UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2012

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 001-35005

VENTRUS BIOSCIENCES, INC.

(Exact name of registrant specified in its charter)

Delaware	**2834**	**20-8729264**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

99 Hudson Street, 5th Floor
New York, New York 10013
(Address of Principal Executive Offices)

(646) 706-5208
(Telephone Number, Including Area Code)

Securities Registered Pursuant to Section 12(b) of the Exchange Act:

Title of Each Class	**Name of Exchange on which Registered**
Common Stock, $0.001 Par Value	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 Section 15(d) of the Exchange 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 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, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐	Accelerated filer ☒
Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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

The aggregate market value of the voting stock held by non-affiliates of the registrant, as of June 30, 2012, was approximately $53.2 million. Such aggregate market value was computed by reference to the closing price of the common stock as reported on the Nasdaq Capital Market on June 29, 2012 (the last trading day before June 30, 2102). For purposes of making this calculation only, the registrant has defined affiliates as including only directors and executive officers and shareholders holding greater than 10% of the voting stock of the registrant as of June 30, 2012.

As of March 12, 2013 there were 19,604,350 shares of the registrant's common stock, $0.001 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the Company's definitive Proxy Statement for its 2013 Annual Meeting of Stockholders are incorporated herein by reference, as indicated in Part III.

VENTRUS BIOSCIENCES, INC.

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This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements are subject to risks and uncertainties, including those set forth under "Item 1A. Risk Factors" and "Cautionary Statement" included in "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report, that could cause actual results to differ materially from historical results or anticipated results.

PART I

Item 1. Business

Overview

We are a development-stage specialty pharmaceutical company currently focused on the development of late-stage prescription drugs for gastrointestinal disorders, specifically anal disorders. Major pharmaceutical progress has been made in the gastrointestinal therapeutic areas of gastroesophageal reflux, peptic ulcer disease and inflammatory bowel disease. However, many major gastrointestinal disorders still lack medical treatments.

Our product candidate portfolio consists of two in-licensed late-stage drugs. Our lead product, VEN 307 (topical diltiazem), is intended to treat pain associated with anal fissures and our secondary product, VEN 308 (topical phenylephrine), is intended to treat fecal incontinence. These candidates are two molecules that were previously approved and are currently marketed for other indications and that have been formulated into our proprietary topical treatments for these new gastrointestinal indications.

There are approximately 1.1 million office visits per year for anal fissures in the U.S. In addition, SDI Physician Drug & Diagnostic Audit estimated that in 2010 there were approximately 730,000 unique patients who visited a physician for anal fissures. Despite these figures, we are aware of only one drug that has received FDA approval for the treatment of pain associated with anal fissures; Rectiv® received approval in late June 2011, and became commercially available in the first quarter of 2012. Rectiv is effective in reducing the pain from anal fissures, but moderate and severe headaches are a frequent side effect of this topical drug whose active ingredient is nitroglycerin.

Diltiazem was first approved in 1982 in oral form for the treatment of angina and high blood pressure. It has been prescribed in the U.S. for millions of patients in oral dosages typically from 240 mg to 360 mg per day. In contrast, daily doses of VEN 307 for treatment of anal fissures will be approximately 30 mg. Because of the extensive patient exposure to diltiazem as a cardiovascular agent and the wide safety margin as a low-dose topical therapy, we intend to develop VEN 307 for the treatment of pain from anal fissures. We intend to develop VEN 307 in a topical formulation as a Section 505(b)(2) new drug application, or NDA, based on our discussions with the U.S. Food and Drug Administration, or FDA, at our pre-IND meeting in August 2007. At this meeting, we discussed necessary preclinical testing, and chemistry and manufacturing data necessary to support an investigational new drug product application, or IND, and received guidance on the design of the pivotal Phase III trials. At a pre-NDA meeting with the FDA in August 2012, we established that it would require a total of two Phase III trials in addition to two provocative skin test trials and a formal PK study comparing VEN 307 to an approved form of diltiazem in anal fissure patients. Our licensor and development partner S.L.A. Pharma conducted the first Phase III VEN 307 clinical trial in Europe, which completed enrollment in December 2011 and for which we reported topline data in May 2012, the results of which are discussed below. We began our second pivotal Phase III trial of VEN 307 in the U.S. in the fourth quarter of 2012. We expect to complete that trial in the fourth quarter of 2013.

We are not aware of any prescription drug treatment for fecal incontinence that has been approved by the FDA for that indication, yet there were approximately 7.0 million Americans suffering from fecal incontinence in the year between July 2010 and June 2011. Solesta®, a hyaluronic acid dermal filler, was approved as a device by the FDA in 2011 for intra-anal injection for fecal incontinence and is currently owned and being marketed by Salix Pharmaceuticals. Phenylephrine has been available since the early 1940s in oral and nasal form for the treatment of nasal congestion. It has also been used as a topical ophthalmic agent since 1936. Phenylephrine is prescribed or used more than 17 million times per year in the U.S., with 99% of the use being for cough/cold oral preparations. The typical oral dosing is 40 mg to 60 mg per day. Because of the extensive patient exposure to phenylephrine, we intend to develop VEN 308 as a topical formulation through a Section 505(b)(2) NDA. In June 2007, we had a pre-IND meeting with the FDA concerning VEN 308 for the treatment of fecal incontinence associated with ileal pouch anal anastomosis (IPAA) where it was established that the next clinical study in the program should be a Phase IIb trial where multiple doses will be assessed and that existing toxicology data are sufficient to support Phase II testing. The FDA has designated fecal incontinence with IPAA as an orphan indication. We intend to do technical development to create a twice daily patentable formulation of VEN 308 in the near future after which we will determine whether to pursue further development of VEN 308.

Our Products and Development Strategy

Our two late-stage product candidates are:

Diltiazem cream (VEN 307), a topical treatment for the relief of pain associated with anal fissures. Anal fissures are small tears or cuts in the skin that lines the anus. They can be extremely painful, cause bleeding and often require surgery, which itself can have unsatisfactory outcomes. In 2010, it was estimated by SDI Health LLC that there were approximately 1.1 million office visits per year for anal fissures. In addition, SDI Physician Drug & Diagnosis Audit estimated that in 2010 there were approximately 730,000 unique patients who visited a physician for anal fissures.. At present, we are aware of only one FDA-approved drug for the treatment of anal fissures. Rectiv (nitroglycerin) ointment 0.4%, for the treatment of moderate to severe pain associated with chronic anal fissures, received FDA approval in late June 2011, and came to market in the first quarter of 2012. Topical nitroglycerin, the active ingredient in Rectiv, has a substantially higher rate of side effects than topical diltiazem, notably moderate and severe headaches, which also are experienced with Rectiv. Topical nitroglycerin also is specially mixed, or compounded, on a patient by patient basis by pharmacists to treat anal fissures, but we have determined that, since the introduction of Rectiv, prescriptions for compounded nitroglycerin have decreased. We also are aware of limited use of Botox® as an injection into the anal sphincter to treat this condition. Several topical forms of nifedipine, a calcium-channel blocker that is compounded by pharmacists, also are used to treat pain from anal fissures. Diltiazem cream, also a calcium-channel blocker, however, is currently used as the preferred treatment prior to surgery by many colorectal surgeons across the U.S. in a compounded version made by pharmacists on a patient by patient basis.

Compounded diltiazem is currently listed in the U.S. and Great Britain anal fissure treatment guidelines as a preferred agent prior to attempting surgery. Neither compounded diltiazem nor nifedipine, however, is FDA-approved for the relief of pain associated with anal fissures nor is the cost typically reimbursed by Medicare or health insurance plans. We expect that VEN 307, if approved by the FDA, would be reimbursable under Medicare and health insurance plans as is Rectiv. When applied topically for the treatment of anal fissures, diltiazem, which has been used for decades for hypertension and angina, dilates the blood vessels supplying the region, reduces anal sphincter tone, and thereby substantially decreases pain. In the majority of multiple clinical trials conducted against placebo or topical nitroglycerin between 1999 and 2002 by various researchers in investigator-initiated trials, topical diltiazem reduced the pain associated with anal fissures and improved healing.

Our product, VEN 307, is a pre-mixed and pre-packaged proprietary formulation of diltiazem that when applied topically yields lower blood levels (at one-tenth the amount) than the lowest oral dose used for cardiovascular treatment. We believe these low blood levels improve the safety profile and lower the risk of side effects. We have potential to capture immediate market share if VEN 307 is approved due to the familiarity of gastroenterologists and surgeons with the current use of diltiazem to treat anal fissures, its ease of prescription as a pre-formulated FDA-approved product with no need for compounding necessary at the pharmacy, and the expected ability for patients to be reimbursed through their health insurance plans or Medicare. We have licensed the exclusive North American rights to VEN 307 for the topical treatment of anal fissures from S.L.A. Pharma, a Swiss corporation and our development partner, who has completed early-stage clinical trials, some toxicology studies and manufacturing for VEN 307 up through a recently completed Phase III trial in Europe. VEN 307 is covered by method of use patents that will expire in February 2018. We expect that we will receive a Hatch-Waxman extension of exclusivity for the three times daily (t.i.d.) formulation of VEN 307 to approximately mid-2019. We also expect to receive a written request from the FDA for pediatric studies for VEN 307, which if undertaken, would extend exclusivity for an additional six months.

In August 2007, we had a pre-IND meeting with the FDA concerning VEN 307 for the treatment of pain from anal fissures where we addressed necessary preclinical testing and product formulation to support an IND, established what clinical safety database would be required, and determined that the next clinical studies needed for approval were two pivotal Phase III trials, preceded (if conducted in the U.S.) by three short-term dermal toxicology studies using final drug product formulation. We are employing a two-pronged development strategy for VEN 307. S.L.A. Pharma conducted the first Phase III VEN 307 clinical trial in the European Union, or E.U., with a three times daily, or t.i.d., formulation which completed enrollment in December 2011 and for which we reported topline data in May 2012. We began our initial Phase III VEN 307 clinical trial in the U.S. in the fourth quarter of 2012 with the same t.i.d. formulation, with completion expected in the fourth quarter of 2013. We intend to initiate development of a different formulation of VEN 307 with new intellectual property in the form of an extended-release, or ER, formulation. There are several proven methodologies for extended-release topical formulations, and we have observed that diltiazem is readily druggable in this regard. We have assessed three to four alternatives preclinically with an external contractor, and we expect to assess in pre-clinical in vivo studies the absorption and the effect on internal anal sphincter, or IAS, pressure with the most promising formulation. Assuming positive outcomes, we plan to file North American patent applications for all formulations that are technically feasible.

S.L.A. Pharma began enrollment in the VEN 307 Phase III trial in November 2010 and completed enrollment of 465 patients at 27 sites in 11 countries in Europe in December 2011. Patients were treated for two months and then observed without treatment for one month in a randomized 1:1:1 double-blind study that compared treatments of 2% VEN 307 and 4% VEN 307 to placebo. The primary endpoint was reduction of worst pain with or following defecation averaged across the fourth week of treatment (Week 4), using a validated numerical rating scale (NRS) for pain. Patients were required to call into an IVRS daily diary to report their pain during the 8 weeks of treatment, as well as for the one week prior to randomization to ensure sufficient pain prior to randomization.

Both the 4% and the 2% diltiazem treatment arms demonstrated statistically significant improvement compared to the placebo arm on the primary endpoint of change from baseline in the Week 4 NRS score for worst anal pain with or following defecation. The mean reduction in the NRS pain score was 0.44 ($p = 0.0107$) and 0.43 ($p = 0.0122$) for the subjects receiving 4% and 2% diltiazem, respectively. The secondary endpoint of overall daily anal-fissure-related pain for Week 4 for the 2% diltiazem arm compared to placebo had a reduction in the pain score of 0.42 ($p = 0.0143$), while the 4% diltiazem arm compared to placebo showed a reduction in the pain score of 0.36 ($p = 0.0289$). At Week 8, healing was improved for the 4% diltiazem arm compared to placebo, with 32.7% ($p = 0.0184$) versus 23.9% showing healing. The 2% diltiazem arm showed healing in 31.2% ($p = 0.0426$ versus placebo) of subjects. On the PGI-I measure, there was a difference favoring 2% diltiazem versus placebo at Week 4 ($p = 0.0084$). There were no significant differences between 4% diltiazem and placebo on the PGI-I measure. AEs were approximately similar for the three trial arms. Reports of headaches were similar in the three arms (14.7% for subjects receiving 4% diltiazem, 12.3% for those receiving 2% diltiazem, and 14.2% for patients receiving placebo).

Based on these results, in June 2012, to begin our U.S. development of VEN 307, we filed an IND for our PK trial in the U.S. for the current formulation of VEN 307. In August 2012, we met with the FDA in a pre-NDA meeting to discuss the Phase III trial, as well as steps to move forward toward an NDA. We were advised that we should submit two provocative skin test trials and a second pivotal study, to, at a minimum, complete the clinical safety data base. In addition, the FDA advised us that it preferred we undertake a more formal standardized definition of healing (similar to that used in wound healing studies) as an endpoint, which would need to be positive in two studies, to support a label claiming improved healing. We determined to not pursue that request, and therefore we do not expect the FDA will allow us to claim improved healing on the product label.

Because diltiazem is approved in oral formulations for the treatment of angina and high blood pressure, it is eligible for the FDA's 505(b)2 registration pathway and we were also advised that we should submit a formal PK comparison of VEN 307 with FDA approved oral diltiazem, done in anal fissure patients in the NDA to support the 505b(2) NDA status.

We initiated a second pivotal Phase III clinical trial of VEN 307 (t.i.d. formulation) in anal fissures in the fourth quarter of 2012, and expect to report top line data in the fourth quarter of 2013. This trial is randomizing in a 1:1 ratio, 400 subjects to either 2% diltiazem cream applied peri-anally three times daily or a placebo cream, at approximately 120 sites primarily in the U.S. with supplemental sites in Canada and Israel. The treatment and the double blind period duration will be four weeks. The primary endpoint is similar to that in the prior Phase III trial conducted by S.L.A. Pharma: worst pain with or following defecation during the fourth week of treatment. The key secondary endpoints are average daily pain and Patients' Global Impression (PGI), also at four weeks. Assuming positive results, we expect to be able to file the NDA in the fourth quarter of 2013 or the first quarter of 2014. Additional studies to be included in the NDA are two provocative skin test safety trials, a cumulative irritation study in 35 healthy volunteers, and a sensitization study in 200 healthy volunteers, following standardized protocols commonly used for the safety evaluation of dermatology products in the U.S. for FDA review, as well as a PK study in patients with anal fissure comparing VEN 307 with an approved oral diltiazem product.

Phenylephrine gel (VEN 308) for the treatment of fecal incontinence associated with ileal pouch anal anastomosis, an FDA orphan indication. Ileal pouch anal anastomosis, or IPAA, is a surgical procedure used as part of a colectomy, which is a surgical treatment for patients with ulcerative colitis. Fecal incontinence resulting from dysfunctional sphincter tone is a common consequence of this procedure. Patients with IPAA, secondary to a total colectomy, tend to have a high incidence of fecal incontinence, up to 30%, according to a 1987 study conducted by Dr. John Pemberton and others at the Mayo Medical School. According to a U.S. community-based epidemiology study (Nelson et al., JAMA, 1995), 2.2% of the U.S. population suffer from fecal incontinence, which we estimate to be approximately 7.0 million people, based on 2010 Census Bureau population estimates. The surgery associated with IPAA can weaken sphincters and muscles necessary for continence and therefore can result in incontinence. About 30% of patients with ulcerative colitis, a form of inflammatory bowel disease which has a prevalence of 700,000 patients in the U.S. (according to Datamonitor 2008) will have had a colectomy, almost always an IPAA procedure (according to McGlauchlin and Clark, Practical Gastroenterology, 8/2008). IPAA-related fecal incontinence is considered an orphan indication by the FDA and the European Medicines Agency, or EMEA. In 2006, the total population of patients with IPAA-related fecal incontinence in the U.S. was estimated to be 50,000 to 100,000, according to IMS Health, Inc. Currently, there are few options available to treat this problem, consisting of over-the-counter, or OTC, bulk laxatives, fiber diets, Imodium, which is a treatment for diarrhea, and invasive surgical procedures. In addition, Solesta, an injectable inert bulking agent product, was approved as a device by the FDA in May 2011 for the treatment of fecal incontinence in adult patients who have failed conservative therapy. Solesta is injected submucosally around the anal sphincter and consequently has to be administered in an outpatient setting by qualified physicians. In addition, Norgine is conducting a European Phase II program with NRL001, a suppository formulation of an alpha adrenergic stimulating agent for the treatment of fecal incontinence. We are not aware of any FDA-approved drugs for fecal incontinence. In several investigator-initiated clinical trials with patients suffering from IPAA-associated fecal incontinence, topical phenylephrine significantly (and in some patients, dramatically) improved patient bowel control. In clinical trials with other forms of incontinence, improvements were also observed following application of topical phenylephrine, depending on the cause of the incontinence.

Our product, VEN 308, is a gel formulation of phenylephrine. Applied topically, VEN 308 increases anal sphincter tone, thereby improving fecal incontinence in patients where sphincter tone is the major cause of their symptoms, such as post-IPAA surgery. We believe VEN 308 potentially has significant advantages over the limited treatment options currently available for fecal incontinence associated with IPAA, including but not limited to, increased efficacy and/or reduced invasiveness. We have licensed the exclusive North American rights to VEN 308 from S.L.A. Pharma who developed the specific formulation of phenylephrine for the topical use in fecal incontinence and developed the manufacturing method. S.L.A. Pharma's previous partner, Solvay, conducted important pharmacokinetic studies. We intend to undertake technical development to create a twice daily patentable formulation of VEN 308 in the near future after which we will determine whether to pursue further development of VEN 308. VEN 308 is covered by a patent that will expire in December 2017. The FDA has granted VEN 308 orphan status for the treatment of IPAA-related fecal incontinence. In the U.S., orphan drug designation is given to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Assuming sufficient resources in the future, which could be supplied from the planned commercialization of VEN 307, we expect to conduct a Phase IIb trial in IPAA patients to be followed by one or two Phase III trials (if results are sufficiently positive) in support of the orphan indication of IPAA-related fecal incontinence. We would expect to submit an orphan NDA for VEN 308 for this indication. Orphan status provides seven years of data exclusivity in the U.S. from the date of approval for a specific indication.

Our Strategy

Our objective is to develop and commercialize highly differentiated products to address critical medical needs of the lower gastrointestinal tract. We are developing our product candidates to treat anal fissures and fecal incontinence. We are aware of only one drug that has received FDA approval for the treatment of pain associated with anal fissures in the U.S.; Rectiv, a topical nitroglycerin, was approved by the FDA in June 2011 and was made commercially available by Aptalis in the first quarter of 2012. There are no FDA-approved prescription drugs for the treatment of incontinence, but Solesta, a hyaluronic acid dermal filler, was approved as a device by the FDA in 2011 for intra-anal injection for fecal incontinence and was launched by Salix Pharmaceuticals in 2012.

To achieve this objective, we intend to:

· complete our second ongoing Phase III trial with the existing three-times-per-day formulation VEN 307, which trial began in the fourth quarter of 2012, and complete two cutaneous safety trials and a PK trial, with the goal to prepare and file an NDA for VEN 307 for the topical treatment of pain associated with anal fissures in the fourth quarter of 2013 or the first quarter of 2014;

· assuming VEN 307 is approved by the FDA, and because topical diltiazem is already used by colorectal surgeons in the U.S., we intend to engage our own contracted gastrointestinal specialty sales force, and marketing staff to commercialize this product and/or engage a suitable partner in the U.S. and to license it for sale in Canada; and depending on the technical feasibility of a twice dally formulation and successful commercialization of the three times daily formulation of VEN 307 and other factors we intend to develop this product in a patentable twice daily extended release formulation and submit the NDA by the end of 2017 to allow several years of commercialization prior to the end of exclusivity of the original VEN 307 product; and

· we intend to do technical development to create a twice daily patentable formulation of VEN 308 in the near future after which we will determine whether to pursue further development of VEN 308.

Iferanserin ointment (VEN 309) for the topical treatment of symptomatic internal hemorrhoids. We previously were developing VEN 309, iferanserin, for the treatment of hemorrhoids. We originally licensed VEN 309 from Sam Amer & Co., Inc., or Amer, in March 2008. In November 2011, we purchased all rights, title and interest to VEN 309 from Amer and terminated the license agreement. On June 25, 2012, we reported that our Phase III, randomized, double-blind, placebo-controlled clinical trial of VEN 309 for the treatment of symptomatic hemorrhoids did not meet its endpoints. Nor could we identify sub-populations in the trial who responded better to drug than placebo. Based on the disappointing results of that Phase III trial and the positive results of our Phase III trial for VEN 307, reported one month earlier in May 2012, we determined that our current resources would be better allocated toward the planned completion of VEN 307 development program in anal fissures. Consequently, we have no immediate plans to continue development of VEN 309 and have ceased all activity related to VEN 309 other than the winding down of the program.

Corporate History

We were incorporated in Delaware in October 2005 under the name South Island Biosciences, Inc. and changed our name to Ventrus Biosciences, Inc. in April 2007. We began operations in April 2007 upon the acquisition of the licenses to VEN 307 and VEN 308 and the hiring of a development team.

