed and holds the marketing approval for the Products, Client requires Patheon to manufacture and label the Products strictly in accordance with the Specifications, cGMPs and Applicable Law, and Client, not Patheon, is best positioned to inform and advise potential users about the circumstances and manner of use of the Products.

ARTICLE 11

CONFIDENTIALITY

11.1 Confidential Information.

"**Confidential Information**" means any information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form) that is non-public, confidential or proprietary including, without limitation, information relating to the Disclosing Party's patent and trademark applications, process designs, process models, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other intellectual property, its clients or client confidential information, finances, marketing, products and processes and all price quotations, manufacturing or professional services proposals, information relating to composition, proprietary technology, and all other information relating to manufacturing capabilities and operations. In addition, all analyses, compilations, studies, reports or other documents prepared by any party's Representatives containing the Confidential Information will be considered Confidential Information. Samples or materials provided hereunder as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. For the purposes of this ARTICLE 11, a party or its Representative receiving Confidential Information under this Agreement is a "**Recipient**," and a party or its Representative disclosing Confidential Information under this Agreement is the "**Disclosing Party**."

11.2 Use of Confidential Information.

The Recipient will use the Confidential Information solely for the purpose of meeting its obligations under this Agreement. The Recipient will keep the Confidential Information strictly confidential and will not disclose the Confidential Information in any manner whatsoever, in whole or in part, other than to those of its Representatives who (i) have a need to know the Confidential Information for the purpose of this Agreement; (ii) have been advised of the confidential nature of the Confidential Information and (iii) have obligations of confidentiality and non-use to the Recipient no less restrictive than those of this Agreement. Recipient will protect the Confidential Information disclosed to it by using all reasonable precautions to prevent the unauthorized disclosure, dissemination or use of the Confidential Information, which precautions will in no event be less than those exercised by Recipient with respect to its own confidential or proprietary Confidential Information of a similar nature.

11.3 Exclusions.

The obligations of confidentiality will not apply to the extent that the information:

(a) is or becomes publicly known through no breach of this Agreement or fault of the Recipient or its Representatives;

(b) is in the Recipient's possession at the time of disclosure by the Disclosing Party other than as a result of the Recipient's breach of any legal obligation;

(c) is or becomes known to the Recipient on a non-confidential basis through disclosure by sources, other than the Disclosing Party, having the legal right to disclose the Confidential Information, provided that the other source is not known by the Recipient to be bound by any obligations (contractual, legal, fiduciary, or otherwise) of confidentiality to the Disclosing Party with respect to the Confidential Information;

(d) is independently developed by the Recipient without use of or reference to the Disclosing Party's Confidential Information as evidenced by Recipient’s written records; or

(e) is expressly authorized for release by the written authorization of the Disclosing Party.

Any combination of information which comprises part of the Confidential Information are not exempt from the obligations of confidentiality merely because individual parts of that Confidential Information were publicly known, in the Recipient’s possession, or received by the Recipient, unless the combination itself was publicly known, in the Recipient’s possession, or received by the Recipient.

11.4 Photographs and Recordings.

Neither party will take any photographs or videos of the other party’s facilities, equipment or processes, nor use any other audio or visual recording equipment (such as camera phones) while at the other party’s facilities, without that party’s express written consent.

11.5 Permitted Disclosure.

Notwithstanding any other provision of this Agreement, the Recipient may disclose Confidential Information of the Disclosing Party to the extent required, as advised by counsel, in response to a valid order of a court or other governmental body or as required by law, regulation or stock exchange rule. But the Recipient will advise the Disclosing Party in advance of the disclosure to the extent practicable

and permissible by the order, law, regulation or stock exchange rule and any other applicable law, will reasonably cooperate with the Disclosing Party, if required, in seeking an appropriate protective order or other remedy, and will otherwise continue to perform its obligations of confidentiality set out herein. If any public disclosure is required by law, the parties will consult concerning the form of announcement prior to the public disclosure being made.