DILTIAZEM CREAM (VEN 307)

Background on anal fissure

Incidence and prevalence

Anal fissure, which is a crack in the skin of the anal canal that results from reduced blood supply to the area and/or from increased sphincter tone, is a common anal disorder characterized by severe anal pain and bleeding with or after bowel movements. Because there have been no approved pharmacological treatments for anal fissure, many cases progress to surgery because of the severe pain. There are no formal epidemiology studies for anal fissure, but its prevalence has been estimated indirectly. When 1,500 unselected neurological inpatients were screened in studies between 1990 and 1998 conducted in the U.S. by Dr. Wolfgang Jost, the prevalence of anal fissure was estimated at 1.6% in males and 2.2% in females. By extrapolation to the 2009 U.S. adult population, we estimate that the general prevalence rate is 1.9%, with approximately 4.3 million current cases. In 2010, it was estimated by SDI Health LLC that there were approximately 1.1 million office visits per year for anal fissures.

Physiology of anal fissure

Although hypertonia, or an increase in tightness of muscle tone, of the internal anal sphincter, or IAS, is associated with anal fissure, its contribution to the cause of anal fissure remains unclear. Hypertonia of the IAS does, however, contribute to chronic anal fissure. Anatomical, angiographic, and blood-flow studies have shown that the vascular supply of the anal epithelium, or tissue lining the anus, is very poor in the posterior midline, the anal area most commonly affected by fissures. Thus, it is possible that decreased anodermal blood supply to this area contributes to the pain and ischemia, or decrease in the blood supply, of traumatized anal epithelium, perpetuating ulceration and preventing healing. Whether the primary event for anal fissure is hypertonia of the IAS or decreased blood supply, hypertonia itself reduces vascular perfusion in the anal area. This reduction of vascular perfusion has been compared with that associated with ischemic pain in the lower limbs.

Current treatments

The clinical goal in treating anal fissures is to reduce the pain associated with the fissure long enough for it to heal naturally and prevent the patient from having to resort to surgery. Currently, most physicians start treatment with diet modification, fiber, sitz baths and stool softeners. If these conservative treatments fail, physicians proceed to pharmacologic therapy, prescribing topical steroids or by directing special pharmacies to create compounded topical formulations by mixing raw diltiazem, and in some cases nifedipine, another calcium-channel blocker, or nitroglycerin, into a cream, ointment or gel for topical use by fissure patients. If these pharmacologic treatments fail to manage the pain, physicians consider, and often perform, surgery. In some instances, physicians initially prescribe pharmacologic therapy in addition to conservative treatments; in other instances because of the severe pain, they initially perform surgery.

The purpose of surgery is to reduce hypertonia of the IAS by either manual dilatation or lateral sphincterotomy. Both procedures are highly successful in relieving the pain and promoting healing of fissures. Although a relatively simple and effective surgical procedure, lateral sphincterotomy is also associated with short-term mild-to-moderate fecal incontinence. This is not an insignificant adverse effect and can become permanent or at least chronic in a fairly high percentage of patients. Studies have shown 6 - 8% of patients had incontinence to flatus or minor fecal soiling at a time greater than five years after surgery. In another study, at a mean follow-up time of 66.6 months (range 30 - 84 months), 10% of patients who had a lateral internal sphincterotomy were incontinent.

Over the last decades, Cellegy Pharmaceuticals, Inc., a drug developer (acquired by ProStrakan Group plc, which is a wholly owned subsidiary of Kyowa Hakko Kirin Co. Ltd.), attempted to gain FDA approval for the topical treatment of anal fissures with nitroglycerin, an agent that reduces IAS and anal fissure pain. Early attempts to develop nitroglycerin utilizing a healing endpoint failed as it was discovered most fissures will heal naturally if the patient can endure the pain for the first several weeks of the disorder. However, it was discovered during development that lowering IAS hypertonia did have a significant benefit in reducing the pain associated with anal fissures. Cellegy’s subsequent multiple pivotal studies with pain as a primary endpoint demonstrated a 33% reduction in pain scores in patients with baseline pain score > 48 (1 - 100 mm on the visual analog scale, or VAS). However because Cellegy did not use minimum pain scores as an inclusion criteria, the overall effect was diluted to 22%. In addition, 63% of subjects reported headaches, which is a known systemic side effect of nitroglycerin. The FDA denied its approval, concluding that the risk benefit ratio for nitroglycerin as topical treatment for anal fissure pain was not favorable due to the modest overall effect and high incidence of systemic side effects. Subsequently Cellegy (now ProStrakan) conducted an additional clinical trial in anal fissures which was filed with the FDA in 2009. ProStrakan received a complete response letter for this new NDA in April 2010, because of issues with statistical significance, according to ProStrakan. However, ProStrakan filed a response to these concerns and, in late June 2011, received approval for the product (Rectiv, a 0.4% concentration of nitroglycerin in ointment) to be applied twice daily for the treatment of pain associated with chronic anal fissures, for up to three weeks duration. This product has been marketed in the U.K. and other European countries and elsewhere since 2007. The professional label in Europe, which is a summary of product characteristics, lists headaches as being very common with a 63% incidence of which 45% were moderate or severe, in three pivotal trials. The U.S. label lists headaches as occurring in 64% of patients, with 938 headaches occurring in 79 patients, in one pivotal trial.

We have planned a clinical program that focuses on pain as the primary endpoint and includes only patients who have adequate pain scores on entry into the studies, which we believe will avoid the modest effects seen in these earlier studies. In addition, based on results of previously published trials (such as Kocher et al. 2002; see **Table 1** below), we believe that the side effects of diltiazem cream are likely to be substantially less than those observed with topical nitroglycerin, which primarily were headaches.

DILTIAZEM CREAM (VEN 307) DEVELOPMENT

Background on diltiazem

Diltiazem, a calcium-channel blocker, was first approved in 1982 in oral form for the treatment of angina and high blood pressure. It has been prescribed in the U.S. for millions of patients in oral dosages typically from 240 mg to 360 mg per day. In contrast, daily doses of VEN 307 for treatment of anal fissures will range from 15 mg to 45 mg. Because of the extensive patient exposure to diltiazem as a cardiovascular agent and the wide safety margin as a low dose topical therapy, we intend to develop the topical formulation as a Section 505(b)(2) NDA, as agreed with the FDA at our pre-IND meeting in August 2007. This special NDA procedure, known as a "section 505(b)(2) application" or a "paper NDA," allows an applicant to seek approval on the basis of a combination of a prior approval of a similar product or published literature, and some new clinical studies conducted or sponsored by the applicant. Section 505(b)(2) applications are often used for changes in a drug that require clinical investigations and thus cannot be handled through the generic drug process, such as a new indication or change in dosage or route of administration.

Compounded diltiazem (prepared by the pharmacist, for each patient, using a general cream base and diltiazem from oral formulations) is currently listed in the U.S. and E.U. anal fissure treatment guidelines as a preferred agent prior to attempting surgery. According to advice we have received from members of our scientific advisory board, who are experts in gastroenterology and gastrointestinal surgery, compounded diltiazem is utilized by many colorectal and gastroenterology specialists each year for the treatment of anal fissures and, according to these experts, has also reduced the number of surgeries required. As a result, awareness and utilization of diltiazem as an effective treatment for anal fissures is high among physicians that treat this disorder. However, compounded diltiazem for anal fissure is not an FDA-approved use nor is it an FDA-approved product, and as such, the cost is not typically reimbursed by Medicare or health insurance plans. Data on unit and dollar volumes of compounded preparations are not routinely collected and not available to us.

Further, to examine the quality of compounded formulations of topical 2% diltiazem, in 2012 (2013?), we undertook a high-performance liquid chromatography (HPLC) analysis of preparations of topical 2% diltiazem hydrochloride gathered from retail pharmacies in a metropolitan region of the U.S. A participating healthcare professional wrote 12 prescriptions, with two refills allowed per prescription, so that three prescriptions could be filled at each of 12 pharmacies (36 total refills) for compounded 2% diltiazem cream. The analysis included an assessment of potency (percentage of claim) and content uniformity, with sampling from eight different pre-specified locations within the compounded formulation containers. The United States Pharmacopoeia (USP) standard for potency is 90% to 115% of claim. Of the 36 preparations, five (13.89%) were supra-potent and 13 (36.11%) were sub-potent. The supra-potent prescriptions ranged in potency from 117.2% to 128.5% of claim, and the sub-potent prescriptions ranged in potency from 34.8% to 89.8% of claim. Fourteen (38.9%) preparations lacked content uniformity according to the USP standard. These results demonstrate that although compounded drugs might be formulated under professional pharmacy standards, these standards are inherently less rigorous than federal GMP quality standards. We believe that a topical 2% diltiazem cream produced under GMP regulations is needed to avoid the large percentage of substandard compounded formulations of a drug specifically recommended by the practice parameters of a medical society.

The use of diltiazem for the treatment of anal fissures was first discovered at St. Mark gastroenterology teaching hospital in London. Professors Kamm and Phillips filed the original method of use patent applications in 1997 in the Great Britain Patent Office. In 1998, a PCT International Application was filed designating the U.S. as National Phase country and which is the current patent application in the U.S. In 2001, North American rights were licensed to Solvay Pharmaceuticals, SA. During the time that Solvay held the rights, it improved the manufacturing processes and formulation and conducted important pharmacokinetic studies. In 2004, the new CEO of Solvay Pharmaceuticals refocused the R&D strategy on CNS and cardio-metabolic programs, discontinuing gastroenterology and women's health projects. Consequently, in 2005, the license rights to diltiazem cream were returned to S.L.A. Pharma. From 2005 to the March 2007 licensing by Paramount BioSciences, S.L.A. Pharma focused on regulatory and manufacturing priorities, preparing diltiazem for further development.

We have the potential to capture immediate market share if VEN 307 is approved due to its known efficacy and the current use of the compounded version. We expect that VEN 307 will be highly competitive with the compounded version because of the ease of prescription (already formulated, and approved by the FDA), with no need for compounding at the pharmacy, and because VEN 307 should be eligible for reimbursement under Medicare and other health plans, which the compounded version is not. For these reasons, we believe that the use of the compounded form of diltiazem will greatly decrease if VEN 307 is approved.

In August 2007, we acquired North American rights to diltiazem from Paramount BioSciences, which previously acquired rights from S.L.A. Pharma in the United Kingdom for developing and marketing a proprietary diltiazem cream for relief of pain associated with anal fissures. We incurred a liability to Paramount BioSciences in the amount of $1,087,876, which represented the fees Paramount BioSciences had paid through August 2007 for both VEN 307 and VEN 308. Paramount BioSciences had acquired the S.L.A. rights in March 2007 and began working with us immediately to advance the development of these assets while an asset transfer agreement was finalized. S.L.A. Pharma is developing diltiazem cream for the European market and S.L.A. Pharma began a Phase III clinical trial in the E.U. in November 2010. We are financially supporting the E.U. trial and are obligated to make monthly payments of $41,500 to S.L.A. Pharma for project management fees for VEN 307.

On November 1, 2011, the U.S. Patent and Trademark Office, or PTO, issued U.S. Patent No. 8,048,875 with claims directed to the use of VEN 307 as a topical treatment for the relief of pain associated with anal fissures. The U.S. patent expires in February 2018. A continuation application was filed on July 8, 2011 claiming priority to U.S. Patent No. 8,048,875 with claims directed to additional uses of VEN 307 for related indications. If the continuation application is issued as a patent, it will also expire in February 2018. If approved by the FDA, VEN 307 will receive three years of data exclusivity in the U.S. under the Hatch-Waxman Act.

In August 2007, we concluded a pre-IND meeting with the FDA in anticipation of our IND submission for permission to initiate Phase III trials in the U.S. This meeting also afforded us an opportunity to gain agreement on the key design issues of the studies (including the one which S.L.A. Pharma is implementing) and additional information required for an approval of an NDA. We anticipate the availability of data from the S.L.A Phase III trial in the second quarter of 2012 and, if the E.U. trial is successful, we plan to initiate the U.S. pivotal program by the second half of 2012, contingent on the availability of additional capital. We expect to collaborate closely with S.L.A. Pharma in order to leverage clinical data for different regulatory agencies and to rationalize manufacturing capacity.

Mechanism of action

The mechanism of action for topical diltiazem cream was demonstrated in human pharmacodynamic studies that showed an anal maximal resting pressure, or MRP, reduction of 28% that was sustained for 3 - 5 hours. This MRP reduction is believed to decrease the pain associated with anal fissures by normalizing internal anal sphincter pressure, which improves vascular blood supply and reduces ischemic pain.

Preclinical safety

Studies have been conducted in rabbits and guinea pigs to assess the topical safety of diltiazem cream. Clinicians treated rabbits in and around the anus with 2% diltiazem or placebo cream twice daily for 90 days to evaluate the chronic safety of the product. Although exterior anal tissue showed an increase in erythema, or redness of the skin, and edema, or accumulation of fluid beneath the skin, the clinicians concluded that these effects were due to the application procedure, to a possible reaction to latex gloves or to both. There were no histological findings. In this study, topical 2% diltiazem cream had no other adverse effects. Clinicians used guinea pigs to assess the potential for 2% diltiazem cream to elicit contact sensitization, or skin reaction to the application. This study did not demonstrate any sensitization potential of the diltiazem cream in guinea pigs.

Investigator-initiated clinical studies (studies sponsored by individual clinicians)

The investigator studies conducted with diltiazem cream applied topically in the perianal area in normal subjects and in patients with anal fissures are summarized in **Table 1.** These studies were conducted by independent investigators and not by us or any partner of ours. The year the study was published is given in the column headed “Study.”

Table 1. Summary of Investigator-initiated clinical studies.

Study	Condition, treatment, dosage	Study design, endpoints	Efficacy	Adverse events
Carapeti, E.A., et al, Gut, 45:719 - 722, 1999	10 normal subjects; placebo (PBO) or diltiazem (DTZ) gel (0.1%, 0.5%, 1%, 2%, 5%, and 10%)	DTZ or PBO gel applied once to anal margin; maximum resting anal pressure (MRP) and anodermal blood flow measured starting 1 hour after treatment	DTZ decreased MRP at concentrations of 1% and higher, maximum decrease of 28% at 2% gel, no further effect of 5% or 10%; effect at 2% lasted 3 - 5 hours; no change in blood flow	No local or systemic adverse events (AEs) reported
Carapeti, E.A., et al, Dis Colon rectum, 43:1359 - 1362, 2000	15 patients with chronic anal fissures (CAF); 2% DTZ gel, three times-per-day (TID) for 8 weeks	DTZ gel applied to anal margin; MRP, anodermal blood flow and healing rate monitored every 2 weeks, daily diary cards for worst pain (scale of 0 - 10) of the day	Fissures healed in 67% of subjects; significant decrease in MRP and pain (decreased from 5.5 pretreatment to 1 post-treatment); no effect on blood flow	No AEs
Bhardwaj, R., et al, Annual Meeting of British Association of Colon proctologists, Brighton, United Kingdom, 2000	44 patients with CAF, 2% DTZ gel, TID for 8 weeks	27 patients assessed at 2 months, 15 patients evaluated at 4 months (included 9 who had healed at 2 months and remained healed); assessed for healing, pain, rectal bleeding, MRP	Fissures healed in 56% of subjects at 2 months, 73% at 4 months; pain abolished in 88%, bleeding in 92%; MRP decreased by 24% at 2 months	1 patient had minor incontinence to flatus
Jonas, M., et al, Dis Colon rectum, 44:1074 - 1078, 2001	50 patients with CAF, 24 treated with oral DTZ (60 mg), 26 with topical DTZ (2% gel), twice per day (BID) for 8 weeks	DTZ gel applied 1cm inside anus and to anal margin; pain, bleeding, perianal irritation (all 3 measured on a scale of 1 - 100 mm), MRP, healing monitored every 2 weeks	Fissures healed in 38% of subjects (oral) vs. 65% (topical) (9 in each group had previously failed on glyceryl trinitrate (GTN); 7 of these healed on topical vs. 1 on oral DTZ); both oral and topical DTZ decreased MRP; pain, bleeding and irritation reduced by both formulations (pain went from 70 to 7 after 8 weeks on oral, from 68 to 3 on topical)	No AEs in topical group; AEs reported in 8 patients on oral DTZ (headaches, nausea and/or vomiting, rash, decreased sense of taste and smell)

Study	Condition, treatment, dosage	Study design, endpoints	Efficacy	Adverse events
Knight, J,S., et al, Br J Surg, 88:553 - 556, 2001	71 patients with CAF, 2% DTZ gel, BID, additional 8 - 12 weeks for subjects who did not heal on original regimen	DTZ applied perianally; healing monitored;	75% healed after 2 - 3 months, a total of 89% healed after a median duration of 9 weeks (range of 2 - 16 weeks); after a median of 32 weeks follow-up (range 14 - 67 weeks) 66% symptom-free, 17% had mild symptoms, and 7% had reoccurrence	4 patients reported perianal dermatitis, 1 reported headache
Griffin, N., et al, Colorectal Dir, 4:430 - 435, 2002	47 patients with CAF who failed topical GTN, 2% DTZ cream, BID for 8 weeks	Treatment administered in anal verge; daily diary for pain, bleeding and itching (scale of 0 - 100); healing monitored	Fissures healed in 48% of subjects; pain and bleeding decreased after 8 weeks, no effect on itching; 2 patients relapsed after median duration of follow-up 45 weeks (range 23 - 54)	1 patient developed a local perianal rash; up to 25% reported increased perianal itch
DasGupta, R., et al, Colorectal Dir, 4:20 - 22, 2002	23 patients with CAF, 2% DTZ gel, TID for up to 12 weeks	DTZ applied to lower half of anal canal, healing monitored	Fissures healed in 48% of subjects, in a median of 8 weeks (range 1 - 12 weeks); of 8 who had previously failed GTN, 6 (75%) healed; no recurrences at 3 months	No AEs
Kocher, H.M., et al, Br J Surg, 89:413 - 417, 2002	60 patients with CAF, 0.2% GTN ointment (29 patients) or 2% DTZ cream (31 patients), BID for 6 - 8 weeks	DTZ or GTN applied to anal verge, monitored every 3 weeks for healing; pain recorded on VAS (0 - 100) scale	At 8 weeks fissures healed or improved in 12 and 13 patients, respectively, after GTN (86%) vs. 8 (healed) and 16 (improved) after DTZ (77%); both decreased pain to approximately same extent; at 12 weeks 2 GTN patients had recurred vs. none in the DTZ group	21/29 GTN subjects (72%) reported AEs vs. 13/31 (42%) in DTZ group; 17/29 in GTN group had headaches, vs. 8/31 of DTZ patients
Bielecki, K., et al, Colorectal Dir, 5:256 - 257, 2003	43 patients with CAF, 0.5% GTN ointment (21 patients) or 2% DTZ ointment (22 patients), BID for 8 weeks	Patients monitored 3 times during treatment	Fissures healed in 86% of GTN, 86% of subjects with DTZ, 3 failures in each group	Mainly headache in 7 GTN patients (33%), no AEs reported in DTZ patients

Study	Condition, treatment, dosage	Study design, endpoints	Efficacy	Adverse events
Shrivastava, U.K., et al, Surg Today, 37:482 - 485, 2007	90 patients with CAF; 2% DTZ ointment (30 patients), 0.2% GTN ointment (30 patients), BID; no treatment (30 patients)	Treatments applied BID to anus, patients monitored for healing and pain (VAS) twice 2 per week then every 2 weeks	Fissures healed in 80%, 73% and 33% for DTZ, GTN and control subjects, respectively; mean time for healing 6.6 weeks, 7.0 weeks and 7.6 weeks for DTZ, GTN and controls, respectively; pain decreased by 75% for DTZ, 59% for GTN and 29% for controls at 6 weeks; recurrence rate 12.5%, 32% and 50% for DTZ, GTN and controls, respectively	No AEs in DTZ patients, 67% of GTN patients had headaches

DTZ = diltiazem; GTN = glyceryltrinitrate (nitroglycerin)

Clinical trials of diltiazem cream sponsored by S.L.A. Pharma

In 2004 and 2005, S.L.A. Pharma assessed the pharmacokinetic profile of topical diltiazem cream over a four-day period in subjects with anal fissure. Clinical dosing was completed in November 2005 and published in January 2007. Clinicians treated patients with eight doses of either 2%, 4%, or 8% diltiazem cream. Clinicians administered a single dose perianally on Day 1, followed by doses three times a day on Days 2 and 3, followed by another single dose on Day 4. The clinicians collected blood over 24 hours on days 1 and 4. Maximum blood levels and area under the curve increased with the dose, and there appeared to be accumulation of diltiazem in blood on Day 4 after multiple dosing. The time to maximum blood levels was five to seven hours, and the plasma half-life was less than 12 hours. However, the maximum amount of diltiazem that was absorbed was much less (at least five-fold less) than observed after oral dosing. Side effects, such as anal irritation, headache, and nausea, were mild.

Blood pressure was measured at the following times after the single dose on Days 1 and 4: predose, 15, 30 and 45 minutes and one, one and a half, two, four and eight hours after dosing. The relatively small maximum mean decreases (mmHg) in blood pressure in patients receiving 2%, 4% and 8% cream (3 - 4 patients per group) by Day 4 ranged from 4 to 8mmHg systolic blood pressure, or SBP, and 4 to 6 mmHg diastolic blood pressure, or DBP. The changes were, in general, transient and asymptomatic and blood pressure had returned to at or near baseline by the next reading. There was no clear dose-related effect among the 2%, 4% and 8% creams with respect to decreases in blood pressure. In clinical trials with oral diltiazem for hypertension, the patients receiving placebo had mean decreases of blood pressure from 2 to 4 mmHg.