11.6 Marking.

The Disclosing Party agrees to use reasonable efforts to summarize in writing the content of any oral disclosure or other non-tangible disclosure of Confidential Information to the Recipient within [***] of the disclosure, but failure to provide this summary will not affect the nature of the Confidential Information disclosed to the Recipient if the Confidential Information was identified as confidential or proprietary when disclosed orally or in any other non-tangible form.

11.7 Return of Confidential Information.

Upon the written request of the Disclosing Party, the Recipient will promptly return the Confidential Information to the Disclosing Party or, if the Disclosing Party directs, destroy all Confidential Information disclosed in or reduced to tangible form including any copies thereof and any summaries, compilations, analyses or other notes derived from the Confidential Information except for one copy which may be maintained by the Recipient for its records. The retained copy will remain subject to all confidentiality provisions contained in this Agreement.

11.8 Remedies.

The parties acknowledge that monetary damages may not be sufficient to remedy a breach by either party of this Agreement and agree that the non-breaching party will be entitled to seek specific performance, injunctive and/or other equitable relief to prevent breaches of this Agreement and to specifically enforce the provisions hereof in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Agreement but will be in addition to any and all other remedies available at law or in equity.

ARTICLE 12

DISPUTE RESOLUTION

12.1 Commercial Disputes.

If any dispute arises out of this Agreement (other than a dispute under Section 6.1(b) or a Technical Dispute, as defined herein), the parties will first try to resolve it amicably. In that regard, any party may send a notice of dispute to the other, and each party will appoint, within [***] from receipt of the notice of dispute, a single representative having full power and authority to resolve the dispute. The representatives will meet as necessary in order to resolve the dispute. If the representatives fail to resolve the matter within [***] from their appointment, or if a party fails to appoint a representative within the [***] period set forth above, the dispute will immediately be referred to the Chief Operating Officer (or another officer as he/she may designate) of each party who will meet and discuss as necessary to try to resolve the

dispute amicably. Should the parties fail to reach a resolution under this Section 12.1, the dispute will be referred to a court of competent jurisdiction in accordance with Section 13.17.

12.2 Technical Dispute Resolution.

If a dispute arises (other than disputes under Sections 6.1(b) or 12.1) between the parties that is exclusively related to technical aspects of the manufacturing, packaging, labelling, quality control testing, handling, storage, or other activities under this Agreement (a "**Technical Dispute**"), the parties will make all reasonable efforts to resolve the dispute by amicable negotiations. In that regard, senior representatives of each party will, as soon as possible and in any event no later than [***] after a written request from either party to the other, meet in good faith to resolve any Technical Dispute. If, despite this meeting, the parties are unable to resolve a Technical Dispute within a reasonable time, and in any event within [***] of the written request, the Technical Dispute will, at the request of either party, be referred for determination to an expert in accordance with Schedule E If the parties cannot agree that a dispute is a Technical Dispute, Section 12.1 will prevail. For greater certainty, the parties agree that the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including Schedule E) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

ARTICLE 13

MISCELLANEOUS

13.1 Inventions.

(a) All Inventions and Intellectual Property generated or derived by Patheon while performing the Manufacturing Services, to the extent it is specific to the development, manufacture, use, and sale of Client's Product or Active Materials that are the subject of the Manufacturing Services, including, but not limited to, any new use, new formulation or any change in the method of producing, testing or storing the Product in each case that are specific to the Product ("**Product Inventions**"), will be the exclusive Intellectual Property of Client. Patheon shall and hereby does assign to Client all right title and interest in and to the Product Inventions. Patheon will execute such instruments as will be required to evidence or effectuate the Client's ownership of Product Inventions, and will cooperate upon reasonable request in the prosecution of patents and other Intellectual Property rights related thereto at Client's cost.

(b) Inventorship of all Inventions and Intellectual Property generated or derived by either party pursuant to this agreement shall be determined in accordance with United States patent law, regardless of where the applicable activities occurred.

(c) Either party will give the other party written notice, as promptly as practicable, of all Inventions which can reasonably be deemed to constitute improvements or other modifications of the Products or processes or technology generated, derived, owned or otherwise controlled by the party during the term of this Agreement.