S.L.A. Pharma compared the effect of 2% diltiazem cream with 0.2% glyceryltrinitrate cream in subjects with chronic anal fissure. This study was completed in January 2001 and published in October 2001. Clinicians applied the preparations in and around the anus twice daily for six weeks. Nine of the 31 patients treated with diltiazem and three of the 29 patients treated with glyceryltrinitrate withdrew from the study by eight weeks. In the diltiazem group, 26% of the patients experienced healed fissures and 52% of patients experienced improved fissures. In the glyceryltrinitrate group, 41% of patients experienced healed fissures and 45% of patients experienced improved fissures. There was no significant difference in the healing rates between the groups. Both treatments resulted in a significant decrease in pain. Four weeks after the end of treatment, no fissures recurred in patients treated with diltiazem, but fissures recurred in two patients treated with glyceryltrinitrate. Compared with 18 treatment-emergent adverse events reported by 13 patients (42%) receiving diltiazem, there were 33 adverse events reported by 21 patients (72%) receiving glyceryltrinitrate. Eight patients receiving diltiazem complained of nine headaches, 17 patients receiving glyceryltrinitrate complained of 20 headaches.

Similar to the early glyceryltrinitrate, or GTN, development program that found healing to be a difficult and inappropriate endpoint for registration trials, S.L.A. Pharma also pursued a healing endpoint strategy in early development. In an exploratory trial sponsored by S.L.A. Pharma that was completed in February 2002 and published in February 2003, the effects of 2% diltiazem cream on healing rates were compared with placebo cream in patients with severe chronic anal fissure. Thirty-one patients were randomized to each treatment group. Creams were applied twice daily for eight weeks. At the end of eight weeks, there was no difference in the healing rates between patients receiving diltiazem (10%) and patients receiving placebo (19%). No difference was observed in the secondary endpoints, including pain, which is likely due to the assessment being made only at the end of the study, not daily as in the other trials, which showed a positive outcome in these endpoints. Fifteen patients receiving diltiazem reported 28 adverse events and 12 patients receiving placebo received 18 adverse events. Seven patients receiving diltiazem and three patients receiving placebo reported a rash or pruritus, or itchiness. Headaches were reported in the same number of patients in both treatment groups.

Summary of studies to date

The topical application of diltiazem cream provides pain relief associated with anal fissure and has also been found to be associated with healing. The effects of diltiazem cream are comparable to those observed for treatment of anal fissure with topical application of GTN, but diltiazem cream is much better tolerated. Based on currently available data and discussion with the FDA, we think it is clear that relief of pain associated with anal fissures is the preferred clinical endpoint. Our belief is supported by the study by U.K. Shrivastava, et al., published in Surgery Today, 37:482 - 485, 2007 (see **Table 1** above), which compared GTN and diltiazem perianally compared with standard care alone. In this trial, pain decreased by 75% for diltiazem compared with 29% for controls at six weeks. In almost all studies with either GTN or diltiazem where pain was measured, results are consistent whereas with healing as an endpoint results are variable.

Our belief that relief of pain associated with anal fissures is the preferred clinical endpoint is further supported by market research that identified clinicians' primary treatment goal as pain relief. Importantly, the diltiazem mechanism of action for pain relief is to reduce IAS pressure which addresses the underlying cause of anal fissure pain.

Diltiazem cream (VEN 307) development plan

In August 2007, we had a pre-IND meeting with the FDA concerning VEN 307 for the treatment of pain from anal fissures where it was established that next clinical studies needed for approval were two pivotal Phase III trials, preceded (if conducted in the U.S.) by three short-term dermal toxicology studies. Prior to conducting clinical Phase III trials in the U.S., we must complete three short-term dermal toxicology studies and file an IND for FDA approval. We plan to employ a two-pronged development strategy for VEN 307. While S.L.A. Pharma has conducted the first Phase III clinical trial in the E.U. using the original three times daily (t.i.d.) formulation, which was completed and reported in May 2012, we have initiated technical development of what we believe is a superior formulation with potentially new intellectual property in the form of an extended release formulation. There are several proven methodologies for extended release topical formulations, and we have observed that diltiazem is readily druggable in this regard. We have assessed three to four alternatives preclinically with an external contractor, and we expect to assess in pre-clinical in vivo studies the absorption and the effect on IAS pressure with the most promising formulation. Assuming positive outcomes, we plan to file North American patent applications for all formulations that are technically feasible.

Assuming the successful launch of VEN 307 (t.i.d.), we will make the final decision on which twice daily (b.i.d.) formulation to pursue depending on several factors, including whether the new formulation is potentially clinically superior (i.e., the same efficacy, tolerability and systemic diltiazem exposure (the maximum plasma concentration, or Cmax) can be achieved with only b.i.d. administration or less), our available resources, revenue, if any, from VEN 307, the observed market size for anal fissures, and existing and projected reimbursement patterns, clinical and regulatory considerations, and our assessment of the then-current state of our intellectual property estate. If the new U.S. developed formulation is superior and the other factors are met, we plan to initiate comparative manometry studies in volunteers for PK and pharmacodynamic (PD) with two of the new formulations, using our base formulation as the comparator and then launch one to two (depending on FDA requirements) pivotal trials with one of the candidates in parallel in order to complete the NDA for an estimated FDA submission prior to the end of 2017 to allow several years of marketing before loss of exclusivity for the original VEN 307 product. We intend to finance the clinical development of the extended release formulation of VEN 307 from operating profit from the planned commercialization of VEN 307 (t.i.d. formulation). We expect to continue to pursue other lifecycle options, such as combination with other drugs.

Supply of clinical trial product

We have in place a primary supplier, and have identified and are qualifying back-up suppliers, for the active pharmaceutical ingredient for VEN 307. We have evaluated and selected a supplier of drug product for our current and planned research studies and clinical trials and also to provide us with our commercial supply of drug product, in the event of FDA approval of VEN 307.

PHENYLEPHRINE GEL (VEN 308)

Background on fecal incontinence

Incidence and prevalence

According to a U.S. community based epidemiology study (Nelson et al., JAMA, 1995), 2.2% of U.S. adults suffer from fecal incontinence, which we estimate to be approximately seven million people, based on 2009 Census Bureau population estimates.

The IPAA orphan population

Patients with an ileal pouch anal anastomosis, or IPAA, secondary to a total colectomy, tend to have a high incidence of fecal incontinence, up to 30%, according to a 1987 study conducted by Dr. John Pemberton and others at the Mayo Medical School. The surgery associated with IPAA can weaken sphincters and muscles necessary for continence and therefore can result in incontinence. About 30% of patients with ulcerative colitis, a form of inflammatory bowel disease which has a prevalence of 700,000 patients in the U.S. (according to Datamonitor 2008) will have had a colectomy, almost always an IPAA procedure (according to McGlauchlin and Clark, Practical Gastroenterology, 8/2008). IPAA-related fecal incontinence is considered an orphan indication by the FDA and the European Medicines Agency, or EMEA. Patients who undergo ileal pouch anal anastomosis are prone to fecal incontinence. In 2006, the total population of patients with IPAA-related fecal incontinence in the U.S. was estimated to be 50,000 to 100,000, according to IMS Health, Inc.

The FDA has granted VEN 308 orphan status for the treatment of IPAA-related fecal incontinence. In the U.S., orphan drug designation is given to a drug intended to treat a rare disease of condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S.

Physiology of fecal incontinence

Continence is a complex physiological action that requires the presence of a series of anatomical barriers preventing the movement of feces through the anus. The puborectalis muscle works with the internal and external anal sphincters to control continence. If any of these three barriers are dysfunctional, incontinence can occur in a wide range of severity. Specifically, anal sphincter weakness has long been associated with fecal incontinence. Abnormal fibrosis, reduced elasticity, insensitivity to norepinephrine and spontaneous relaxation are associated with anal sphincter weakness.

Current treatments

To our knowledge, there are no FDA-approved drugs for the treatment of fecal incontinence. Most physicians start with conservative therapy, which consists of diet modification, sitz baths and over-the-counter antidiarrheal medication. In addition to conservative therapy, physicians might prescribe antidiarrheal medication or recommend surgery.

The most common surgical procedure is sphincteroplasty for patients with physical injury to the anal sphincter. Success rates for this type of surgery are low and most of the benefit decreases with time. Solesta is an injectable inert bulking agent product approved as a device by the FDA in May 2011 for the treatment of fecal incontinence in adult patients who have failed conservative therapy. Solesta is injected submucosally around the anal sphincter and consequently has to be administered in an outpatient setting by qualified physicians. In addition, Norgine plans to conduct a European Phase I trial with NRL001, a suppository formulation of an alpha adrenergic stimulating agent for the treatment of fecal incontinence, which is anticipated to start in Europe in early 2011.

Background on phenylephrine

Phenylephrine has been available since the early 1940s in oral and nasal form for the treatment of nasal congestion. It has also been used as a topical ophthalmic agent since 1936. Phenylephrine is prescribed more than 17 million times per year in the U.S., with 99% of the prescriptions being for cough/cold oral preparations. The typical oral dosing is 40 mg to 60 mg per day. Because of the extensive patient exposure to phenylephrine, we intend to develop the topical formulation as a Section 505(b)(2) NDA. The use of phenylephrine for the treatment of fecal incontinence was first discovered at St. Mark gastroenterology teaching hospital in London. Professors Kamm and Phillips filed the original method of use patents in 1996. In 1997, phenylephrine patent application and rights were assigned to S.L.A. Pharma. In 2001, S.L.A. Pharma licensed North American rights to Solvay Pharmaceuticals, SA. During the time that Solvay held the rights, it improved the manufacturing processes and formulation and conducted important pharmacokinetic studies. In 2004, the new CEO of Solvay Pharmaceuticals refocused its R&D strategy on CNS and cardio-metabolic programs, discontinuing gastroenterology and women's health projects. Consequently, in 2005, the licensed rights to phenylephrine gel were returned to S.L.A. Pharma. From 2005 to the March 2007 licensing by Paramount BioSciences, S.L.A. Pharma focused on regulatory and manufacturing priorities, preparing the asset for further development.

In August 2007, we acquired North American rights to phenylephrine gel from Paramount BioSciences, which previously acquired rights from S.L.A. Pharma in the United Kingdom in March 2001 for developing and marketing a proprietary phenylephrine gel for the treatment of fecal incontinence. We incurred a liability to Paramount BioSciences of $1,087,876, which represented the fees Paramount BioSciences had paid through August 2007 for both VEN 307 and VEN 308. Paramount BioSciences had acquired the S.L.A. rights in March 2007 and began working with Ventrus immediately to advance the development of these assets while an asset transfer agreement was finalized.

We expect to collaborate closely with S.L.A. Pharma to leverage clinical data for different regulatory agencies and to rationalize manufacturing capacity.

Our total payment obligation for VEN 308 will not exceed $1,200,000. S.L.A. Pharma has billed us for, and we have paid, $973,500 of services through December 31, 2011. This leaves $226,500 in possible additional payments. However, we currently have no further payment obligations for VEN 308 unless we agree with S.L.A. Pharma to additional services outside the scope of the agreement.

Mechanism of action (MOA)

The MOA for topical phenylephrine gel is to increase resting anal sphincter pressure, thus increasing patient bowel control. Phenylephrine gel's MOA makes it an attractive candidate for any patient population that suffers from incontinence characterized as leaking/seeping fecal incontinence.

Preclinical safety

A mouse lymph node assay conducted by S.L.A. Pharma did not show phenylephrine hydrochloride to be a sensitizer (meaning a chemical that induces an allergic reaction after repeated exposure) because the drug was not associated with any type of delayed hypersensitization. In another S.L.A. Pharma study, contact sensitization potential, as measured in guinea pigs, under the conditions of the study, a 20% gel was considered to be a strong sensitizer to guinea pig skin. A 28-day study by S.L.A. Pharma in rabbits, in which 10% and 20% phenylephrine gel (900 mg) was applied three times each day to the dorsum, demonstrated mild inflammation which may have been exacerbated by animals biting the site of application. These studies were primarily conducted at St. Mark's Hospital in the U.K. in the 1990s.

Investigator-initiated clinical studies

A number of investigator studies have been conducted with phenylephrine applied topically for the treatment of fecal incontinence and are summarized in **Table 2** . These studies were conducted by independent investigators and not by us or any partner of ours. The year the study was published is given under the column headed “Study.” One of these studies was conducted in patients with IPAA-related fecal incontinence. In one specific randomized controlled trial, phenylephrine significantly reduced the incontinence score ($P = 0.015$) and improved subjective measures ($P = 0.04$) compared with placebo. For some patients in this study, phenylephrine totally eliminated nocturnal episodes of fecal incontinence. No patient discontinued treatment during the study due to side effects. Studies in patients whose incontinence was more related to factors other than anal sphincter tone (many patients in the passive fecal incontinence studies) showed less response. As a result, our development plan will initially focus on the orphan IPAA indication.

Table 2. Investigator-initiated studies of topical phenylephrine gel for treatment of fecal incontinence.

Study	Condition, treatment, dosage	Summary of results
Carapeti, E.A., et al, Br J Surg. 86:267 - 270, 1999	Normal subjects, phenylephrine gel (5%, 10%, 20%, 30%) applied once to anal verge	Resting anal pressure increased by 8% to 33%, effect lasted for median of 7 hours, no change in pulse
Carapeti, E.A., et al, Dis Colon rectum, 43:1059 - 1063, 2000	IPAA-related FI, 10% phenylephrine or placebo gel, 2 times/day for 4 weeks	50% (6/12) of phenylephrine subjects improved vs 8% (1/12) placebo, 33% had cessation of FI on phenylephrine, 0% on placebo, phenylephrine increased anal pressure. No reported side effects.
Carapeti, E.A., et al, Br J Surg, 87:35 - 42, 2000	Passive FI, 10% phenylephrine vs placebo cream, 2 times/day for 4 weeks	No effect of phenylephrine or placebo on incontinence or anal pressure, 17% of phenylephrine and 6% of placebo patients had > 75% improvement
Cheetham, M.J., et al, 2000	Passive FI, 20% phenylephrine or placebo gel, 2 times/day for 4 weeks	No effect of phenylephrine or placebo on incontinence, anal pressure, blood pressure, or pulse rate
Sasse, K.L., et al, Dis Colon rectum, 43:A2, 2000	FI, 10% phenylephrine cream, 24 weeks	Increased anal pressure, improved incontinence
Cheetham, M.J., et al, Gut, 43:356 - 359, 2001	Passive FI, placebo or phenylephrine gel (10%, 20%, 30%, or 40%) as single application	Anal pressure increased in dose-related manner after phenylephrine, no effect on pulse, transient perianal burning
Mutch, M.G., et al, 2002	Passive FI, 10% phenylephrine cream, 3 times/day for 30 days	Phenylephrine improved incontinence score, anal pressure, and anal sphincter length

FI = fecal incontinence; IPAA = ileal pouch anal anastomosis

Clinical trials

Solvay Pharmaceuticals assessed the safety and pharmacokinetic profile of intra-anal and perianal application of phenylephrine gel in healthy volunteers in 2004 in a study completed in March 2004 and published in May 2004. The phenylephrine gel was applied as a single dose either intra-anally at doses of 5, 10, 25, 50, or 100 mg, or perianally at doses of 100, 200, or 400 mg. Blood samples were collected out to 24 hours after dosing.

Perianal application of phenylephrine gel resulted in much less absorption than intra-anal application: at a perianal dose of 400 mg, blood levels were comparable to what was seen after intra-anal treatment with 10 mg to 25 mg.

Intra-anal application of phenylephrine was associated with increased blood pressure that lasted for approximately three hours, whereas these effects were not seen with perianal treatment. The most frequent side effects were headache and goosebumps after intra-anal application of phenylephrine gel which were not seen with perianal application, and anal/rectal pain after perianal application of phenylephrine gel.

Summary of studies to date

Topical phenylephrine gel has demonstrated efficacy for the treatment of fecal incontinence associated with IPAA. Pharmacokinetic studies have shown a superiority of perianal dosing which yielded low systemic absorption while still providing the desired local therapeutic effect. No hemodynamic effects where observed when phenylephrine gel was administered perianally at up to eight times the therapeutic dose. Therefore, further development of the drug will focus solely on perianal application.

Phenylephrine gel (VEN 308) development plan

We intend to do technical development to create a twice daily patentable formulation of VEN 308 in the near future after which we will determine whether to pursue further development of VEN 308.

Supply of clinical trial product

At this time, we are not actively pursuing the development of VEN 308 and have not undertaken any clinical supply activities for VEN 308.

License Agreements and Intellectual Property

General

Our goal is to obtain, maintain and enforce patent protection for our products, formulations, processes, methods and other proprietary technologies, preserve our trade secrets and operate without infringing on the proprietary rights of other parties, both in the U.S. and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the U.S. and abroad. However, patent protection may not afford us with complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management and research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently rely and will in the future rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

License Agreements - VEN 307 and 308

In March 2007, pursuant to an Exclusive License Agreement, S.L.A. Pharma granted Paramount BioSciences, Inc., or PBS, an exclusive, royalty-bearing license to sell, make, use and import diltiazem for treatment, through topical administration, of anal fissures and phenylepherine for treatment, through topical administration, of fecal incontinence in the U.S., Canada and Mexico. Pursuant to the Exclusive License Agreement, PBS was obligated to form a company to develop the technologies referenced in the Exclusive License Agreement and issue to S.L.A. Pharma that number of shares equal to 5% of such company's outstanding common stock as of the effective date of the Exclusive License Agreement. To satisfy this obligation, PBS formed our company and we issued 18,401 shares of our common stock to S.L.A. Pharma in August 2007. In the event we closed an equity financing with gross proceeds of not less than $5,000,000 and the 18,401 shares issued to S.L.A. Pharma did not have a fair market value at least equal to $500,000 (calculated by multiplying the number of shares by the price per share paid in the financing), we were required to issue to S.L.A. Pharma that number of additional shares of our common stock so that, when added to the 18,401 shares initially issued, the new and old shares would have a fair market value equal to $500,000 (based on the price per share paid in the financing). As a result, upon the closing of our initial public offering on December 22, 2010, based on the initial offering price of $6.00, we issued S.L.A. Pharma 64,933 shares of our common stock.

In August 2007, pursuant to an Assignment and Assumption Agreement, PBS sold all of its rights in and arising out of the Exclusive License Agreement with S.L.A. Pharma to us for $1,087,876. The corresponding U.S. and foreign patents and applications for the two compounds have been licensed to us under the Assignment and Assumption Agreement (the technology referred to collectively as the Compound Technology). As consideration in part for the rights to the Compound Technology, an initial licensing fee of $250,000 was paid to S.L.A. Pharma and $50,000 for reimbursement of clinical development costs incurred by S.L.A. Pharma (these amounts were paid by PBS and was included in the consideration paid by us to PBS in connection with the Assignment and Assumption Agreement). In the event that the Compound Technology is commercialized, we are obligated to pay to S.L.A. Pharma annual royalties ranging from the mid to upper single digit percentages, based upon net sales of the product. In addition, we are required to make payments to S.L.A. Pharma up to an aggregate amount of $20 million upon the achievement of various milestones related to regulatory events. Should we make any improvements regarding the Compound Technology, we are required to grant S.L.A. Pharma licenses to use such improvements.

We also are required to reimburse S.L.A. Pharma for clinical development costs associated with the technology development of both VEN 307 and VEN 308. Our total payment obligation for these development costs for VEN 307 will not exceed $4,200,000. From August 2007 through December 31, 2012, we made $4,200,000 of such payments. Additionally, upon receipt of a quality controlled final study report for the Phase III trial for VEN 307 in Europe, the cap on the amount of payments we must make to S.L.A. Pharma in respect of VEN 307 development costs will be increased to $4,600,000, and we must pay S.L.A. Pharma $400,000, which we paid in February 2013 upon the receipt of the report that month.

We remain obligated to pay S.L.A. Pharma $41,500 a month for project management fees for VEN 307, which we began paying in October 2010, until S.L.A. Pharma is no longer managing the development program for VEN 307. From October 2010 through December 31, 2012, we have paid $1,079,000 in project management fees for VEN 307.

From August 2007 through December 31, 2012, we had paid $973,500 in project management fees to S.L.A. Pharma relating to the development of VEN 308. These project management fees were terminated effective October 1, 2010. We do not expect to continue developing VEN 308 in the short term and therefore do not expect to make any additional payments.

We issued an additional 2,016 shares of our common stock to S.L.A. Pharma pursuant to the terms of the fourth amendment to the license agreement entered into in December 2009 and issued a warrant to purchase 13,605 shares of our common stock at an exercise price of $1.24 per share pursuant to the terms of the sixth amendment entered into on August 30, 2010. The sixth amendment benefited us by providing for an extension of the next $600,000 development fee, due September 30, 2010 to December 31, 2010 and the cancellation of all future VEN 308 monthly project management fees of $41,500 per month beginning after September 30, 2010, resulting in significant short term savings.