13.2 Intellectual Property.

(a) For the term of this Agreement, Client hereby grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license of Client's Intellectual Property which Patheon must use in order to perform the Manufacturing Services.

(b) Patheon hereby grants to Client a perpetual, irrevocable, non-exclusive, paid-up, royalty-free, transferable license (with the right to sublicense) to use the Patheon Intellectual Property used by Patheon to perform the Manufacturing Services to enable Client to manufacture or have manufactured the Product(s).

(c) Subject to Section 13.1, all Client Intellectual Property, including Product Inventions, will be the exclusive property of Client, and all Patheon Intellectual Property will be the exclusive property of Patheon.

(d) Neither party has, nor will it acquire, any interest in any of the other party's Intellectual Property unless otherwise expressly agreed to in writing. Neither party will use any Intellectual Property of the other party, except as specifically authorized by the other party or as required for the performance of its obligations under this Agreement.

(e) Each party hereby acknowledges that it does not have, and will not acquire any interest in any of the other party's trademarks or trade names unless otherwise expressly agreed. Each party agrees not to use any trademarks or trade names of the other party, except as specifically authorized by the other party in writing both as to the names or marks which may be used and as to the manner and prominence of use. All goodwill in any trademarks will inure to the benefit of the trademark owner. Client, in its sole discretion, will determine the trademarks and trade names owned or licensed by Client to be used in connection with the Products, including without limitation, the trademarks and trade names which will appear on the labels, packaging, and any promotional or other materials related to the Products. Patheon will use those trademarks and trade names notified by Client to Patheon for use in the labelling and packaging of the Products, and Patheon will use only such notified trademarks and trade names for such purpose. Upon expiration or termination of this Agreement, Patheon will immediately cease using all of Client's trademarks and trade names.

(f) Each party will be solely responsible for the costs of filing, prosecution, and maintenance of its own Intellectual Property, including trademarks and trademark applications and patents and patent applications.

13.3 Insurance.

Each party will maintain commercial general liability insurance, including blanket contractual liability insurance covering the obligations of that party under this Agreement through the term of this Agreement and for a period of [***] thereafter. This insurance will have policy limits of not less than (i) [***] for each occurrence for personal injury or property damage liability; and (ii) [***] in the aggregate per annum for product and completed operations liability. If requested each party will give the other a certificate of insurance evidencing the above and showing the name of the issuing company, the policy number, the effective date, the expiration date, and the limits of liability. The insurance certificate will further provide for a minimum of 30 days' written notice to the insured of a cancellation of, or material change in, the insurance.

If a party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the party will forthwith notify the other party in writing and the parties will in good faith negotiate appropriate amendments to the insurance provision of this Agreement in order to provide adequate assurances.

13.4 Independent Contractors.

The parties are independent contractors and this Agreement will not be construed to create between Patheon and Client any other relationship such as, by way of example only, that of employer-employee, principal agent, joint-venturer, co-partners, or any similar relationship, the existence of which is expressly denied by the parties.

13.5 No Waiver.

Either party's failure to require the other party to comply with any provision of this Agreement will not be deemed a waiver of the provision or any other provision of this Agreement, with the exception of Sections 6.1 and 8.2 of this Agreement.

13.6 Assignment.

(a) Patheon may not assign this Agreement or any of its associated rights or obligations without the written consent of Client, this consent not to be unreasonably withheld. But Patheon may arrange for subcontractors to perform specific testing services arising under this Agreement without the consent of Client; provided, however, the Patheon will provide advance notice of the name and function of any such subcontractor. Further it is specifically agreed that Patheon may subcontract any part of the Manufacturing Services under this Agreement to any of its Affiliates. Patheon will remain solely liable to Client for its obligations under this Agreement, and for the obligations of the applicable Affiliate of Patheon under the Quality Agreement, if the Manufacturing Services are subcontracted.