The Exclusive License Agreement with S.L.A. Pharma is terminable by us for any reason upon 90 days' written notice, and by either party in the event of a material breach or default of the Exclusive License Agreement or either party becomes bankrupt or insolvent. In the event that we are not current in our payments under the license agreement, S.L.A. Pharma may terminate the Exclusive License Agreement if we have not brought the payments current within three business days of receipt of notice from S.L.A. Pharma. If the Exclusive License Agreement is terminated in any of these situations, we would have no further payment obligations to S.L.A. Pharma. In the event we have a "change in control" prior to the completion of the Phase III trial for VEN 307 and we terminate the Exclusive License Agreement within 30 days of the change in control, we must pay the balance of all payments owed for VEN 307 even if S.L.A. Pharma has not actually incurred those costs. In the event we have a "change in control" after the completion of the Phase III trial for VEN 307 and we terminate the Exclusive License Agreement within 30 days of the change in control, we must pay the balance of all payments owed for VEN 307 even if S.L.A. Pharma has not actually incurred those costs plus any other development expenses mutually agreed upon, but excluding the $41,500 monthly payments for VEN 307 and any monthly payments that might have been agreed to and initiated for VEN 308. A "change in control" is defined as a merger or other reorganization of our company in which our stockholders prior to the transaction do not own a majority of the voting stock of the surviving or successor entity, the sale by one or more of our stockholders of a majority of our voting securities, or the sale of all or substantially all of our assets related to VEN 307 and VEN 308. A "change in control" does not include a bona fide financing transaction in which voting control transfers to one or more persons or entities who acquire our securities in the transaction.

The U.S. patent for VEN 307 for topical treatment of pain associated with anal fissures was filed with the PTO on August 12, 1999 (No. 09/335,928) and a notice of allowance was issued by the PTO on May 26, 2011. A patent application was filed under the Patent Treaty Cooperation Act on February 23, 1998, entered the national stage in Canada on August 23, 1999 and a patent was issued on November 11, 2006 (No. 2,281,755). The expiration date for the patent in both the U.S. and Canada is February 23, 2018, if all maintenance fees are paid. The patent was filed in the name of Michael A. Kamm and Robin K. S. Phillips as the inventors and S.L.A. Pharma as the assignee.

The U.S. patent expires in February 2018. If approved, VEN 307 will have three years of data exclusivity in the U.S. under the Hatch-Waxman Act.

A patent application for VEN 308 for fecal incontinence was filed under the Patent Treaty Cooperation Act on December 23, 1997, entered the national stage in the U.S. on August 24, 1999 and in Canada on June 18, 1999. A patent was issued in the U.S. on October 21, 2003 (No. 6,635,678) and in Canada on March 18, 2008 (No. 2,275,663). The expiration date for the patent in both the U.S. and Canada is December 23, 2017, if all maintenance fees are paid. The patent was filed in the name of Michael A. Kamm and Robin K. S. Phillips as the inventors and S.L.A. Pharma as the assignee.

Under the S.L.A. Pharma Exclusive License Agreement, we are also responsible for the costs of prosecution of the patents, as well as any new patent filings for the licensed products. While we will pay these costs, S.L.A. Pharma will retain ownership of the patents although we will have the rights to license the technology underlying the patents for the duration of the Exclusive License Agreement.

License Agreements - VEN 309

On June 5, 2011, we entered into an asset purchase agreement with Amer to acquire all rights, title and interest to VEN 309. We paid $500,000 on execution and paid $12 million for the asset at closing, which took place on November 14, 2011. We also paid Amer $50,000 on execution and paid Amer $5,000 per month for consulting services through the closing. Prior to the purchase, we had licensed the rights to VEN 309 from Amer.

There are four patent filings for VEN 309, all of which, except as noted below, were filed in the name of Dr. Sam Amer as the inventor and Amer as the assignee (we now own all of the rights to VEN 309). The patent filing for the VEN 309 compound that we are developing was filed in the U.S. (No. 5,780,487), Europe (Germany, Great Britain, France, Switzerland and Spain) (No. EP 0973741), Japan (No. 520835/98), Norway (No. 19994181) and Korea (No. 10-997007763). Patents have been granted in the U.S. and Europe, while applications are pending in Norway, Japan and Korea. The U.S. patent will expire on August 7, 2015 and all foreign patents will expire on January 23, 2018, if all maintenance fees are timely paid.

The second patent filing is for the treatment of hemorrhoids with 5-HT $_2$ antagonists and has been filed in the U.S. (No. 5,266,571), Europe (Germany, Great Britain, Austria, Greece, France, Portugal, Luxemburg, Ireland, Spain, Denmark, Switzerland, Belgium, Sweden, and Netherland) (No. EP 0684816), Japan (No. 2807092) and Korea (No. 0278522), in all of which the patent has been granted. The U.S. patent will expire on January 9, 2012 and all foreign patents will expire on February 19, 2013, if all maintenance fees are timely paid.

The third patent filing for VEN 309 is for 5-HT $_2$ receptor antagonist compositions useful in treating venous conditions. This patent has been filed in the U.S. only (No. 5,605,902) and has been granted. The patent will expire on January 9, 2012, if all maintenance fees are timely paid.

The fourth patent filing for VEN is a concentration of range patent for the treatment of internal and external hemorrhoids that was filed in the U.S. (No. 12/860,974) and internationally on August 23, 2010 (No. PCT/US2010/046260). This patent is still pending. If issued, any patent will expire on August 23, 2030.

We are solely responsible for the prosecution of the patent for VEN 309. Because we have ceased development of VEN 309, and to conserve resources, we have determined to not make maintenance fee payments on the patents for VEN 309.

Competition

As of the date of this report, we believe that there are no FDA-approved drug products that compete with VEN 308 nor are we aware of any products that could potentially compete against any of our products for which FDA approval is currently being sought. However, a competing product could be filed for FDA approval in the future. Further, non-FDA-approved products could be introduced in the future that could compete with our planned products.

In late June 2011, ProStrakan Group plc received approval for Rectiv, a 0.4% concentration of nitroglycerin in ointment to be applied intra- and peri-anally twice daily for the treatment of pain associated with chronic anal fissures for a duration of up to three weeks. The U.S. label (professional package insert) for Rectiv lists headache occurring in 64% of patients with 938 headaches occurring in 79 patients, in the one pivotal trial described. In January 2012, Aptalis Pharma announced that it had signed an exclusive license agreement with ProStrakan Group plc to market Rectiv in the U.S; Rectiv became commercially available in the first quarter of 2012.

The American Gastroenterology Association, in a technical review of anal fissure management in 2003 (Madoff, R.D. & Fleshman, J.W. (2003) AGA Technical Review on the Diagnosis and Care of Patients With Anal Fissure, *Gastroenterology*, 124, 235-245) states, “Based on the relatively limited data available to date, topical anal fissure therapy with calcium-channel blockers appears to be roughly as effective as treatment with topical nitrates. Moreover, the side effect profile of topical calcium-channel blockers appears superior, specifically with respect to fewer reported headaches.” Rectiv is a topical nitrate.

In the U.S., topical nitroglycerin, compounded in a twice daily ointment, has been used for over a decade while diltiazem cream has been in use for approximately five to seven years. Solvay Pharmaceuticals Inc., the original licensee for VEN 307 in the U.S., commissioned in 2003 an extensive quantitative market research study by Eidetics in 206 general practitioners, gastroenterologists and colorectal surgeons. In 2003, compounded topical nitroglycerin had been in use for several years but diltiazem cream had not yet seen appreciable use. The product profile presented to physicians described equivalent efficacy of diltiazem to nitroglycerin for pain relief and healing, but also described meaningful differences in headache incidence, and this is the comparative profile we expect if VEN 307 is approved. In response to this comparative profile, diltiazem was the preferred prescription treatment for anal fissures with 35% overall preference share for topical diltiazem, 23% for topical hydrocortisone and 14% for topical nitroglycerin.

Topical nitroglycerin has also been marketed in the U.K. and other European countries and elsewhere as Rectogesic ^{TM} since 2007 while at the same time diltiazem cream, though not approved, has been used on a named patient basis or compounded. The professional label in Europe for Rectiv marketed as Rectogesic lists headaches as being very common with a 63% incidence, of which 45% were moderate or severe. Indeed, the Association of Coloproctology of Great Britain and Ireland in their guidelines of 2008 (Cross, K.L.R., et al., (2008), The Management of Anal Fissure: ACPGBI Position Statement, Colorectal Disease, 10 (Suppl. 3), 1-7) states that, “ Topical diltiazem has similar efficacy to GTN (nitroglycerin) but with fewer side effects and should be recommended as first line treatment in the management of anal fissure”.

Based on results of previously published trials (such as Kocher et al. 2002 and Shrivastava 2007, see **Table 1** above under the heading “Diltiazem Cream (VEN 309) Development - Investigator-initiated clinical studies (studies sponsored by individual clinicians)”, we believe that the efficacy of diltiazem cream is likely to be similar to Rectiv in the relief of pain from chronic anal fissures while we believe that the side effects, particularly moderate and severe headaches, are likely to be substantially less than those observed with topical nitroglycerin, and we expect to observe this in our subsequent trials, some or all of which are expected to have a comparative arm of Rectiv. Consequently, considering existing professional society views in the U.S. and the U.K., even though VEN 307 is not yet approved in those countries, and considering existing data (some of which is directly comparative) on both products, we believe that, if approved, VEN 307 will be highly competitive with Rectiv.

In addition, in 2011, an Israeli company, RDD Pharma Ltd., completed in Israel a 20 patient single-arm open label study of the effect of coated suppositories of nifedipine, a calcium channel blocker, on pain and healing in the treatment of chronic anal fissures.

Our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. We believe that 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, price 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 indications we are targeting could render our drugs non-competitive or obsolete.

Government Regulation

General

The production, distribution, and marketing of products employing our technology, and its development activities, are subject to extensive governmental regulation in the U.S. and in other countries. In the U.S., our products are regulated as drugs and are subject to the Federal Food, Drug, and Cosmetic Act, as amended, and the regulations of the FDA, as well as to other federal, state, and local statutes and regulations. These laws, and similar laws outside the U.S., govern the clinical and preclinical testing, manufacture, safety, effectiveness, approval, labeling, distribution, sale, import, export, storage, recordkeeping, reporting, advertising, and promotion of our products. Product development and approval within this regulatory framework, if successful, will take many years and involve the expenditure of substantial resources. Violations of regulatory requirements at any stage may result in various adverse consequences, including the FDA's and other health authorities' delay in approving or refusal to approve a product. Violations of regulatory requirements also may result in enforcement actions.

The following provides further information on legal and regulatory matters that have the potential to affect our operations or future marketing of products.

Research, Development and Product Approval Process

The research, development, and approval process in the U.S. and elsewhere is intensive and rigorous and generally takes many years to complete. The typical process the FDA requires before a therapeutic drug may be marketed in the U.S. includes:

- preclinical laboratory and animal tests performed under the FDA's Good Laboratory Practices regulations, or GLPs;

- submission to the FDA of an application for an IND, which must become effective before human clinical trials may commence;

- preliminary human clinical studies to evaluate the drug and its manner of use;
- adequate and well-controlled human clinical trials to establish whether the drug is safe and effective for its intended uses;
- FDA review of whether the facility in which the drug is manufactured, processed, packed, or held meets standards designed to assure the product's continued quality; and
- submission of a marketing application to the FDA, and review and approval of the application by the FDA.

During preclinical testing, studies are performed with respect to the chemical and physical properties of candidate formulations. These studies are subject to GLP requirements. Biological testing is typically done in animal models to demonstrate the activity of the compound against the targeted disease or condition and to assess the apparent effects of the new product candidate on various organ systems, as well as its relative therapeutic effectiveness and safety. An IND must be submitted to the FDA and become effective before studies in humans may commence.

Clinical trial programs in humans generally follow a three-phase process. Typically, Phase I trials are conducted in small numbers of healthy volunteers or, on occasion, in patients afflicted with the target disease. Phase I trials are conducted to determine the metabolic and pharmacological action of the product candidate in humans and the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. In Phase II, studies are generally conducted in larger groups of patients having the target disease or condition in order to validate clinical endpoints, and to obtain preliminary data on the effectiveness of the product candidate and optimal dosing. This phase also helps determine further the safety profile of the product candidate. In Phase III, large-scale clinical trials are generally conducted in patients having the target disease or condition to provide sufficient data for the statistical proof of effectiveness and safety of the product candidate as required by U.S. and foreign regulatory agencies.

Before proceeding with a study, sponsors may seek a written agreement from the FDA regarding the design, size, and conduct of a clinical trial. This is known as a Special Protocol Assessment, or SPA. Among other things, SPAs can cover clinical studies for pivotal trials whose data will form the primary basis to establish a product's efficacy. SPAs help establish up-front agreement with the FDA about the adequacy of a clinical trial design to support a regulatory approval, but the agreement is not binding if new circumstances arise. There is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to an SPA.

U.S. law requires that studies conducted to support approval for product marketing be "adequate and well controlled." In general, this means that either a placebo or a product already approved for the treatment of the disease or condition under study must be used as a reference control. Studies must also be conducted in compliance with good clinical practice requirements, and informed consent must be obtained from all study subjects.

The clinical trial process for a new compound can take 10 years or more to complete. The FDA may prevent clinical trials from beginning or may place clinical trials on hold at any point in this process if, among other reasons, it concludes that study subjects are being exposed to an unacceptable health risk. Trials may also be prevented from the beginning or may be terminated by institutional review boards, which must review and approve all research involving human subjects. Side effects or adverse events that are reported during clinical trials can delay, impede, or prevent marketing authorization. Similarly, adverse events that are reported after marketing authorization can result in additional limitations being placed on a product's use and, potentially, withdrawal of the product from the market.

Following the completion of clinical trials, the data are analyzed to determine whether the trials successfully demonstrated safety and effectiveness and whether a product approval application may be submitted. In the U.S., if the product is regulated as a drug, a new drug application, or NDA, must be submitted and approved before commercial marketing may begin. The NDA must include a substantial amount of data and other information concerning the safety and effectiveness of the compound from laboratory, animal, and human clinical testing, as well as data and information on manufacturing, product quality and stability, and proposed product labeling. This special NDA procedure, known as a "section 505(b)(2) application" or a "paper NDA," allows an applicant to seek approval on the basis of a combination of a prior approval of a similar product or published literature, and some new clinical studies conducted or sponsored by the applicant. Section 505(b)(2) applications are often used for changes in a drug that require clinical investigations and thus cannot be handled through the generic drug process, such as a new indication or change in dosage form or route of administration.

Each domestic and foreign manufacturing establishment, including any contract manufacturers we may decide to use, must be listed in the NDA and must be registered with the FDA. The application generally will not be approved until the FDA conducts a manufacturing inspection, approves the applicable manufacturing process for the drug product, and determines that the facility is in compliance with cGMP requirements.

Each NDA submitted for FDA approval is usually reviewed for administrative completeness and reviewability within 45 to 60 days following submission of the application. If deemed complete, the FDA will "file" the NDA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established performance goals for the review of NDAs - six months for priority applications and 10 months for standard applications. However, the FDA is not legally required to complete its review within these periods, and these performance goals may change over time. Moreover, the outcome of the review, even if generally favorable, typically is not an actual approval but an "action letter" that describes additional work that must be done before the application can be approved. The FDA's review of an application may involve review and recommendations by an independent FDA advisory committee. Even if the FDA approves a product, it may limit the approved therapeutic uses for the product as described in the product labeling, require that warning statements be included in the product labeling, require that additional studies be conducted following approval as a condition of the approval, impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval.

Significant legal and regulatory requirements also apply after FDA approval to market under an NDA. These include, among other things, requirements related to adverse event and other reporting, product advertising and promotion and ongoing adherence to cGMPs, as well as the need to submit appropriate new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. The FDA also enforces the requirements of the Prescription Drug Marketing Act which, among other things, imposes various requirements in connection with the distribution of product samples to physicians.

The regulatory framework applicable to the production, distribution, marketing, and/or sale, of our products may change significantly from the current descriptions provided herein in the time that it may take for any of our products to reach a point at which an NDA is approved.

Overall research, development, and approval times depend on a number of factors, including the period of review at FDA, the number of questions posed by the FDA during review, how long it takes to respond to the FDA's questions, the severity or life-threatening nature of the disease in question, the availability of alternative treatments, the availability of clinical investigators and eligible patients, the rate of enrollment of patients in clinical trials, and the risks and benefits demonstrated in the clinical trials.

Orphan Drugs

Under the Orphan Drug Act, special incentives exist for companies to develop products for rare diseases or conditions, which are defined to include those diseases or conditions that affect fewer than 200,000 people in the U.S. Companies may request that the FDA grant a drug orphan designation prior to approval. Products designated as orphan drugs are eligible for special grant funding for research and development, FDA assistance with the review of clinical trial protocols, potential tax credits for research, reduced filing fees for marketing applications, and a special seven-year period of market exclusivity after marketing approval. Orphan drug exclusivity prevents FDA approval of applications by others for the same drug and the designated orphan disease or condition. The FDA may approve a subsequent application from another entity if the FDA determines that the application is for a different drug or different use, or if the FDA determines that the subsequent product is clinically superior, or that the holder of the initial orphan drug approval cannot assure the availability of sufficient quantities of the drug to meet the public's need. A grant of an orphan designation is not a guarantee that a product will be approved. If a sponsor receives orphan drug exclusivity upon approval, there can be no assurance that the exclusivity will prevent another entity or a similar drug from receiving approval for the same or other uses.

Other U.S. Regulatory Requirements

In the U.S., the research, manufacturing, distribution, sale, and promotion of drug and biological products are potentially subject to regulation by various federal, state, and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services (for example, the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing, and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provision of the Health Insurance Portability and Accountability Act, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection, unfair competition, and other laws. Moreover, we are now, and in the future may become subject to, additional federal, state, and local laws, regulations, and policies relating to safe working conditions, laboratory practices, the experimental use of animals, and/or the use, storage, handling, transportation, and disposal of human tissue, waste, and hazardous substances, including radioactive and toxic materials and infectious disease agents used in conjunction with our research work.

Foreign Regulatory Requirements

We and our collaborative partners may be subject to widely varying foreign regulations, which may be quite different from those of the FDA, governing clinical trials, manufacture, product registration and approval, and pharmaceutical sales. Whether or not FDA approval has been obtained, we or our collaboration partners must obtain a separate approval for a product by the comparable regulatory authorities of foreign countries prior to the commencement of product marketing in these countries. In certain countries, regulatory authorities also establish pricing and reimbursement criteria. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. In addition, under current U.S. law, there are restrictions on the export of products not approved by the FDA, depending on the country involved and the status of the product in that country.

Reimbursement and Pricing Controls

In many of the markets where we or our collaborative partners would commercialize a product following regulatory approval, the prices of pharmaceutical products are subject, by law, to direct price controls and to drug reimbursement programs with varying price control mechanisms. Public and private health care payors control costs and influence drug pricing through a variety of mechanisms, including through negotiating discounts with the manufacturers and through the use of tiered formularies and other mechanisms that provide preferential access to certain drugs over others within a therapeutic class. Payors also set other criteria to govern the uses of a drug that will be deemed medically appropriate and therefore reimbursed or otherwise covered. In particular, many public and private health care payors limit reimbursement and coverage to the uses of a drug that are either approved by the FDA or that are supported by other appropriate evidence (for example, published medical literature) and appear in a recognized drug compendium. Drug compendia are publications that summarize the available medical evidence for particular drug products and identify which uses of a drug are supported or not supported by the available evidence and whether or not such uses have been approved by the FDA. For example, in the case of Medicare coverage for physician-administered oncology drugs, the Omnibus Budget Reconciliation Act of 1993, with certain exceptions, prohibits Medicare carriers from refusing to cover unapproved uses of an FDA-approved drug if the unapproved use is supported by one or more citations in the American Hospital Formulary Service Drug Information, the American Medical Association Drug Evaluations, or the U.S. Pharmacopoeia Drug Information. Another commonly cited compendium, for example under Medicaid, is the DRUGDEX Information System.

Available Information

Our website address is www.ventrusbio.com. Information on our website is not incorporated herein by reference. We make available free of charge through our website our press releases, Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after electronically filed with or furnished to the Securities and Exchange Commission.

Employees

As of February 28, 2013, we had eight employees and had contracted with seven consultants and three contract research organizations excluding S.L.A Pharma, on manufacturing, preclinical and clinical aspects of our drug programs. We use consulting agreements to avoid the costs customarily associated with employees to save resources.

Item 1A. Risk Factors

This report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this report and in any documents incorporated in this report by reference.

If any of the following risks, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Risks Related to Our Business

We have a limited operating history and a history of operating losses, and expect to incur significant additional operating losses.

We were established in October 2005, began active operations in the spring of 2007 and have only a limited operating history. Therefore, there is limited historical financial information upon which to base an evaluation of our performance. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by companies in their early stages of operations. We have generated losses since we began operations and, as of December 31, 2012, we had a deficit accumulated during the development stage of $92.3 million. We expect to incur substantial additional losses over the next two years as we continue to pursue our research, development and clinical trial activities, especially for VEN 307. Such losses could continue beyond that time frame if we do not successfully launch and commercialize VEN 307 as planned. The amount of future losses and when, if ever, we will achieve profitability are uncertain. We have no products that have generated any commercial revenue, do not expect to generate revenues from the commercial sale of products unless and until VEN 307 is approved by the FDA for sale, and we might never generate revenues from the sale of products.

We are not currently profitable and might never become profitable.

We have a history of losses and expect to incur significant operating and capital expenditures and resultant substantial losses and negative operating cash flow for the next two years, and beyond if we do not successfully launch and commercialize VEN 307 as planned. We might never achieve or maintain profitability. Even if we succeed in developing and commercializing VEN 307 or other product candidates, we could incur substantial losses in the future. We anticipate that our expenses will continue to be substantial in the foreseeable future as we:

- continue to undertake non-clinical and clinical trials for product candidates, especially VEN 307;
- seek regulatory approvals for our product candidates, including VEN 307;
- implement additional internal systems and infrastructure; and
- hire additional personnel, including additional personnel related to the planned launch of VEN 307.

As a result, we will need to generate significant revenues in order to achieve and maintain profitability. Our ability to generate revenue and achieve profitability will depend on, among other things:

- successful completion of research and clinical trials for VEN 307 and our other product candidates;
- obtaining necessary regulatory approvals from the FDA and international regulatory agencies;
- establishing manufacturing, sales, and marketing arrangements with third parties; and
- raising sufficient funds to finance our activities, if and when needed.

We might not succeed at any of these undertakings. If we are unsuccessful at some or all of these undertakings, our business, prospects, and results of operations might be materially adversely affected.

We have no approved products.

To date, we have no approved product on the market and have generated no product revenues. Unless and until we receive approval from the FDA for VEN 307 and approvals from the FDA and other regulatory authorities for our other product candidates, we cannot sell our drugs and will not have product revenues. Therefore, until the planned launch and commercialization of VEN 307, and thereafter if approval is not granted or the launch is not successful, we will have to fund all of our operations and capital expenditures from cash on hand, any licensing fees and any future securities offerings or debt financings. We intend to devote substantially all of our resources for the next two years to the development of our lead product candidate, VEN 307. In the event we do not obtain regulatory approval of or successfully launch VEN 307, our business will be materially and adversely affected.

Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive, can take many years to complete and its outcome is highly uncertain. Failure can occur at any time during the clinical trial process due to inadequate performance of a drug or inadequate adherence by patients or investigators to clinical trial protocols. In addition, the results of pre-clinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. For example, in late June 2012, we reported that our Phase III randomized, double-blind, placebo-controlled clinical trial of iferanserin (VEN 309) in patients with hemorrhoidal disease did not meet its endpoints, despite favorable Phase II trial results. As a result, we have determined that our current resources would be better allocated toward the planned completion of VEN 307 for the treatment of anal fissures for which we reported positive results from our Phase III randomized, double-blind, placebo-controlled clinical trial conducted in Europe by S.L.A. Pharma. The failure to obtain positive results in our ongoing Phase III trial for VEN 307 in the U.S. would seriously impair the development prospects, and even prevent regulatory approval, of VEN 307. Such a failure also would have a material adverse effect on our business, financial condition, results of operations and prospects.

Our recently begun second Phase III trial for VEN 307 may be more expensive and time consuming than we currently expect. The FDA could insist that we submit the NDA for review with two U.S. Phase III trials for VEN 307, or after the review of an NDA submission based on the S.L.A. Pharma trial and our first Phase III trial in the U.S., require a second U.S. study for approval which would eliminate possible time and cost savings for the submission of the NDA for VEN 307, and which would add to the time and cost of VEN 307's development.

We are a development-stage company and might not be able to commercialize any product candidates.

We are a development-stage company and have not demonstrated our ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

· continuing to undertake research and development and clinical trials;

· participating in regulatory approval processes;

· formulating and manufacturing products; and

· conducting sales, marketing and distribution activities.

Our development of current and future product candidates is subject to the risks of failure and delay inherent in the development of new pharmaceutical products and products based on new technologies, including:

· delays in product development, clinical testing, or manufacturing;

· unplanned expenditures in product development, clinical testing, or manufacturing;

· failure of a product candidate to demonstrate acceptable safety and efficacy;

· failure to receive regulatory approvals;

· emergence of superior or equivalent products;

· inability to manufacture and sell on our own, or through any others, product candidates on a commercial scale or at a financially viable cost; and

· failure to achieve market acceptance.

Because of these risks, our research and development efforts might not result in any commercially viable products. If we do not successfully complete a significant portion of these development efforts, obtain required regulatory approvals, and have commercial success with any approved products, our business, financial condition and results of operations will be materially harmed.

The results of our ongoing second Phase III trial for VEN 307 might not be positive or as positive as the results of the first Phase III trial.

While the results of the first Phase III trial, announced in May 2012, were positive, the results of our ongoing second Phase III trial may not be as positive as the results for the first Phase III trial, if at all. Further, the results of any additional studies or trials designed to show efficacy and safety of VEN 307, including our two cutaneous safety trials, may not be positive. Lastly, unforeseen safety issues could emerge in any future study or trial, which could severely hamper the likelihood of FDA or other regulatory approval of VEN 307. If any of these events were to occur, the development of VEN 307 could be significantly delayed and more expensive than anticipated, and could lead us to abandon our development efforts entirely, any of which would have a significant adverse effect on our business.

We may need additional financing to complete the development of VEN 307 and fund our activities in the future.

We anticipate that we will incur operating losses for the next two years as we continue to develop VEN 307 and will require substantial funds during that time to support our operations. We anticipate that to complete the clinical trial process to obtain the approval of VEN 307 will cost approximately $15 million. We expect that our current resources will provide us with sufficient capital to fund our operations to develop VEN 307 through to FDA approval and commercial launch. However, we might consume our available capital before that time if, for example, we are not efficient in managing our resources, including the conducting of our ongoing Phase III trial or if we encounter unforeseen costs, delays or other issues or if regulatory requirements change. If that happens, we may need additional financing to complete the development of VEN 307. Thereafter, if VEN 307 is not approved or the launch is not successful, we will need additional capital to fund our operations in the future. However, there is no assurance that we will be successful in raising any necessary additional capital on terms that are acceptable to us, or at all. If such event or other unforeseen circumstances occurred and we were unable to raise capital, we could be forced to discontinue product development, forego sales and marketing efforts, sacrifice attractive business opportunities, cease operations entirely and sell or otherwise transfer all or substantially all of our remaining assets.

We are dependent on a license relationship for VEN 307 and VEN 308.

We have acquired, by license from S.L.A. Pharma, the rights to VEN 307 and VEN 308, which are critical to our business, and we might enter into additional licenses in the future. The license with S.L.A. Pharma contains, and we expect that any future licenses will contain, provisions requiring up-front, milestone, and royalty payments to the licensor. In addition, we are obligated to pay S.L.A. Pharma monthly project management fees of $41,500 until S.L.A. Pharma is no longer managing the development program for VEN 307. In the event we breach these obligations to S.L.A. Pharma, we could lose our rights to VEN 307 or VEN 308, or both, depending on the breach, which would have a material adverse effect on our business and prospects. If we fail to comply with similar obligations to any other licensor, it would have the right to terminate the license, in which event we would not be able to commercialize drug candidates or technologies that were covered by the license. Also, the milestone and other payments associated with licenses will make it less profitable for us to develop our drug candidates than if we owned the technology ourselves.

We have had negative cash flows from operations and might not be able to generate sufficient cash to meet our substantial obligations to S.L.A. Pharma, which could result in the termination of our license or put substantial burdens on our financial position.

We license both of our product candidates, VEN 307 and VEN 308, from S.L.A. Pharma, and have obligations related to VEN 308 and to fund S.L.A. Pharma's development efforts for VEN 307 in the E.U. Under the license, we are obligated to pay S.L.A. Pharma monthly project management fees of $41,500 until S.L.A. Pharma is no longer managing the development program for VEN 307. Further, if we commercialize a product candidate, we must pay S.L.A. Pharma annual royalties ranging from the mid to upper single digit percentages, based upon net sales of the product. We also are required to make future milestone payments totaling up to $20 million upon the achievement of various milestones related to regulatory events for both VEN 307 and VEN 308, the earliest of which is not anticipated until late 2014 or early 2015.

We expect to experience negative cash flow for at least the next two years as we fund our operating losses and capital expenditures for the development of VEN 307 and VEN 308. In the event that we are not current in our payments under the license agreement, S.L.A. Pharma may terminate the license agreement if we have not brought the payments current within three business days of receipt of notice from S.L.A. Pharma. In the event we breach these obligations, we could lose our rights to VEN 307 or VEN 308, or both, depending on the breach, which would have a material adverse effect on our business and prospects.

Corporate and academic collaborators might take actions to delay, prevent, or undermine the success of our products.

Our operating and financial strategy for the development, clinical testing, manufacture, and commercialization of drug candidates heavily depends on collaborating with corporations, academic institutions, licensors, licensees, and other parties. However, there can be no assurance that we will successfully establish these collaborations. In addition, should a collaboration be terminated, replacement collaborators might not be available on attractive terms, or at all. The activities of any collaborator will not be within our control and might not be within our power to influence. There can be no assurance that any collaborator will perform its obligations to our satisfaction or at all, that we will derive any revenue or profits from these collaborations, or that any collaborator will not compete with us. If any collaboration is not successful, we might require substantially greater capital to undertake development and marketing of our proposed products and might not be able to develop and market these products effectively, if at all. In addition, a lack of development and marketing collaborations might lead to significant delays in introducing proposed products into certain markets and/or reduced sales of proposed products in such markets.

We rely on data provided by our collaborators and others that has not been independently verified and could prove to be false, misleading, or incomplete.

We rely on third-party vendors, scientists, and collaborators to provide us with significant data and other information related to our projects, clinical trials, and our business. If these third parties provide inaccurate, misleading, or incomplete data, our business, prospects, and results of operations could be materially adversely affected.

We rely exclusively on third parties to formulate and manufacture our product candidates.

While we have contracted with a highly experienced head of manufacturing to oversee the manufacture of our clinical trial supplies, we do not have and do not intend to establish our own manufacturing facilities. Consequently, we lack the physical plant to formulate and manufacture our own product candidates, which are currently being manufactured entirely by commercial third parties, albeit under close supervision by our contractors. If any product candidate we might develop or acquire in the future receives FDA approval, we will rely on one or more third-party contractors to manufacture our products. If, for any reason, we become unable to rely on our current source or any future source to manufacture our product candidates, either for clinical trials or, at some future date, for commercial quantities, then we would need to identify and contract with additional or replacement third-party manufacturers to manufacture compounds for preclinical, clinical and commercial purposes. We might not be successful in identifying additional or replacement third-party manufacturers, or in negotiating acceptable terms with any that we do identify. If we are unable to secure and maintain third-party manufacturing capacity, the development and sales of our products and our financial performance might be materially affected.

In addition, before any of our collaborators can begin to commercially manufacture our product candidates, each must obtain regulatory approval of the manufacturing facility and process. Manufacturing of drugs for clinical and commercial purposes must comply with the FDA's Current Good Manufacturing Practices, or cGMPs, and applicable non-U.S. regulatory requirements. The cGMP requirements govern quality control and documentation policies and procedures. Complying with cGMP and non-U.S. regulatory requirements will require that we expend time, money, and effort in production, recordkeeping, and quality control to assure that the product meets applicable specifications and other requirements. Our contracted manufacturing facilities must also pass a pre-approval inspection prior to FDA approval. Failure to pass a pre-approval inspection might significantly delay FDA approval of our products. If any of our collaborators fails to comply with these requirements, it would be subject to possible regulatory action which could limit the jurisdictions in which we are permitted to sell our products. As a result, our business, financial condition, and results of operations might be materially harmed.

Our reliance on a limited number of third-party manufacturers exposes us to the following risks:

· We might be unable to identify manufacturers for commercial supply on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. This approval would generally require compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.

· Our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality required to meet our clinical and commercial needs, if any.

· Our contract manufacturers might not perform as agreed or might not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products.

· Currently, our contract manufacturers are all foreign, which increases the risk of shipping delays and adds the risk of import restrictions.

· Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have complete control over third-party manufacturers' compliance with these regulations and standards although we have agents in plant that monitor the production process.

· If any third-party manufacturer makes improvements in the manufacturing process for our products, we might not own, or might have to share, the intellectual property rights to the innovation with our licensors.

· We might compete with other companies for access to these manufacturers' facilities and might be subject to manufacturing delays if the manufacturers give other clients higher priority than us.

Each of these risks could delay our clinical trials or the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates and could result in higher costs or deprive us of potential product revenues. As a result, our business, financial condition, and results of operations might be materially harmed.

Preclinical and clinical trials required for our product candidates are expensive and time-consuming, and their outcome is uncertain.

In order to obtain FDA approval to market a new drug product, we must demonstrate safety and effectiveness in humans. To meet these requirements, we must conduct extensive preclinical testing and sufficient adequate and well-controlled clinical trials. Conducting clinical trials is a lengthy, time consuming, and expensive process. The length of time might vary substantially according to the type, complexity, novelty, and intended use of the product candidate, and often can be several years or more per trial. Delays associated with products for which we are directly conducting preclinical or clinical trials might cause us to incur additional operating expenses. The commencement and rate of completion of clinical trials might be delayed by many factors, including, for example:

· the lack of effectiveness during clinical trials;

· the emergence of unforeseen safety issues;

· inability to manufacture sufficient quantities of qualified materials under cGMP for use in clinical trials;

· slower than expected rates of patient recruitment;

· failure to recruit a sufficient number of patients;

· modification of clinical trial protocols;

· changes in regulatory requirements for clinical trials;

· delays, suspension, or termination of clinical trials by the institutional review board responsible for overseeing the study at a particular study site; and

· government, institutional review board or other regulatory delays or clinical holds requiring suspension or termination of the trials.

The results from preclinical testing and early clinical trials are not necessarily predictive of results obtained in later clinical trials. Accordingly, even if we obtain or have obtained positive results from preclinical or early clinical trials, we might not achieve the same success in future clinical trials. For example, although positive results have been observed in earlier and recent clinical trials of each of VEN 307 and VEN 308, there is no assurance that any of our future clinical trials will be successful. Clinical trials might not provide statistically significant data supporting a product candidate's safety and effectiveness to meet the requisite regulatory approvals.

We are using and intend to continue to rely on one or more contract research organizations, or CROs, to conduct our clinical trials for VEN 307. We are highly dependent on these CROs to conduct our trials in accordance with the requirements of the FDA and good scientific practice. In the event the CROs fail to perform their duties in such a fashion, we may not obtain regulatory approval for any of our product candidates.

The failure of clinical trials to demonstrate safety and effectiveness for the desired indications could harm the development of that product candidate and other product candidates. This failure could cause us to abandon a product candidate and could delay development of other product candidates. Any delay in, or termination of, our clinical trials would delay the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. Any change in, or termination of, our clinical trials could materially harm our business, financial condition, and results of operation.

Unforeseen safety issues could hinder the development of our product candidates and their adoption, if approved.

Both VEN 307 and VEN 308 have been safely used extensively for decades when given orally at much higher exposures (blood levels) than currently under study in the topical application of VEN 307 and VEN 308. Despite these safety records, other safety issues could arise during testing of our products, which might delay testing or prevent further development entirely. If a product is approved, any limitation on use that might be necessary could hinder its adoption in the marketplace. In addition, if any product is approved, it could be used against any instructions that we publish that limit its use, which could subject us to litigation.

If we cannot compete successfully for market share against other drug companies, we might not achieve sufficient product revenues and our business will suffer.

If our product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing drugs might provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or might offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we might not achieve sufficient product revenues and our business will suffer.

We might compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

· developing drugs;

· undertaking pre-clinical testing and human clinical trials;

· obtaining FDA and other regulatory approvals of drugs;

· formulating and manufacturing drugs; and

· launching, marketing and selling drugs.

We might not obtain the same resources and experience as our competitors. If we are unable to perform these tasks effectively and efficiently, our results of operations might be materially adversely affected.

Developments by competitors might render our products or technologies obsolete or non-competitive.

The pharmaceutical and biotechnology industries are intensely competitive. We might compete with organizations that are developing treatments for the indications that our products target.

To our knowledge, there is currently only one FDA-approved drug for the treatment of anal fissures. Rectiv, a topical nitroglycerin treatment, was approved in late June 2011 by the FDA, and came to market in the first quarter of 2012. For the treatment of fecal incontinence, Solesta, an injectable therapy developed by Oceana Therapeutics, was approved as a device by the FDA in 2011 and came to market in 2012. To our knowledge, there are no other products approved or in development although there are two non-drug products in development. If our competitors develop effective treatments for anal fissure or fecal incontinence and successfully commercialize those treatments, our business and prospects might be materially harmed.

If we are not able to develop collaborative marketing relationships with licensees or partners, or create an effective internal sales, marketing, and distribution capability, we might be unable to market our products successfully.

To market our products, we will have to establish our own marketing and sales force or out-license our product candidates to, or collaborate with, larger firms with experience in marketing and selling pharmaceutical products. There can be no assurance that we will be able to successfully establish our own marketing capabilities or establish marketing, sales, or distribution relationships with third parties; that such relationships, if established, will be successful; or that we will be successful in gaining market acceptance for our products. To the extent that we enter into any marketing, sales, or distribution arrangements with third parties, our product revenues will be lower than if we marketed and sold our products directly, and any revenues we receive will depend upon the efforts of such third parties. If we are unable to establish such third-party sales and marketing relationships, or choose not to do so, we will have to establish our own in-house capabilities. Although our employees have extensive experience in the commercialization of drug products, we, as a company, have no experience in marketing or selling pharmaceutical products and currently have no sales, marketing, or distribution infrastructure. To market any of our products directly, we would need to develop a marketing, sales, and distribution force that both has technical expertise and the ability to support a distribution capability. To establish our own marketing, sales, and distribution capacity would significantly increase our costs, and require substantial additional capital. In addition, there is intense competition for proficient sales and marketing personnel, and we might not be able to attract individuals who have the qualifications necessary to market, sell, and distribute our products. There can be no assurance that we will be able to establish internal marketing, sales, or distribution capabilities.

Physicians and patients might not accept and use our drugs.

Even if the FDA approves one of our product candidates, physicians and patients might not accept and use it. Acceptance and use of our products will depend upon a number of factors, including:

- perceptions by members of the health care community, including physicians, about the safety and effectiveness of our product;
- cost-effectiveness of our product relative to competing product or therapies;
- availability of reimbursement for our product from government or other healthcare payors; and
- effective marketing and distribution efforts by us and our licensees and distributors, if any.

If our current product candidates are approved, we expect sales to generate substantially all of our revenues for the foreseeable future, and as a result, the failure of these products to find market acceptance would harm our business and would require us to seek additional financing.

Our ability to generate product revenues will be diminished if our products sell for inadequate prices or patients are unable to obtain adequate levels of reimbursement.

Our ability to commercialize our products, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

- government and health administration authorities;
- private health maintenance organizations and health insurers; and
- other healthcare payors.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payors, including Medicare, are challenging the prices charged for medical products and services. Government and other healthcare payors increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. Even if our product candidates are approved by the FDA, insurance coverage might not be available, and reimbursement levels might be inadequate, to cover our products. If government and other healthcare payors do not provide adequate coverage and reimbursement levels for our products, once approved, market acceptance of such products could be reduced.

Proposals to modify the current health care system in the U.S. to improve access to health care and control its costs are continually being considered by the federal and state governments. In March 2010, the U.S. Congress passed landmark healthcare reform legislation. We cannot predict what impact on federal reimbursement policies and regulatory compliance landscape this legislation will have in general or on our business specifically. We expect continued judicial and legislative review and assessment of this legislation and possibly alternative health care reform proposals. We cannot predict judicial results or whether new proposals will be made or adopted, when they may be adopted or what impact they may have on us if they are adopted.

Health administration authorities in countries other than the U.S. may not provide reimbursement for our products at rates sufficient for us to achieve profitability, or at all. Like the U.S., these countries could adopt health care reform proposals and could materially alter their government-sponsored health care programs by reducing reimbursement rates.

Any reduction in reimbursement rates under Medicare or private insurers or foreign health care programs could negatively affect the pricing of our products. If we are not able to charge a sufficient amount for our products, then our margins and our profitability will be adversely affected.

If we lose key management or scientific personnel, cannot recruit qualified employees, directors, officers, or other significant personnel or experience increases in our compensation costs, our business might materially suffer.

We are highly dependent on the services of our Chairman, Chief Executive Officer and acting Chief Medical Officer, Dr. Russell H. Ellison. Our employment agreement with Dr. Ellison does not ensure his retention. This is also true for our other management team members, both present and future.

Furthermore, our future success also depends, in part, on our ability to identify, hire, and retain additional management team members as our operations grow. We expect to experience intense competition for qualified personnel and might be unable to attract and retain the personnel necessary for the development of our business. Finally, we do not currently maintain, nor do we intend to obtain in the future, “key man” life insurance that would compensate us in the event of the death or disability of any of the members of our management team.

If we cannot enforce non-compete and confidentiality provisions applicable to our employees and consultants, our business might materially suffer.

We include a non-compete provision in any employment agreement we enter into with an employee, including Dr. Ellison, that runs during the term of the agreement and for six months after termination, and, in the case of Thomas Rowland, who resigned as our Chief Business Officer effective September 30, 2012, up to one year from the date of his resignation. This non-compete provision, with a six-month duration after termination, was also included in employment agreements with our former chief medical officer and chief scientific officer, which have lapsed.

We include a confidentiality provision in any employment or consulting agreement we enter into with an employee or a consultant. The confidentiality provision runs during the term of the agreement and thereafter without limit. As a result, the confidentiality provisions contained in the employment agreements with our former chief business officer, chief medical officer and chief scientific officer remain in effect and are in effect under all of our current consulting agreements.

For future employees with whom we do not enter into an employment agreement, we will enter into a confidentiality agreement with the same provisions described above.

To be able to enforce these non-compete and confidentiality provisions we would need to know of any breach and have sufficient funds to enforce the provisions. We cannot assure you that we would know of or be able to afford enforcement of any breach. In addition, such provisions are subject to state law and interpretation by courts, which could limit the scope and duration of these provisions. Any limitation on or non-enforcement of these non-compete and confidentiality provisions could have an adverse effect on our business.

If we are unable to hire additional qualified personnel, our ability to grow our business might be harmed.