(b) Subject to Section 8.2(d), Client may assign this Agreement or any of its associated rights or obligations without approval from Patheon. But Client will give Patheon prior written notice of any assignment (where and to the extent possible), any assignee will covenant in writing with Patheon to be bound by the terms of this Agreement, and Client will remain liable hereunder. Any partial assignment will be subject to Patheon's cost review of the assigned Products and Patheon may terminate this Agreement or any assigned part thereof, on [***] prior written notice to Client and the assignee if good faith discussions do not lead to agreement on amended Manufacturing Service fees within a reasonable time.

(c) Despite the foregoing provisions of this Section 13.6, either party may assign this Agreement to any of its Affiliates or to a successor to or purchaser of all or substantially all of its business, but the assignee must execute an agreement with the non-assigning party whereby it agrees to be bound hereunder.

13.7 Force Majeure.

Neither party will be liable for the failure to perform its obligations under this Agreement if the failure is caused by an event beyond that party's reasonable control, including, but not limited to, strikes or other labor disturbances, lockouts, riots, quarantines, communicable disease outbreaks, wars, acts of terrorism, fires, floods, storms, interruption of or delay in transportation, defective equipment, lack of or inability to obtain fuel, power or components, or compliance with any order or regulation of any government entity acting within colour of right (a "**Force Majeure Event**"). A party claiming a right to excused performance under this Section 13.7 will immediately notify the other party in writing of the extent of its inability to perform, which notice will specify the event beyond its reasonable control that prevents the performance. Neither party will be entitled to rely on a Force Majeure Event to relieve it from an obligation to pay money (including any interest for delayed payment) which would otherwise be due and payable under this Agreement.

13.8 Additional Product.

Additional products may be added to this Agreement and the additional products will be governed by the general conditions hereof with any special terms (including, without limitation, price) governed by executed amendments to Schedules A, B, C, and D as applicable.

13.9 Notices.

Any notice, approval, instruction or other written communication required or permitted hereunder will be sufficient if made or given to the other party by personal delivery, by telecopy, facsimile communication, or confirmed receipt email or by sending the same by first class mail, postage prepaid to the respective addresses, telecopy or facsimile numbers or electronic mail addresses set forth below:

If to Client:

Evoke Pharma, Inc.
420 Stevens Ave, Suite 370
Solana Beach, California 92075 USA

Attention: Matt D'Onofrio

Email address:MDOnofrio@EvokePharma.com

If to Patheon:

Patheon UK Limited
Kingfisher Drive
Covingham
Swindon Wiltshire SN3 5BZ
England

Attention: Legal Director

Facsimile No: [***]
Email address: [***]

or to any other addresses, telecopy or facsimile numbers or electronic mail addresses given to the other party in accordance with the terms of this Section 13.9. Notices or written communications made or given by personal delivery, telecopy, facsimile, or electronic mail will be deemed to have been sufficiently made or given when sent (receipt acknowledged), or if mailed, five days after being deposited in the United States, Canada, or European Union mail, postage prepaid or upon receipt, whichever is sooner.

13.10 Severability.

If any provision of this Agreement is determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable in any respect, that determination will not impair or affect the validity, legality, or enforceability of the remaining provisions, because each provision is separate, severable, and distinct.

13.11 Entire Agreement.

This Agreement, together with the Quality Agreement, constitutes the full, complete, final and integrated agreement between the parties relating to the subject matter hereof and supersedes all previous written or oral negotiations, commitments, agreements, transactions, or understandings concerning the subject matter hereof. Any modification, amendment, or supplement to this Agreement must be in writing and signed by authorized representatives of both parties. In case of conflict, the prevailing order of documents will be this Agreement and the Quality Agreement.

13.12 Other Terms.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by Client or Patheon will have any effect on the rights, duties, or obligations of the parties under or otherwise modify this Agreement, regardless of any failure of Client or Patheon to object to the terms, provisions, or conditions unless the document specifically refers to this Agreement and is signed by both parties.

13.13 No Third Party Benefit or Right.

For greater certainty, nothing in this Agreement will confer or be construed as conferring on any third party any benefit or the right to enforce any express or implied term of this Agreement.