At February 28, 2013, we had eight employees, seven consultants and three contract research organizations with whom we have contracted to carry out the development of VEN 307. While we believe this will provide us with sufficient staffing to develop VEN 307 through to FDA approval, we might need to hire or contract with additional qualified personnel with expertise in clinical research and testing, government regulation, formulation and manufacturing and sales and marketing to commercialize VEN 307. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for these individuals is intense, and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success.

We might not successfully manage our growth.

Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our current and future management and other administrative and operational resources. To manage this growth, we must expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business would be harmed.

We might seek to develop our business through acquisitions of or investment in new or complementary businesses, products or technologies, and the failure to manage these acquisitions or investments, or the failure to integrate them with our existing business, could have a material adverse effect on us.

We might consider opportunities to acquire or invest in other technologies, products and businesses that might enhance our capabilities or complement our current product candidates. Potential and completed acquisitions and strategic investments involve numerous risks, including potential problems or issues associated with the following:

- assimilating the purchased technologies, products or business operations;
- maintaining uniform standards, procedures, controls and policies;
- unanticipated costs associated with the acquisition or investment;
- diversion of our management’s attention from our preexisting business;
- maintaining or obtaining the necessary regulatory approvals or complying with regulatory standards; and
- adverse effects on existing business operations.

We have no current commitments with respect to any acquisition or investment in other technologies or businesses. We do not know if we will identify suitable acquisitions, whether we will be able to successfully complete any acquisitions, or whether we will be able to successfully integrate any acquired product, technology or business into our business or retain key personnel, suppliers or collaborators.

Our ability to successfully develop our business through acquisitions would depend on our ability to identify, negotiate, complete and integrate suitable target businesses or technologies and obtain any necessary financing. These efforts could be expensive and time consuming and might disrupt our ongoing operations. If we are unable to efficiently integrate any acquired business, technology or product into our business, our business and financial condition might be adversely affected.

Risks Related to Our Regulatory and Legal Environment

We are subject to extensive and costly government regulation.

Product candidates employing our technology are subject to extensive and rigorous domestic government regulation including regulation by the FDA, the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments, and their respective foreign equivalents. The FDA regulates the research, development, preclinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution, import, and export of pharmaceutical products. The FDA regulates small molecule chemical entities, whether administered orally, topically or by injection, as drugs, subject to an NDA, under the Federal Food, Drug, and Cosmetic Act. If products employing our technologies are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not they have obtained FDA approval for a given product and its uses. Such foreign regulation might be equally or more demanding than corresponding U.S. regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. We or our collaborators must obtain and maintain regulatory authorization to conduct clinical trials and approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires submitting extensive preclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy for each intended use. The development and approval process might take many years, requires substantial resources, and might never lead to the approval of a product.

Even if we are able to obtain regulatory approval for a particular product, the approval might limit the intended medical uses for the product, limit our ability to promote, sell, and distribute the product, require that we conduct costly post-marketing surveillance, and/or require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, might require further regulatory review and approval. Once obtained, any approvals might be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our collaborators, or our contract manufacturers fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal of a regulatory authority, including the FDA, to review pending market approval applications or supplements to approved applications; untitled letter or warning letters; fines; import and export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications or licenses; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

We might not obtain the necessary U.S. or worldwide regulatory approvals to commercialize any product candidate.

We cannot assure you that we will receive the approvals necessary to commercialize for sale any of our product candidates, or any product candidate we acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the U.S. and approvals from the FDA-equivalent regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA an NDA demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research, pre-clinical studies, and clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. We cannot predict whether our research and clinical approaches will result in drugs that the FDA considers safe for humans and effective for their indicated uses. The FDA has substantial discretion in the drug approval process and might require us to conduct additional pre-clinical and clinical testing, perform post-marketing studies or otherwise limit or impose conditions on any approval we obtain. For example, the FDA proposed that we include an additional treatment arm in our pivotal Phase III trail for VEN 309, which increased the cost of that trial.

The approval process might also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals might:

- delay commercialization of, and our ability to derive product revenues from, our product candidates;
- impose costly procedures on us; and
- diminish any competitive advantages that we might otherwise enjoy.

Even if we comply with all FDA requests, the FDA might ultimately reject one or more of our NDAs. We cannot be sure that we will ever obtain regulatory approval for our product candidates. Failure to obtain FDA approval of our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any source of revenues, until another product candidate could be developed or obtained. There is no guarantee that we will ever be able to develop or acquire another product candidate.

In foreign jurisdictions, we must receive approval from the appropriate regulatory authorities before we can commercialize any drugs. The risks associated with foreign regulatory approval processes are similar to the risks associated with the FDA approval procedures described above. We cannot assure you that we will receive the approvals necessary to commercialize our product candidates for sale outside the U.S.

Even if approved, our products will be subject to extensive post-approval regulation.

Once a product is approved, numerous post-approval requirements apply. Among other things, the holder of an approved NDA is subject to ongoing FDA oversight monitoring and reporting obligations, including obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the NDA. Application holders must submit new or supplemental applications and obtain FDA approval for changes to the approved product, product labeling, or manufacturing process. Application holders also must submit advertising and other promotional material to the FDA and report on ongoing clinical trials. The FDA also has the authority to require changes in the labeling of approved drug products and to require post-marketing studies.

Advertising and promotional materials must comply with FDA rules in addition to other applicable federal and state laws. The distribution of product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act. Manufacturing facilities remain subject to FDA inspection and must continue to adhere to the FDA's cGMP requirements. Application holders must obtain FDA approval for product, manufacturing, and labeling changes, depending on the nature of the change. Sales, marketing, and scientific/educational grant programs, among other activities, must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veteran's Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Depending on the circumstances, failure to meet these post-approval requirements can result in criminal prosecution, fines, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal to allow us to enter into supply contracts, including government contracts. In addition, even if we comply with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval.

We face the risk of product liability claims and might not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that are inherent in the development of drugs. If the use of one or more of our or our collaborators' drugs harms people, we might be subject to costly and damaging product liability claims brought against us by clinical trial participants, consumers, health care providers, pharmaceutical companies or others selling our products. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop. We obtained clinical trial insurance for VEN 307 prior to beginning the Phase III trial in late 2012. We cannot predict all of the possible harms or side effects that might result and, therefore, the amount of insurance coverage we hold now or in the future might not be adequate to cover all liabilities we might incur. We intend to expand our insurance coverage to include product liability insurance covering the sale of commercial products if we obtain marketing approval for our drug candidates in development, but we might be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. If we are unable to obtain insurance at an acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which might materially and adversely affect our business and financial position. If we are sued for any injury allegedly caused by our or our collaborators' products, our liability could exceed our total assets and our ability to pay the liability. A successful product liability claim or series of claims brought against us would decrease our cash and could cause the value of our common stock to decrease.

We might be exposed to liability claims associated with the use of hazardous materials and chemicals.

Our research, development and manufacturing activities and/or those of our third-party contractors might involve the controlled use of hazardous materials and chemicals. Although we will strive to have our safety procedures, and those of our contractors, for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages, and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products might require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations. We currently do not carry hazardous materials liability insurance. We intend to obtain such insurance in the future if necessary.

Risks Related to Our Intellectual Property

Our business depends on protecting our intellectual property.

If we and our licensor S.L.A. Pharma do not obtain protection for our respective intellectual property rights, our competitors might be able to take advantage of our research and development efforts to develop competing drugs.

Our success, competitive position and future revenues, if any, depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. To date, we hold some exclusive patent rights, including rights under U.S. patents and patent applications as well as rights under foreign patents and patent applications. We anticipate filing additional patent applications both in the U.S. and in other countries, as appropriate. However, the patent process is subject to numerous risks and uncertainties, and there can be no assurance that we will be successful in protecting our products by obtaining and defending patents. These risks and uncertainties include the following:

- Our patent rights might be challenged, invalidated, or circumvented, or otherwise might not provide any competitive advantage;

- Our competitors, many of which have substantially greater resources than we do and many of which might make significant investments in competing technologies, might seek, or might already have obtained, patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential products either in the U.S. or in international markets;

- As a matter of public policy regarding worldwide health concerns, there might be significant pressure on the U.S. government and other international governmental bodies to limit the scope of patent protection both inside and outside the U.S. for disease treatments that prove successful; and

- Countries other than the U.S. might have less restrictive patent laws than those upheld by U.S. courts, allowing foreign competitors the ability to exploit these laws to create, develop, and market competing products.

In addition, the U.S. Patent and Trademark Office and patent offices in other jurisdictions have often required that patent applications concerning pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Thus, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated.

In addition to patents, we also rely on trade secrets and proprietary know-how. Although we take measures to protect this information by entering into confidentiality and inventions agreements with our employees, scientific advisors, consultants, and collaborators, we cannot provide any assurances that these agreements will not be breached, that we will be able to protect ourselves from the harmful effects of disclosure if they are breached, or that our trade secrets will not otherwise become known or be independently discovered by competitors. If any of these events occurs, or we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

Patent and other intellectual property protection is crucial to the success of our business and prospects, and there is a substantial risk that such protections will prove inadequate. Our business and prospects will be harmed if these protections prove insufficient.

We rely on trade secret protections through confidentiality agreements with our employees, customers and other parties, and the breach of these agreements could adversely affect our business and prospects.

We rely on trade secrets, which we seek to protect, in part, through confidentiality and non-disclosure agreements with our employees, collaborators, supplies, and other parties. There can be no assurance that these agreements will not be breached, that we would have adequate remedies for any such breach or that our trade secrets will not otherwise become known to or independently developed by our competitors. We might be involved from time to time in litigation to determine the enforceability, scope and validity of our proprietary rights. Any such litigation could result in substantial cost and divert management's attention from our operations.

If we infringe the rights of third parties we might have to forgo selling our future products, pay damages, or defend against litigation.

If our product candidates, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we might have to:

- obtain licenses, which might not be available on commercially reasonable terms, if at all;
- abandon an infringing product candidate;
- redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others;
- pay damages; and/or
- defend litigation or administrative proceedings which might be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

Any of these events could substantially harm our earnings, financial condition and operations.

Risks Related to Our Common Stock

We might not be able to maintain the listing of our common stock on The NASDAQ Capital Market.

Our common stock is listed on The NASDAQ Capital Market under the symbol "VTUS." We might not be able to maintain the listing standards of that exchange. If we fail to maintain the listing requirements, our common stock might trade on the OTC Bulletin Board or in the "pink sheets" maintained by Pink OTC Markets, Inc. These alternative markets are generally considered to be markets that are less efficient and less broad than The NASDAQ Capital Market.

The price of our common stock might fluctuate significantly, and you could lose all or part of your investment.

Since we went public on December 22, 2010 and through February 28, 2013, the price of our common stock has fluctuated between $1.99 and $21.00, with significant volatility after we announced on June 25, 2012 that VEN 309 failed to meet the endpoints of our Phase III trial. Continued volatility in the market price of our common stock might prevent you from being able to sell your shares of our common stock at or above the price you paid for such shares. The trading price of our common stock might be volatile and subject to wide price fluctuations in response to various factors, including:

- results of our clinical trials and other studies involving VEN 307;
- availability of capital;
- future sales of our common stock;
- sale of shares of our common stock by our significant stockholders or members of our management;
- additions or departures of key personnel;
- investor perceptions of us and the pharmaceutical industry;
    - issuance of new or changed securities analysts' reports or recommendations, or the announcement of any changes to our credit rating;
- success or failure of our product candidates;
    - introduction of new products or announcements of significant contracts, acquisitions or capital commitments by us or our competitors;
- threatened or actual litigation and government investigations;
- legislative, political or regulatory developments;
- the overall performance of the equity markets;
- actual or anticipated fluctuations in our quarterly financial and operating results;
- general economic conditions;
- changes in interest rates; and
- changes in accounting standards, policies, guidance, interpretations or principles.

These and other factors might cause the market price of our common stock to fluctuate substantially, which might limit or prevent investors from readily selling their shares of our common stock and might otherwise negatively affect the liquidity of our common stock. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has had a significant impact on the market price of securities issued by many companies across many industries. The changes frequently appear to occur without regard to the operating performance of the affected companies. Accordingly, the price of our common stock could fluctuate based upon factors that have little or nothing to do with our company, and these fluctuations could materially reduce our share price.

We do not intend to pay dividends for the foreseeable future and our stock may not appreciate in value.

We currently intend to retain our future earnings, if any, to finance the operation and growth of our business and do not expect to pay any cash dividends in the foreseeable future. As a result, the success of an investment in shares of our common stock will depend upon any future appreciation in its value. There is no guarantee that shares of our common stock will appreciate in value or that the price at which our stockholders have purchased their shares will be able to be maintained.

The requirements of being a public company adds to our operating costs and might strain our resources and distract our management.

As a public company, we face increased legal, accounting, administrative and other costs and expenses not faced by private companies. We are subject to the reporting requirements of the Securities Exchange Act of 1934, which requires that we file annual, quarterly and current reports with respect to our business and financial condition, and the rules and regulations implemented by the SEC, the Sarbanes-Oxley Act of 2002, and The NASDAQ Capital Market, each of which imposes additional reporting and other obligations on public companies. These rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly, although we are currently unable to estimate these costs with any degree of certainty. Complying with these requirements might divert management's attention from other business concerns, which could have a material adverse effect on our prospects, business, and financial condition.

Additionally, the expenses incurred by public companies generally for reporting and corporate governance purposes have been increasing. These increased costs will require us to divert a significant amount of money that we could otherwise use to develop our product candidates or otherwise expand our business. If we are unable to satisfy our obligations as a public company, we could be subject to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

Several provisions of the Delaware General Corporation Law and our Amended and Restated Certificate of Incorporation and Bylaws could discourage, delay or prevent a merger or acquisition, which could adversely affect the market price of our securities.

Several provisions of the Delaware General Corporation Law and our Amended and Restated Certificate of Incorporation and Bylaws could discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, and the market price of our securities could be reduced as a result. These provisions include:

- "blank check" preferred stock;
- prohibiting us from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder unless certain provisions are met;
- prohibiting cumulative voting in the election of directors;
- limiting the persons who may call special meetings of stockholders;
- establishing advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings; and
- The ability of our board of directors to increase its size and fill vacancies.

If securities analysts downgrade our stock or cease coverage of us, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. Currently, six financial analysts publish reports about us and our business. We do not control these or any other analysts. Furthermore, there are many large, well-established, publicly traded companies active in our industry and market, which may mean that it is less likely that we will receive widespread analyst coverage. If any of the analysts who cover us downgrade our stock, our stock price would likely decline rapidly. If these analysts cease coverage of our company, we could lose visibility in the market, which in turn could cause our stock price to decline.

Substantial future sales of our common stock in the public market may depress our stock price and make it difficult for you to recover the full value of your investment in our shares of securities.

As of February 28, 2013, we had 19,604,350 shares of common stock outstanding. Substantially all of these shares are available for public sale, subject in some cases to volume and other limitations or delivery of a prospectus. In addition, the issuance of up to 2,200,000 shares of our common stock upon conversion of the Series A Preferred Stock issued in February 2013 would be substantially dilutive to the outstanding shares of our common stock. The market price of our common stock may decline if our common stockholders sell a large number of shares of our common stock in the public market, or the market perceives that such sales may occur. In addition, at February 28, 2013, we had outstanding options and warrants to purchase an aggregate of 1,878,475 shares and 874,651 shares, respectively, of our common stock. If these options or warrants are exercised and the shares issued upon exercise are sold, the market price of our securities may also decline. These factors also could impair our ability to raise needed capital by depressing the price at which we could sell our securities.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We occupy space on the 5 th floor at 99 Hudson Street, New York, New York 10013. We rent this space pursuant to a lease that runs until August 2014. We believe our current facilities are suitable and adequate for our activities until such time as we hire a significant number of additional employees or consultants. We intend to renew the lease prior to its expiration.

Item 3. Legal Proceedings

We are not a party to any legal proceedings and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

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

Our common stock is traded under the symbol "VTUS" and is quoted on the NASDAQ Capital Market. The following table sets forth the high and low sales prices for shares of our common stock, as reported by NASDAQ for the periods indicated.

	2011	
	High	**Low**
First Quarter	$ 11.98	$ 5.75
Second Quarter	$ 21.00	$ 11.02
Third Quarter	$ 15.10	$ 7.84
Fourth Quarter	$ 9.94	$ 6.96

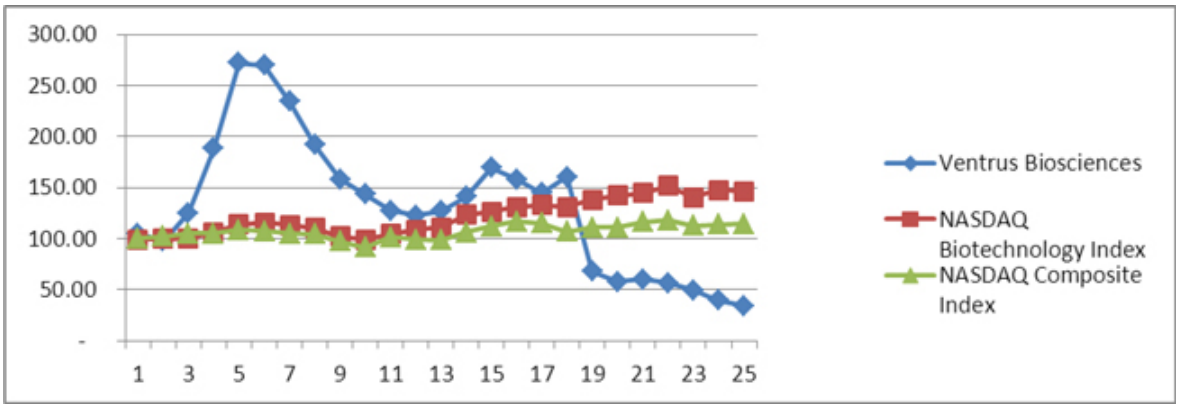
	2012	
	High	**Low**
First Quarter	$ 12.00	7.68
Second Quarter	$ 13.53	$ 4.20
Third Quarter	$ 4.40	$ 3.46
Fourth Quarter	$ 3.81	$ 1.99

On March 12, 2013, the closing price for the common stock as reported on the NASDAQ Capital Market was $3.32.

As of March 12, 2013, there were 105 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers.

Performance Graph

The following graph compares our cumulative total stockholder return from December 17, 2010 with those of the Nasdaq Composite Index and the Nasdaq Biotech Index and assumes that all dividends were reinvested. The graph assumes that U.S. $100 was invested on December 17, 2010 in (1) our common stock, (2) the Nasdaq Biotech Index and (3) the Nasdaq Composite Index. The measurement points utilized in the graph consist of the last trading day in each calendar year, which closely approximates the last day of our respective fiscal year. The historical stock performance presented below is not intended to and may not be indicative of future stock performance.



Company/Peer Company/ Market	12/31/10	12/31/2011	12/31/2012
Ventrus Biosciences	$ 105.08	$ 127.11	$ 34.29
NASDAQ Biotechnology Index	$ 99.10	$ 110.80	$ 146.15
NASDAQ Composite Index	$ 100.37	$ 98.57	$ 114.25

Dividend Policy

We currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain our future earnings, if any, for use in the operation and expansion of our business. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as earnings levels, capital requirements, our overall financial condition and any other factors our board deems relevant.

Equity Compensation Plans

The information required by Item 4 of Form 10-K regarding equity compensation plans is incorporated herein by reference to “Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters” in this report.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and the financial statements and the notes thereto included elsewhere in this report.

Statement of Operations Data:

	Year Ended December 31,				
	2012	2011	2010	2009	2008
	(in thousands)				
Operating expenses	$ 24,855	$ 34,002	$ 4,766	$ 3,340	$ 7,164
Loss from operations	(24,855)	(34,002)	(4,766)	(3,340)	(7,164)
Interest income	65	76	6	-	13
Interest expense		(419)	(10,530)	(1,199)	(1,635)
Net loss	(24,790)	(34,345)	(15,291)	(4,539)	(8,786)

Balance Sheet Data:

	As of December 31,				
	2012	2011	2010	2009	2008
Total assets	$ 20,556	$ 37,046	$ 14,617	$ 166	$ 870
Deferred financing costs, net	-	-	27	69	-
Total stockholders' equity (deficiency)	17,810	34,533	11,626	(13,363)	(9,457)

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

Overview

We are a development-stage specialty pharmaceutical company currently focused on the development of late-stage prescription drugs for gastrointestinal disorders, specifically anal disorders.

We have in-licensed our two proprietary product candidates that are in clinical development that address large market opportunities, including our most advanced product candidate, VEN 307. VEN 307 is a pre-mixed and pre-packaged proprietary topical formulation of the drug diltiazem which we are developing for the treatment of anal fissures. VEN 308 is intended to treat fecal incontinence.

Our development partner, S.L.A. Pharma, conducted a Phase III trial of VEN 307 in Europe, the positive results of which we announced in May 2012. Based on those results, we initiated a second pivotal Phase III clinical trial of VEN 307 in anal fissures in the fourth quarter of 2012, and expect to report top line data in the fourth quarter of 2013. We intend to undertake technical development to create a twice daily patentable formulation of VEN 307 after which we will determine whether to pursue further development of an extended release formulation of VEN 307.

Based on disappointing results of our Phase III trial of VEN 309 for the treatment of hemorrhoids, which we reported in June 2012, we have ceased all activity related to VEN 309 other than the winding down of the program..