13.14 Execution in Counterparts.

This Agreement may be executed in two or more counterparts, by original, facsimile or “pdf” signature, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

13.15 Use of Client Name.

Patheon will not make any use of Client's name, trademarks or logo or any variations thereof, alone or with any other word or words, without the prior written consent of Client, which consent will not be unreasonably withheld. Despite this, Client agrees that Patheon may include Client's name and logo in customer lists or related marketing and promotional material for the purpose of identifying users of Patheon's Manufacturing Services. Client will have right to disclose name of Patheon as manufacturing partner to regulatory, financial and public investors.

13.16 Taxes.

(a) The Client will bear all taxes, duties, levies and similar charges (and any related interest and penalties) ("**Tax**" or "**Taxes**"), however designated, imposed as a result of the provision by the Patheon of Services under this Agreement, except:

(i) any Tax based on net income or gross income that is imposed on Patheon by its jurisdiction of formation or incorporation ("**Resident Jurisdiction**");

(ii) any Tax based on net income or gross income that is imposed on Patheon by jurisdictions other than its Resident Jurisdiction if this tax is based on a permanent establishment of Patheon; and

(iii) any Tax that is recoverable by Patheon in the ordinary course of business for purchases made by Patheon in the course of providing its Services, such as Value Added Tax (as more fully defined in subparagraph (d) below), Goods & Services Tax ("**GST**") and similar taxes.

(b) If the Client is required to bear a tax, duty, levy or similar charge under this Agreement by any state, federal, provincial or foreign government, including, but not limited to, Value Added Tax, the Client will pay the tax, duty, levy or similar charge and any additional amounts to the appropriate taxing authority as are necessary to ensure that the net amounts received by Patheon hereunder after all such payments or withholdings equal the amounts to which Patheon is otherwise entitled under this Agreement as if the tax, duty, levy or similar charge did not exist.

(c) Patheon will not collect an otherwise applicable tax if the Client's purchase is exempt from Patheon's collection of the tax and a valid tax exemption certificate is furnished by the Client to Patheon.

(d) If Section 13.16 (a)(iii) does not apply, any payment due under this Agreement for the provision of Services to the Client by Patheon is exclusive of value added taxes, turnover taxes, sales taxes or similar taxes, including any related interest and penalties (hereinafter all referred to as "**VAT**"). If any VAT is payable on a Service supplied by Patheon to the Client under this Agreement, this VAT will be added to the invoice amount and will be for the account of (and reimbursable to Patheon by) the Client. If VAT on the supplies of Patheon is payable by the Client under a reverse charge procedure (i.e., shifting of liability, accounting or payment requirement to recipient of supplies), the Client will ensure that Patheon will not effectively be held liable for this VAT by the relevant taxing authorities or other parties. Where applicable, Patheon will use its reasonable commercial efforts to ensure that its invoices to the Client are issued in such a way that these invoices meet

the requirements for deduction of input VAT by the Client, if the Client is permitted by law to do so.

(e) Any Tax that Client pays, or is required to pay, but which Client believes should properly be paid by Patheon pursuant hereto may not be offset against sums due by Client to Patheon whether due pursuant to this Agreement or otherwise.

13.17 Governing Law.

This Agreement will be construed and enforced in accordance with the laws of the State of New York, New York, U.S.A. without regard to the application of principles of conflicts of law. In relation to such matters, both Parties shall submit to the exclusive jurisdiction of the state and federal courts located in the State of New York, New York. THE PARTIES EXPRESSLY WAIVE THEIR RESPECTIVE RIGHTS TO A JURY TRIAL IN RESPECT OF ANY MATTER RELATING TO THIS AGREEMENT OR ITS FORMATION. Notwithstanding the foregoing, Patheon and Client agree that either party will be entitled to seek interim relief (injunctive or otherwise) from any court of competent jurisdiction if there is a breach of this Agreement. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement.

[Signature page to follow]

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Agreement as of the Effective Date.

PATHEON UK LIMITED

By: /s/ Mark Newton

Name: Mark Newton

Title: Sr. Dir. G.C.S.

EVOKE PHARMA, INC.