Since our inception, we have had no revenue from product sales, and have funded our operations principally through debt financings, our initial public offering in 2010, a public offering of our common stock in July 2011, sales of our common stock in mid-2012 pursuant to an at-the-market program, and a public offering of our common stock and Series A non-voting convertible preferred stock in February 2013. Our operations to date have been primarily limited to organizing and staffing our company, licensing our product candidates, developing clinical trials for our product candidates, establishing manufacturing for our product candidates, maintaining and improving our patent portfolio and raising capital. We have generated significant losses to date, and we expect to continue to generate losses as we progress towards the commercialization of VEN 307 and VEN 308. As of December 31, 2012, we had a deficit accumulated during the development stage of $92,319,514. Because we do not generate revenue from any of our product candidates, our losses will continue as we advance our product candidates towards regulatory approval and eventual commercialization. We do not anticipate FDA approval and launch of VEN 307 until at least late 2014 or early 2015. As a result, our operating losses are likely to be substantial over the next two years as we continue the development and undertake commercialization of VEN 307 and thereafter if approval is not received or VEN 307 is not successfully launched. We are unable to predict the extent of any future losses or when we will become profitable, if at all.

We believe that our existing cash will be sufficient to fund our projected operating requirements through FDA approval of VEN 307 and its initial launch and commercialization. Thereafter, we will need revenue from commercial sales of VEN 307, if any, or additional capital to continue operations.

Financial Operations Overview

Critical Accounting Policies

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. Our significant accounting policies are more fully described in Note 2 to the December 31, 2012 audited financial statements included in this report. The following accounting policies are critical to fully understanding and evaluating our financial results.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires our management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements as well as the reported revenue, if any, and expenses during the reporting periods. On an ongoing basis, management evaluates their estimates and judgments. Management bases estimates on historical experience and on various other factors that they 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. Actual results might differ from these estimates under different assumptions or conditions.

Stock-Based Compensation

We account for stock options granted to employees, measured at grant date, based on the estimated fair value of the award, which is recognized as expense over the employee's requisite service period on a straight-line basis. We account for stock options and warrants granted to non-employees on a fair value basis. The initial non-cash charge to operations for nonemployee options and warrants with vesting are revalued at the end of each reporting period based upon the change in the fair value of the options and recognized as consulting expense over the related service period. For the purpose of valuing options and warrants granted to employees and non-employees, we use the Black-Scholes option pricing model. To determine the risk-free interest rate, we utilize the U.S. Treasury yield curve in effect at the time of grant with a term consistent with the expected term of the awards. We estimate the expected life of the options granted based on anticipated exercises in the future periods assuming the success of our business model as currently forecasted. For warrants and non-employee options, we use the contractual term of the warrant, the length of the note or option as the expected term. The expected dividend yield reflects our current and expected future policy for dividends on our common stock. The expected stock price volatility for our stock options will be calculated by examining historical volatilities for publicly traded industry peers as we do not now and for the near future will not have any significant trading history for our common stock. Forfeiture rates will be calculated based on the expected service period for our employees.

Research and Development Expense

Research and development expenses consist primarily of costs associated with: (i) internal costs associated with our development activities; (ii) payments we make to third party contract research organizations, contract manufacturers, and consultants; (iii) technology and intellectual property license costs; and (iv) patent reimbursements. All research and development is expensed as incurred. License fees and pre-approved milestone payments due under each research and development arrangement that are paid prior to regulatory approval are expensed when the license is entered into or the milestone is achieved.

Conducting a significant amount of research and development is central to our business model. Since our inception on October 7, 2005 to December 31, 2012, we incurred $59,043,406 in research and development expenses. Product candidates in later-stage clinical development generally have higher development costs than those in earlier stages of development, primarily due to the significantly increased size and duration of the clinical trials. Included in research and development expense is the full $12.5 million purchase price we paid in 2011 for VEN 309.

We plan to continue research and development expenses for the at least the next two years in order to complete development of our most advanced product candidate, VEN 307. On June 25, 2012, we reported that a Phase III, randomized, double-blind, placebo-controlled clinical trial of VEN 309 for the treatment of symptomatic hemorrhoids did not meet its endpoints. Based on the disappointing results of that Phase III trial, we have determined that our current resources would be better allocated toward the planned completion of VEN 307 development program in anal fissures. Consequently, we have no immediate plans to continue development of VEN 309 and have ceased all activity related to VEN 309 other than the winding down of the program.

The following table summarizes the research and development expenses incurred since inception.

	YE 2010	YE 2011	YE 2012	Period from October 7, 2005 (inception) to December 31, 2012
VEN 307	$ 1,309,501	$ 1,921,922	$ 5,565,280	$ 11,289,203
VEN 309	$ 379,237	$ 22,230,856	$ 13,102,375	$ 43,773,214
Other	$ 161,928	$ 1,124,904	$ 846,508	$ 3,980,989

The process of conducting pre-clinical studies and clinical trials necessary to obtain FDA approval is costly and time consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the quality of the product candidate's clinical data, regulatory conversations with FDA, manufacturing capabilities and commercial viability. As a result of the uncertainties discussed above, the uncertainty associated with clinical trial enrollments and the risks inherent in the development and regulatory process, we are unable to determine with certainty the duration and completion costs of current or future clinical stages of our product candidate or when, or to what extent, we will generate revenues from the commercialization and sale of our product candidate. Based on its current status, we anticipate that to complete the clinical trial process and commercialize our lead product candidate VEN 307 will cost approximately $15 million. This estimate could change significantly depending on the progress, timing and results of non-clinical and clinical trials associated with VEN 307. We believe the Company currently has sufficient funds to meet its operating requirements and scheduled regulatory and development activities through FDA approval and initial launch and commercialization of diltiazem. Assuming such approval and launch, thereafter, if the Company cannot generate significant cash from its operations, it intends to obtain any additional funding it requires through strategic relationships, public or private equity or debt financings, or other arrangements and it cannot assure such funding will be available on reasonable terms, or at all.

Our significant accounting policies are described in more detail in Note 1 to our audited financial statements included in this report.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, including the use of structured finance, special purpose entities or variable interest entities.

Contractual Obligations

The following table summarizes our future contractual obligations and commercial commitments at December 31, 2012.

	Less than 1 year	1-2 years
SLA Pharma	$ 498,000	$ -
Regus (office lease)	$ 74,046	$ 58,800
Total contractual obligations	$ 572,046	$ 58,800

Results of Operations

Comparison of the Years Ended December 31, 2012 and December 31, 2011

Research and Development Expense

Research and development expense was $19,514,163 for the year ended December 31, 2012, a decrease of $5,763,519 or 22.80%, from $25,277,682 for the same period in 2011. The primary reason for the decrease was the $12.5 million purchase price for VEN 309 that was paid to Sam Amer in 2011, which was offset by costs associated with preparing for and initiating the second clinical trial for VEN 307 in 2012.

General and Administrative Expense

General and administrative expense consists primarily of salaries, consulting fees and other related costs, professional fees for legal services and accounting services, insurance and travel expenses, as well as the option expense associated with the grants of options to our employees and directors in 2012. We expect that our general and administrative expenses will increase as we add additional personnel to continue our commercialization plans for VEN 307.

General and administrative, or G&A, expense was $5,341,333 for the year ended December 31, 2012, a decrease of $3,383,058, or approximately 38.77%, from $8,724,391 for the year ended December 31, 2011. The biggest decrease in G&A expense in 2012 was associated with stock-based compensation expense for employees, consultants and directors which decreased by $3,524,000, as well as a decrease in investor relations expenses of $112,000, which was offset by increases in board fees of $105,000, directors and officers insurance of $86,000, and consulting fees of $65,000.

Interest Expense and Income

We had no outstanding loans during the year ended December 31, 2012 due to repayment of all loans in July 2011 and therefore had no interest expense for the year, a decrease of $116,664 from the year ended December 31, 2011. Interest income was $65,066 for the year ended December 31, 2012 compared to $76,334 for the year ended December 31, 2011.

Comparison of the Years Ended December 31, 2011 and December 31, 2010

Research and Development Expense

Research and development expense was $25,277,682 for the year ended December 31, 2011, an increase of $23,427,016, or 1265%, from $1,850,666 for the year ended December 31, 2010. The primary reason for the increase was the increased development activities of VEN 309, which commenced after we received the proceeds from our initial public offering in December 2010. We have incurred higher development costs due to initiation of the Phase III clinical trial as well as product development and manufacturing costs to support the clinical study. Additionally, we expensed $12,500,000 relating to the acquisition of title and rights to VEN 309 from Sam Amer.

General and Administrative Expense.

General and administrative, or G&A, expense was $8,724,391 for the year ended December 31, 2011, an increase of $5,808,801, or approximately 199%, from $2,915,590 for the year ended December 31, 2010. We had limited operations and related operating expenses in the first half of 2010 due to the lack of funds. We began increasing our operating activities in the second half of 2010. The largest G&A expense incurred in the year 2011 was associated with stock-based compensation expense for employees, consultants and directors which increased by $3,550,080 as well as G&A salaries of $1,331,211 which did not exist in 2010.

Interest Expense

Interest expense of $116,664 in 2011 consisted of interest incurred on related party note which was paid in full in July 2011. Additionally, there was $302,327 of amortization of debt discount and deferred financing costs. Interest expense in 2010 consisted of interest incurred on the 5% related parties' promissory notes which were issued from October 2005 to June 2008, the 8% related parties' promissory notes which were issued from July 2008 to December 2010, the 10% Paramount Credit Partners notes from January 2009 to June 2010, the 8% senior convertible notes which were issued from December 2007 to December 2008, the 10% senior convertible notes from December 2008 to December 2010, the 8% 2010 senior convertible notes which were issued from February 2010 to December 2010, our letter of credit borrowings and interest due on our license fee payments. Additionally, interest expense included the beneficial conversion charge of conventional convertible debt that was converted below market value as well as amortization of debt discount and deferred financing costs, as well as the debt discount for warrants issued in connection with debt financings.

Liquidity and Capital Resources

As a result of our significant research and development expenditures and the lack of any FDA-approved products to generate product sales revenue, we have not been profitable and have generated operating losses since we were incorporated in October 2005. We have funded our operations through December 31, 2012 principally with debt (which in connection with the initial public offering, all of the convertible notes, and accrued interest thereon, were converted into common stock) and equity financing, including raising approximately $15.2 million in net proceeds in our initial public offering, which closed on December 22, 2010, and approximately $2.4 million in net proceeds upon the exercise on January 7, 2011 of the over-allotment option granted to the underwriter of our initial public offering. In addition, in July 2011, we raised $47.6 million in net proceeds in a registered public offering of our common stock.

We also filed a shelf registration statement with the Securities and Exchange Commission, or SEC which was declared effective on February 10, 2012 under which we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of $100,000,000. As part of the shelf registration statement, we included a prospectus for an at-the-market common equity sales program for the sale of up to $20,000,000 of our common stock. In May and June 2012, we raised $4,166,000 in net proceeds under the at-the-market common equity sales program. In February 2013, we raised approximately $20.7 million in net proceeds in a public offering of our common stock and our Series A non-voting convertible preferred stock, all of which shares were sold off of the shelf registration statement.

Net Cash Used in Operating Activities

Net cash used in operating activities was $21,379,790 for the year ended December 31, 2012 and funded our research and development program build out and general and administrative expenses. The net loss of $24,790,430 for the year ended December 31, 2012 was greater than cash used in operating activities by $3,410,640. The primary reason for the difference is attributed to a stock-based compensation charge of $3,171,093.

Net Cash Used in Investing Activities

Net cash used in investing activities was $3,241 for the year ended December 31, 2012.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $4,896,816 for the year ended December 31, 2012. Net cash provided by financing activities during the year ended December 31, 2012 consisted of the sale of common stock in an at-the-market program of $4,166,494. We also received $730,322 from the exercise of warrants and options in 2012.

Funding Requirements

We expect to incur losses for at least the next two years as we develop VEN 307 and thereafter if the FDA does not approve VEN 307 or we do not launch it successfully. We expect to incur increasing research and development expenses for VEN 307. We expect that our general and administrative expenses will also increase as we add infrastructure for the planned commercialization of VEN 307, and continue to incur costs related to being a public company, including increased professional fees. Our future capital requirements will depend on a number of factors, including the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims and other intellectual property rights, the acquisition of licenses to new products or compounds, the status of competitive products, the availability of financing, and our success in developing markets for our product candidates.

We anticipate that to complete the clinical trial process to obtain the approval of VEN 307 will cost approximately $15 million. Based on our cash position at December 31, 2012, and our analysis of our future development costs, we believe that our existing cash and cash equivalents will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through the initial launch and commercialization of VEN 307. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect, which would cause us to require additional capital earlier. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials.

We do not anticipate that we will generate product revenue for at least the next two years, assuming the FDA approves VEN 307 and we successfully launch that product. In the absence of additional funding, we expect our continuing operating losses to result in increases in our cash used in operations over the next two years as we continue the development of VEN 307 and prepare for its commercialization.

We may need to finance our future cash needs through public or private equity offerings, debt financings, corporate collaboration and licensing arrangements, or a bank credit facility or other financing vehicle if one or more of our assumptions prove to be incorrect or if we choose to expand our product development efforts more rapidly than we presently anticipate, and we may decide to raise additional funds even before we need them if the conditions for raising capital are favorable. We do not currently have any commitments for future external funding. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations.

Additional equity or debt financing or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If we need additional capital and adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Recent Accounting Pronouncements

In May 2011, the financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, NO. 2011-04, *Fair Value Measurement (Topic 820): Amendments to Achieve Common Fair Value Measurement and Disclosure Requirements in U.S. GAAP and IFRS*. This ASU represents the converged guidance of the FASB and the International Accounting Standards Board, or IASB (together, the "Board") on fair value measurement. The collective efforts of the Boards and their staffs, reflected in ASU No. 2011-04, have resulted in common requirements for measuring fair value and for disclosing information about fair value measurements, including a consistent meaning of the term "fair value." The Boards have concluded the common requirements will result in greater comparability of fair value measurements presented and disclosed in financial statements prepared in accordance with U.S. GAAP and international financial reporting standards, or IFRS. The amendments to the FASB Accounting Standards Codification in this ASU are to be applied prospectively. The amendments are effective for annual periods beginning after December 15, 2011. The application of ASU No. 2011-04 did not have a material effect on our financial statements.

Cautionary Statement

We operate in a highly competitive environment that involves a number of risks, some of which are beyond our control. The following statement highlights some of these risks. For more detail, see "Item 1A. Risk Factors".

Statements contained in this Form 10-K that are not historical facts, are or might constitute forward-looking statements under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Although we believe the expectations reflected in such forward-looking statements are based on reasonable assumptions, our expectations might not be attained. Forward-looking statements involve known and unknown risks that could cause actual results to differ materially from expected results. Factors that could cause actual results to differ materially from our expectations expressed in the report include, among others: risks related to the costs, timing, regulatory review and results of our studies and clinical trials; our ability to obtain FDA approval of our product candidates; differences between historical studies on which we have based our planned clinical trials and actual results from our trials; our anticipated capital expenditures, our estimates regarding our capital requirements, and our need for future capital; our liquidity and working capital requirements; our expectations regarding our revenues, expenses and other results of operations; the unpredictability of the size of the markets for, and market acceptance of, any of our products, including VEN 307; our ability to sell any approved products and the price we are able realize; our ability to obtain future funding on acceptable terms; our ability to retain and hire necessary employees and to staff our operations appropriately; our ability to compete in our industry and innovation by our competitors; our ability to stay abreast of and comply with new or modified laws and regulations that currently apply or become applicable to our business; estimates and estimate methodologies used in preparing our financial statements; the future trading prices of our common stock and the impact of securities analysts' reports on these prices; and the risks set out in our filings with the SEC.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates.

We do not believe that our cash and equivalents have significant risk of default or illiquidity. Under our current investment policies, we invest our cash and cash equivalents in money market funds which invest in short-term U.S. Treasury securities with insignificant rates of return. While we believe our cash and equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and equivalents at one or more financial institutions that are in excess of federally insured limits.

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 results of operations during 2010, 2011 or 2012.

Our purchases of raw materials and finished goods are denominated in U.S. dollars. Consequently, we have not considered it necessary to use foreign currency contracts or other derivative instruments to manage changes in currency rates. We do not now, nor do we plan to, use derivative financial instruments for speculative or trading purposes. However, these circumstances might change.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found on page F-1.

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

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain a system of disclosure controls and procedures, as defined in Exchange Act Rule 13a-15(e),which is designed to provide reasonable assurance that information, which is required to be disclosed in our reports filed pursuant to the Securities and Exchange Act of 1934, as amended (the "Exchange Act"), is accumulated and communicated to management in a timely manner. At the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15(b). Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures as of the end of the period covered by this report were effective.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. A control system, no matter how well designed and operated, can only provide reasonable, not absolute, assurance that the objectives of the control system are met. Because of these inherent limitations, management does not expect that our internal controls over financial reporting will prevent all error and all fraud. Under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control-Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in *Internal Control-Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2012.

The effectiveness of our internal control over financial reporting as of December 31, 2012, has been audited by EisnerAmper LLP, an independent registered public accounting firm, as stated in their report which is included on page F-3 herein.

Changes in Internal Control over Financial Reporting

During 2011 and 2012, we took the following measures to address the material weaknesses that we had identified in 2010 and improve our periodic financial statement reporting process:

- upgraded our accounting software system in the first quarter of 2011
- limited access to the accounting and information systems and related data to strengthen segregation of duties;
- hired a controller in April 2011;
- began third party proofing of our quarterly and annual financial statements during the second half of 2011; and
- implemented recommendations of our outside consultants regarding our processes and controls.

Our audit committee, board of directors and management discussed among themselves and with EisnerAmper LLP the material weaknesses identified in fiscal year 2010 and assigned the highest priority to correct the issue. We actively sought the guidance and expertise of external consultants to help evaluate and recommend a stronger internal control structure. We hired outside consultants after the second quarter of fiscal year 2011 who have reviewed and tested our internal controls. Based on recommendations by the consultants, management implemented additional procedures and refined controls. As of December 31, 2012, we believe we have effectively remediated the previously identified material weaknesses.

Other than the matters discussed above, there were no other significant changes in our internal control over financial reporting or in other factors that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The other information required by this Item is incorporated by reference to the information under the sections captioned “Proposal No. 1 - Election of Directors,” “Section 16(A) Beneficial Ownership Reporting Compliance,” and “Corporate Governance and Board Matters” in our definitive proxy statement for our 2013 annual meeting of stockholders, referred to herein as the 2013 proxy statement, that we intend to file on or before April 30, 2013.

Item 11. Executive Compensation

The information required by this Item is incorporated by reference to the information under the sections in the 2013 proxy statement captioned “Executive Compensation,” “Director Compensation,” “Proposal No. 1 - Election of Directors,” “Section 16(A) Beneficial Ownership Reporting Compliance,” and “Corporate Governance and Board Matters”

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

Equity Compensation Plans

The following table sets forth the indicated information as of December 31, 2012 with respect to our equity compensation plans:

Plan Category	Number of Securities to be issued upon exercise of outstanding options, warrants and rights		Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans
Equity compensation plans approved by our shareholders:				
2007 Stock Plan	2,016	$	6.00	-0-
2010 Stock Plan:	1,878,475	$	6.72	1,920,485
Equity compensation plans not approved by our shareholders:				
2008 Warrants	9,947	$	66.46	-0-
2009 Placement Agent Warrants	39,657	$	12.40	-0-
2009 PCP Warrants	104,867	$	6.60	-0-
2010 Warrants	342,579	$	6.60	-0-
Licensor Warrants	13,605	$	1.24	-0-
Consultant Warrants	84,545	$	6.16	-0-
2010 Placement Agent Warrants	82,251	$	7.50	-0-
Underwriter Warrants	197,200	$	7.50	-0-
Total	2,755,142	$	7.02	1,920,485

Our equity compensation plan consists of the 2007 Stock Plan and the 2010 Stock Plan, both of which were approved by our stockholders. Our equity compensation arrangements that have not been approved by our stockholders consist of warrants to purchase shares of our common stock issued to: Paramount BioCapital as placement agent in our 2008 common stock offering; S.L.A. Pharma to whom we issued a warrant for 13,605 shares as part of an amendment to the license agreement between us and S.L.A. Pharma for VEN 307 and VEN 308; three consultants; National Securities Corporation as placement agent in our 2010 convertible note offering; and the underwriters of our initial public offering.

The other information required by this Item is incorporated by reference to the information under the section captioned “Security Ownership of Certain Beneficial Owners and Management” in the 2013 proxy statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item is incorporated by reference to the information under the section captioned “Certain Relationships and Related Transactions” and “Corporate Governance and Board Matters - Independence of Directors” contained in the proxy statement.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated by reference to the information under the section in the 2013 proxy statement captioned “Audit and Audit Committee Matters.”