By: /s/ David A. Gonyer

Name: David A. Gonyer

Title: President and CEO

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE A

PRODUCT AND SPECIFICATIONS

Product

[***]

Specifications

[***]

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE B

ANNUAL VOLUME

[***]

MINIMUM ORDER QUANTITY AND PRICE

[***]

The following cost items are included in the Price for the Products:

[***]

The following cost items are not included in the Price for the Products:

[***]

Manufacturing Parameters

[***]

Packaging Parameters

[***]

Testing Conditions

[***]

SCHEDULE C

ANNUAL STABILITY TESTING [and VALIDATION ACTIVITIES (if applicable)]

[***]

-

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE D

ACTIVE MATERIALS

Active Materials	Supplier
[***]	[***]

ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

PRODUCT	ACTIVE MATERIALS	ACTIVE MATERIALS CREDIT VALUE
[***]	[***]	[***]

MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Agreement in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

PRODUCT	MAXIMUM CREDIT VALUE
[***]	[***]

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE E

TECHNICAL DISPUTE RESOLUTION

Technical Disputes which cannot be resolved by negotiation as provided in Section 12.2 of the Agreement will be resolved in the following manner:

1. **Appointment of Expert**. Within [***] after a party requests under Section 12.2 of the Agreement that an expert be appointed to resolve a Technical Dispute, the parties will jointly appoint a mutually acceptable expert with experience and expertise in the subject matter of the dispute. If the parties are unable to so agree within the [***] period, or if there is a disclosure of a conflict by an expert under Paragraph 2 hereof which results in the parties not confirming the appointment of the expert, then an expert (willing to act in that capacity hereunder) will be appointed by an experienced arbitrator on the roster of the American Arbitration Association.

2. **Conflicts of Interest**. Any person appointed as an expert will be entitled to act and continue to act as an expert even if at the time of his appointment or at any time before he gives his determination, he has or may have some interest or duty which conflicts or may conflict with his appointment if before accepting the appointment (or as soon as practicable after he becomes aware of the conflict or potential conflict) he fully discloses the interest or duty and the parties will, after the disclosure, have confirmed his appointment.

3. **Not Arbitrator**. No expert will be deemed to be an arbitrator and the provisions of the American Arbitration Act or of any other applicable statute (foreign or domestic) and the law relating to arbitration will not apply to the expert or the expert's determination or the procedure by which the expert reaches his determination under this Schedule E.

4. **Procedure**. Where an expert is appointed:

   (a) Timing. The expert will be so appointed on condition that (i) he promptly fixes a reasonable time and place for receiving representations, submissions or information from the parties and that he issues the authorizations to the parties and any relevant third party for the proper conduct of his determination and any hearing and (ii) he renders his decision (with full reasons) within [***] (or another other date as the parties and the expert may agree) after receipt of all information requested by him under Paragraph 4(b) hereof.

   (b) Disclosure of Evidence. The parties undertake one to the other to give to any expert all the evidence and information within their respective possession or control as the expert may reasonably consider necessary for determining the matter before him which they will disclose promptly and in any event within [***] of a written request from the relevant expert to do so.

(c) Advisors. Each party may appoint any counsel, consultants and advisors as it feels appropriate to assist the expert in his determination and so as to present their respective cases so that at all times the parties will co-operate and seek to narrow and limit the issues to be determined.

(d) Appointment of New Expert. If within the time specified in Paragraph 4(a) above the expert will not have rendered a decision in accordance with his appointment, a new expert may (at the request of either party) be appointed and the appointment of the existing expert will thereupon cease for the purposes of determining the matter at issue between the parties except if the existing expert renders his decision with full reasons prior to the appointment of the new expert, then this decision will have effect and the proposed appointment of the new expert will be withdrawn.

(e) Final and Binding. The determination of the expert will, except for fraud or manifest error, be final and binding upon the parties.

(f) Costs. Each party will bear its own costs for any matter referred to an expert hereunder and, in the absence of express provision in the Agreement to the contrary, the costs and expenses of the expert will be shared equally by the parties.

For greater certainty, the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including this Schedule E) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE F

QUARTERLY ACTIVE MATERIALS INVENTORY REPORT

TO: EVOKE PHARMA, INC.

FROM: PATHEON UK LIMITED [or applicable Patheon Affiliate]

RE: Active Materials quarterly inventory report under Section 2.2(a) of the Manufacturing Services Agreement dated • (the "**Agreement**")

Reporting quarter:

Active Materials on hand
at beginning of quarter:kg (A)

Active Materials on hand
at end of quarter:kg (B)

Quantity Received during quarter:kg (C)

Quantity Dispensed during quarter:[1] kg
[***]

Quantity Converted during quarter:kg
(total Active Materials in Products produced
and not rejected, recalled or returned)

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

PATHEON UK LIMITED DATE:
[or applicable Patheon Affiliate]

Per:
Name:
Title:

---

1 [***]

CERTAIN MATERIAL (INDICATED BY ASTERISKS) HAS BEEN OMITTED FROM THIS DOCUMENT PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT. THE OMITTED MATERIAL HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

SCHEDULE G

REPORT OF ANNUAL ACTIVE MATERIALS INVENTORY RECONCILIATION AND CALCULATION OF ACTUAL ANNUAL YIELD

TO: EVOKE PHARMA, INC.

FROM: PATHEON UK LIMITED [or applicable Patheon Affiliate]

RE: Active Materials annual inventory reconciliation report and calculation of Actual Annual Yield under Section 2.2(a) of the Manufacturing Services Agreement dated 31 October, 2017 (the "**Agreement**")

Reporting Year ending:

Active Materials on hand
at beginning of Year:kg (A)

Active Materials on hand
at end of Year:kg (B)

Quantity Received during Year:kg (C)

Quantity Dispensed during Year:[2] kg (D)
[***]

Quantity Converted during Year:kg (E)
(total Active Materials in Products produced
and not rejected, recalled or returned)

Active Materials Credit Value:EUR / kg(F)

---

[2] [***]

Target Yield:_%(G)

Actual Annual Yield:%(H)
[***]

Shortfall: EUR(I)
[***] (if a negative number, insert zero)

Based on the foregoing reimbursement calculation Patheon will reimburse Client the amount of EUR .

Surplus Credit:EUR(J)
[***]

Based on the foregoing reimbursement calculation Patheon may carry forward one Year a Surplus Credit in the amount of EUR .

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

DATE:

PATHEON UK LIMITED
[or applicable Patheon Affiliate]

Per:
Name:
Title:

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Evoke Pharma, Inc.
Solana Beach, California

We hereby consent to the incorporation by reference in Registration Statements on Form S-3 (No. 333-221556) and Forms S-8 (No. 333-219960, 333-211302 and 333-191518) of Evoke Pharma, Inc. of our report dated March 7, 2018, relating to the financial statements, which appears in this Annual Report on Form 10-K. Our report contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

/s/ BDO USA, LLP

San Diego, California
March 7, 2018

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David A. Gonyer, certify that:

1. I have reviewed this Annual Report on Form 10-K of Evoke Pharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2018

/s/ David A. Gonyer
David A. Gonyer
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Matthew J. D'Onofrio, certify that:

1. I have reviewed this Annual Report on Form 10-K of Evoke Pharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2018

/s/ Matthew J. D'Onofrio
Matthew J. D'Onofrio
Executive Vice President, Chief Business Officer,
Treasurer and Secretary
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Evoke Pharma, Inc. (the "Company") for the period ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, David A. Gonyer, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 7, 2018

/s/ David A. Gonyer
David A. Gonyer
President and Chief Executive Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (SUBSECTIONS (A) AND (B) OF SECTION 1350, CHAPTER 63 OF TITLE 18, UNITED STATES CODE)

In connection with the Annual Report on Form 10-K of Evoke Pharma, Inc. (the "Company") for the period ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Matthew J. D'Onofrio, Executive Vice President, Chief Business Officer, Treasurer and Secretary of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 7, 2018

/s/ Matthew J. D'Onofrio
Matthew J. D'Onofrio
Executive Vice President, Chief Business Officer,
Treasurer and Secretary

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.