Item 15. Exhibits, Financial Statement Schedules

(a) *Exhibits.* The following exhibits are filed as part of this registration statement:

Exhibit No.	Description
1.1	Form of Underwriting Agreement dated December 22, 2010. (1)
1.2	Form of Underwriting Agreement dated July 13, 2011. (10)
1.3	Controlled Equity Offering Sales Agreement, dated January 30, 2012 between Ventrus Biosciences, Inc. and Cantor Fitzgerald & Co. (6)
1.4	Underwriting Agreement, dated January 30, 2013, by and between Ventrus Biosciences, Inc. and William Blair & Company, L.L.C. (9)
1.5	Underwriting Agreement, dated January 30, 2013, by and between Ventrus Biosciences, Inc. and William Blair & Company, L.L.C. (9)
3.1	Amended and Restated Certificate of Incorporation dated November 11, 2010. (2)
3.2	Amended and Restated Bylaws dated July 12, 2010. (5)
3.3	Certificate of Designation of Series A Non-Voting Convertible Preferred Stock of Ventrus Biosciences, Inc. filed on January 30, 2013. (8)
4.1	Specimen of Common Stock Certificate. (3)
4.2	Form of Convertible Promissory Note issued to investors between December 2007 and March 2008, as amended in December 14, 2009. (5)
4.3	Form of Warrant issued to investors between June and September 2008. (5)
4.4	Form of Convertible Promissory Note issued to Paramount BioSciences, LLC and Capretti Grandi, LLC in 2008 and 2009, as amended on December 21, 2009. (4)
4.5	Warrants issued to Paramount Credit Partners, LLC on January 23, March 25, June 1 and June 24, 2009. (4)
4.6	Form of Convertible Promissory Note issued to investors and Paramount BioCapital, Inc. in February, March and April 2010. (5)
4.7	Form of Convertible Promissory Note issued to investors in May 2010. (4)
4.8	Form of Warrant issued to investors in February and March, 2010. (4)
4.9	Form of Warrant issued to investors in May 2010. (4)
4.10	Form of Placement Agent Warrant issued to Paramount BioCapital, Inc. on March 11, 2008. (5)
4.11	Placement Agent Warrants issued to National Securities Corporation on February 26, March 31 and May 6, 2010, as amended October 28, 2010 and November 30, 2010. (1)
4.12	Warrant issued to S.L.A. Pharm AG on August 30, 2010. (4)
4.13	Form of underwriters warrant dated December 22, 2010. (1)

Exhibit No.	Description
10.1*	Exclusive License Agreement dated March 23, 2007 by and between S.L.A. Pharma AG, and Paramount Biosciences, LLC, as amended on July 24, 2008, November 20, 2008, June 1, 2009, December 18, 2009 and June 24, 2010 and letter agreements dated October 27, 2008, November 20, 2008 and January 22, 2009. (2)
10.2	Assignment and Assumption Agreement dated August 2, 2007, by and between Paramount Biosciences LLC and Ventrus Biosciences, Inc. (5)
10.3*	License Agreement dated March 10, 2008 by and between Sam Amer & Co., Inc. and Ventrus Biosciences, Inc., as amended on July 31, 2008, September 29, 2008, November 17, 2008, and letter agreements dated March 13, 2009, August 18, 2009, May 13, 2009 and December 15, 2009. (5)
10.4	Amended and Restated Consulting Agreement dated July 19, 2010 between Russell H. Ellison and Ventrus Biosciences, Inc. (5)
10.5	Amended and Restated Employment Agreement dated July 19, 2010 between Russell H. Ellison and Ventrus Biosciences, Inc. (5)
10.6	Amended and Restated Consulting Agreement dated July 19, 2010 between David J. Barrett and Ventrus Biosciences, Inc. (5)
10.7	2007 Stock Incentive Plan. (5)
10.8	Consulting Agreement dated March 1, 2009 between John Dietrich and Ventrus Biosciences, Inc. (4)
10.9	Consulting Agreement dated May 11, 2010 between Timothy Hofer and Ventrus Biosciences, Inc. (4)
10.10	Amendment No. 6, dated August 30, 2010, to Exclusive License Agreement between S.L.A. Pharma AG and Paramount BioSciences, LLC (assigned to Ventrus Biosciences). (4)
10.11	Senior promissory notes issued by Ventrus Biosciences, Inc. to Paramount Credit Partners, LLC on January 23, March 25, June 1 and June 24, 2010 and Waiver Agreement and Amendment dated as of August 30, 2010. (3)
10.12	Employment Agreement dated November 11, 2010 between David J. Barrett and Ventrus Biosciences, Inc. (2)
10.14	2010 Equity Incentive Plan. (4)
10.15	Asset Purchase Agreement dated June 5, 2011 between Ventrus Biosciences, Inc. and Sam Amer & Co., Inc. (5)
10.16	Amendment No. 7, dated June 6, 2011, to Exclusive License Agreement between S.L.A. Pharma AG and Paramount BioSciences, LLC (assigned to Ventrus Biosciences). (5)
10.17	Amendment No. 1, dated August 24, 2011, to Employment Agreement between David J. Barrett and Ventrus Biosciences, Inc. (7)
10.18	Amendment No. 1, dated August 24, 2011, to Amended and Restated Employment Agreement between Russell Ellison and Ventrus Biosciences, Inc. (7)
10.19	Employment Agreement dated September 1, 2011 between Thomas Rowland and Ventrus Biosciences, Inc. (7)
23.1	Consent of EisnerAmper LLP, Independent Registered Public Accounting Firm.
31.1	Certification of the Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of the 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 the Chief Financial Officer Pursuant to 18 U.S. C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Certain information in this exhibit has been omitted and filed separately with the Securities and Exchange Commission pursuant to a confidential treatment request.

(1) Incorporated by reference to the exhibit filed in the Registrant's Amendment No. 4 to Registration Statement on Form S-1 filed on December 6, 2010.

(2) Incorporated by reference to the exhibit filed in the Registrant's Amendment No. 3 to Registration Statement on Form S-1 filed on November 16, 2010.
(3) Incorporated by reference to the exhibit filed in the Registrant's Amendment No. 2 to Registration Statement on Form S-1 filed on October 29, 2010.
(4) Incorporated by reference to the exhibit filed in the Registrant's Amendment No. 1 to Registration Statement on Form S-1 filed on October 4, 2010.
(5) Incorporated by reference to the exhibit filed in the Registrant's Registration Statement on Form S-1 filed on July 20, 2010.
(6) Incorporated by reference to the exhibit filed in the Registrant's Registration Statement on Form S-3 filed on January 31, 2012.
(7) Incorporated by reference to the exhibit filed in the Registrant's Current Report on Form 8-K filed on August 25, 2011.
(8) Incorporated by reference to the exhibit filed in the Registrant's Current Report on Form 8-K filed on February 4, 2013.
(9) Incorporated by reference to the exhibit filed in the Registrant's Current Report on Form 8-K filed on January 30, 2013.
(10) Incorporated by reference to the exhibit filed in the Registrant's Current Report on Form 8-K filed on July 14, 2011.

SIGNATURES

In accordance with Section 13 or 15(d) of the Securities Exchange Act, the Registrant caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

VENTRUS BIOSCIENCES, INC.

Date: March 18, 2013

By: /s/ Russell H. Ellison
Name: Russell H. Ellison
Title: Chief Executive Officer

SIGNATURES

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 in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Russell H. Ellison Russell H. Ellison	Chief Executive Officer (Principal Executive Officer) and Director	March 18, 2013
/s/ David J. Barrett David J. Barrett	Chief Financial Officer (Principal Financial and Accounting Officer)	March 18, 2013
/s/ Anthony E. Altig Anthony E. Altig	Director	March 18, 2013
/s/ Mark Auerbach Mark Auerbach	Director	March 18, 2013
/s/ Joseph Felder Joseph Felder	Director	March 18, 2013
/s/ Myron Z. Holubiak Myron Z. Holubiak	Director	March 18, 2013

FINANCIAL STATEMENTS

VENTRUS BIOSCIENCES, INC.

(A Development Stage Company)

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders
Ventrus Biosciences, Inc.

We have audited the accompanying balance sheets of Ventrus Biosciences, Inc. (a development stage company) (the "Company") as of December 31, 2012 and 2011, and the related statements of operations, stockholders' equity (deficiency), and cash flows for each of the years in the three-year period ended December 31, 2012 and for the period from October 7, 2005 (inception) to December 31, 2012. The financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ventrus Biosciences, Inc. as of December 31, 2012 and 2011, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2012 and for the period from October 7, 2005 (inception) to December 31, 2012, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Ventrus Biosciences, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"), and our report dated March 14, 2013 expressed an unqualified opinion thereon.

/s/ EisnerAmper LLP

New York, New York
March 14, 2013

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Ventrus Biosciences, Inc.

We have audited Ventrus Biosciences, Inc.'s (a development stage company) (the "Company") internal control over financial reporting as of December 31, 2012, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) 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.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Ventrus Biosciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on criteria established in *Internal Control - Integrated Framework* issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Ventrus Biosciences, Inc. as of December 31, 2012 and 2011, and the related statements of operations, stockholders' equity (deficiency) and cash flows for each of the years in the three-year period ended December 31, 2012 and for the period from October 7, 2005 (inception) to December 31, 2012, and our report dated March 14, 2013 expressed an unqualified opinion thereon.

/s/ EisnerAmper LLP

New York, New York
March 14, 2013

VENTRUS BIOSCIENCES, INC.
(A Development Stage Company)

Balance Sheets

	December 31, 2012	December 31, 2011
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 20,489,219**	**$ 36,975,434**
Other current assets	**59,584**	**62,129**
Total current assets	**20,548,803**	**37,037,563**
Computer equipment, net of accumulated depreciation of $33,050 and $28,432	**6,841**	**8,218**
Total assets	**$ 20,555,644**	**$ 37,045,781**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	**$ 1,847,245**	**$ 2,342,074**
Accrued expenses	**898,213**	**171,000**
Total liabilities	**$ 2,745,458**	**$ 2,513,074**
Stockholders' equity:		
Preferred stock, $.001 par value; 5,000,000 shares authorized, none issued	-	-
Common stock, $.001 par value; 50,000,000 authorized; 12,934,350 and 12,406,406 issued and outstanding	**12,934**	**12,406**
Additional paid-in capital	**110,116,766**	**102,049,385**
Deficit accumulated during the development stage	**(92,319,514)**	**(67,529,084)**
Total stockholders' equity	**17,810,186**	**34,532,707**
Total liabilities and stockholders' equity	**$ 20,555,644**	**$ 37,045,781**

The accompanying notes are an integral part of these financial statements

VENTRUS BIOSCIENCES, INC.
(A Development Stage Company)

Statements of Operations

	Year Ended December 31, 2012	Year Ended December 31, 2011	Year Ended December 31, 2010	Period from October 7, 2005 (Inception) to December 31, 2012
Operating expenses:				
Research and development	**$ 19,514,163**	$ 25,277,682	$ 1,850,666	**$ 59,043,406**
General and administrative	**5,341,333**	8,724,391	2,915,590	**19,586,401**
Loss from operations	**(24,855,496)**	(34,002,073)	(4,766,256)	**(78,629,807)**
Other income (expense):				
Interest income	**65,066**	76,334	5,730	**161,119**
Interest expense:				
Beneficial conversion charge	-	-	(6,001,496)	**(6,001,496)**
Amortization of debt discount and warrants	-	(302,327)	(2,484,927)	**(2,865,758)**
Interest expense	-	(116,664)	(2,043,676)	**(4,983,572)**
Total other income (expense)	**65,066**	(342,657)	(10,524,369)	**(13,689,707)**
Net loss	**$ (24,790,430)**	$ (34,344,730)	$ (15,290,625)	**$ (92,319,514)**
Basic and diluted net loss per common share	**$ (1.94)**	$ (3.57)	$ (24.67)	
Weighted average common shares outstanding - basic and diluted	**12,726,551**	9,613,900	619,923	

The accompanying notes are an integral part of these financial statements

VENTRUS BIOSCIENCES, INC.
(A Development Stage Company)

Statements of Cash Flows

	Year ended December 31, 2012	Year ended December 31, 2011	Year ended December 31, 2010	Period from October 7, 2005 (Inception) to December 31, 2012
Cash flows from operating activities:				
Net loss	**$ (24,790,430)**	$ (34,344,730)	$ (15,290,625)	**$ (92,319,514)**
Adjustments to reconcile net loss to net cash used in operating activities:				
Stock-based compensation	**2,831,651**	2,982,949	2,356,087	**8,771,922**
Stock - based payments to consultants	**339,442**	3,990,817	-	**4,330,259**
Stock issued in connection with license agreement	-	-	389,597	**414,825**
Charge resulting from beneficial conversion feature	-	-	6,001,496	**6,001,496**
Stock issued to vendor	-	-	-	**5,000**
Warrants issued in connection with related party note conversion	-	-	915,118	**1,255,978**
Amortization of deferred financing costs and debt discount	-	328,958	2,327,193	**3,466,010**
Non-cash research and development	-	-	-	**1,087,876**
Interest payable - 2007 Senior convertible notes	-	-	611,266	**1,598,104**
Interest payable - 2010 Senior convertible notes	-	-	354,269	**354,269**
Expenses paid on behalf of the Company satisfied through the issuance of notes	-	-	-	**227,910**
Interest payable - related parties	-	-	94,912	**266,279**
Interest payable - Paramount Credit Partners, LLC	-	-	79,696	**187,536**
Depreciation	**4,618**	3,746	12,525	**35,623**
Changes in operating assets and liabilities:				
Prepaid research and development	-	-	-	-
Other current assets	**2,545**	(43,214)	(16,396)	**(59,584)**
Accounts payable and accrued expenses	**232,384**	2,012,642	(3,049,564)	**2,557,921**
Net cash used in operating activities	**(21,379,790)**	(25,068,832)	(5,214,427)	**(61,818,090)**

	Year ended December 31, 2012	Year ended December 31, 2011	Year ended December 31, 2010	Period from October 7, 2005 (Inception) to December 31, 2012
Cash flows from investing activities:				
Purchase of office and computer equipment	**(3,241)**	(11,964)	-	**(42,464)**
	(3,241)	(11,964)		**(42,464)**
Cash flows from financing activities:				
Net proceeds from initial public offering and other offerings	**4,166,494**	49,988,823	15,184,344	**69,339,661**
Proceeds from private placement	-	-	-	**1,146,024**
Proceeds from exercise of warrants and options	**730,322**	288,732	-	**1.019,054**
Proceeds from 2010 Senior convertible notes	-	-	3,425,000	**3,425,000**
Proceeds from notes payable to Paramount Credit Partners, LLC	-	-	-	**1,573,000**
Repayment of Paramount Credit Partners, LLC Note	-	(1,573,000)	-	**(1,573,000)**
Proceeds from notes payable to related parties	-	-	950,562	**5,041,953**
Repayment of notes payable - related party	-	-	-	**(1,500,000)**
Proceeds from 2007 Senior convertible notes	-	-	-	**5,305,000**
Payment for deferred financing costs	-	-	(755,092)	**(1,431,603)**
Proceeds from utilization of short-term note and line of credit	-	-	99,380	**419,380**
Repayment of debt facilities	-	(419,380)	-	**(419,380)**
Proceeds from term note payable	-	-	800,000	**800,000**
Repayment of term note payable	-	(800,000)	-	**(800,000)**
Proceeds from receipt of subscriptions	-	-	-	**4,684**
Net cash provided by financing activities	**4,896,816**	47,485,175	19,704,194	**82,349,773**
Net (decrease) increase in cash and cash equivalents	**(16,486,215)**	22,404,379	14,489,767	**20,489,219**
Beginning of period	**36,975,434**	14,571,055	81,288	-
End of period	**$ 20,489,219**	**$ 36,975,434**	$ 14,571,055	**$ 20,489,219**

	Year ended December 31, 2012	Year ended December 31, 2011	Year ended December 31, 2010	Period from October 7, 2005 (Inception) to December 31, 2012
Supplemental schedule of non-cash financing activities:				
Warrants issued to placement agent	-	-	-	**$ 341,334**
Warrants issued to investors in connection with convertible notes	-	-	$ 1,166,989	**$ 1,166,989**
Debt discount on Paramount Credit Partners, LLC notes	-	$ 302,327	-	**$ 782,376**
Debt discount on 2010 senior convertible notes	-	-	-	**$ 1,468,254**
Related party notes and accrued interest converted to 2010 Senior convertible notes	-	-	$ 2,192,433	**$ 3,995,667**
Notes and accrued interest converted to common stock	-	-	$ 14,003,158	**$ 14,003,158**
Supplemental disclosure - cash paid for interest	-	$ 277,324	$ 76,899	**$ 685,397**

The accompanying notes are an integral part of these financial statements

VENTRUS BIOSCIENCES, INC.
(A Development Stage Company)

Statements of Changes in Stockholders' Equity (Deficiency)
Period from October 7, 2005 (Inception) to December 31, 2012

	Common Stock				
	Shares	Amount	Additional Paid-in Capital	Deficit Accumulated During the Development Stage	Total
Issuance of common stock to founders and employees at $0.0124 per share in March and April 2007		$ 368	$ 4,196	-	$ 4,564
Issuance of common stock to founders and employees at $0.0124 per share in May and June 2007	9,677	10	110	-	120
Issuance of common stock to licensor at $0.0124 per share in August 2007	18,401	18	210	-	228
Stock-based compensation for the period from January to December 2007	-	-	16,655	-	16,655
Warrants issued in connection with senior convertible notes in 2007	-	-	164,284	-	164,284
Net loss	-	-	-	(4,567,894)	(4,567,894)
Balance at December 31, 2007	396,090	396	185,455	(4,567,894)	(4,382,043)
Warrants issued in connection with senior convertible notes in January, February and March 2008	-	-	177,050	-	177,050
Common stock issued in financing at $60.39 per share in June and September 2008 net of related costs	18,977	19	929,438	-	929,457
Conversion of related party notes and interest payable at $60.39 per share in June 2008	29,861	30	1,803,204	-	1,803,234
Warrants issued in connection with related party note conversion in June 2008	-	-	340,860	-	340,860
Stock-based compensation for the period from January to December 2008	-	-	460,822	-	460,822
Net loss	-	-	-	(8,786,430)	(8,786,430)
Balance at December 31, 2008	444,928	445	3,896,829	(13,354,324)	(9,457,050)
Stock-based compensation for the period from January to December 2009	-	-	123,758	-	123,758
Warrants issued in connection with Paramount Credit Partner LLC notes in January, March and June 2009	-	-	480,049	-	480,049

	Common Stock				
	Shares	Amount	Additional Paid-in Capital	Deficit Accumulated During the Development Stage	Total
Common Stock issued to licensor in December 2009 at $12.40 per share	2,016	2	24,998	-	25,000
Common Stock issued to vendor in December 2009 at $12.40 per share	403	-	5,000	-	5,000
Net loss	-	-	-	(4,539,405)	(4,539,405)
Balance at December 31, 2009	447,347	447	4,530,634	(17,893,729)	(13,362,648)
Warrant issued to licensor in connection with amendment to the agreement in August 2010	-	-	161,552	-	161,552
Stock-based compensation for the period from January to December 2010	-	-	2,194,535	-	2,194,535
Conversion of notes and accrued interest to common stock in December 2010 at $4.20 per share	3,334,085	3,334	13,999,824	-	14,003,158
Beneficial conversion charge recorded on notes and interest converted to common stock in December 2010	-	-	6,001,496	-	6,001,496
Common stock issued in IPO in December 2010 at $6.00 per share net of related costs	2,900,000	2,900	15,181,444	-	15,184,344
Fair value of warrants issued with Senior convertible notes in December 2010	-	-	2,344,708	-	2,344,708
Common Stock issued to Licensor for amendment in December 2010 at $6.00 per share	64,933	65	389,532	-	389,597
Net loss	-	-	-	(15,290,625)	(15,290,625)
Balance at December 31, 2010	6,746,365	6,746	44,803,724	(33,184,354)	11,626,116
Common Stock issued in January 2011 at $6.00 per share to fulfill over-allotment option from IPO, net of related costs	435,000	435	2,420,341		2,420,776
Warrants exercised	50,034	50	288,682		288,732
Additional shares issued in January 2011 in connection with the December 22, 2010 conversion of notes into common stock at $4.20 per share	7				
Shares issued in a stock offering in July 2011, at $10.00 per share net of related costs	5,175,000	175	47,562,872		47,568,047
Stock- based compensation for the period from January 1 to December 31, 2011 to employees and directors			2,982,949		2,982,949

	Common Stock				
	Shares	**Amount**	**Additional Paid-in Capital**	**Deficit Accumulated During the Development Stage**	**Total**
Stock-based payments for the period from January 1 to December 31, 2011 for options issued to consultants			3,990,817		3,990,817
Net loss				(34,344,730)	(34,344,730)
Balance at December 31, 2011	12,406,406	$ 12,406	$ 102,049,385	$ (67,529,084)	$ 34,532,707
Common Stock-issued for options exercised between January and December 2012	68,240	68	427,749	-	427,817
Stock based compensation for the period from January to December 2012 to employees and directors	-	-	2,831,651	-	2,831,651
Stock-based payments for the period from January 1 to December 31, 2012 for options issued to consultants.	-	-	339,442	-	339,442
Proceeds from common stock sold (at an average $12.45 per share), net of costs	354,700	355	4,166,139	-	4,166,494
Shares issued in cashless exercise of warrants	11,620	11	(11)	-	
Warrants exercised from January 1, 2012 and December 31, 2012	45,834	46	302,459	-	302,505
Shares issued in a cashless exercise of options	47,550	48	(48)	-	
Net loss				(24,790,430)	(24,790,430)
Balance at December 31, 2012	**12,934,350**	**$ 12,934**	**$ 110,116,766**	**$ (92,319,514)**	**$ 17,810,186**

The accompanying notes are an integral part of these financial statements

VENTRUS BIOSCIENCES, INC.
(A Development Stage Company)

Notes to Financial Statements

Note 1 - Organization, Business and Basis of Presentation:

Organization and business:

Ventrus BioSciences Inc. ("Ventrus" or the "Company") is a development-stage specialty pharmaceutical company focused on the late-stage development and commercialization of gastrointestinal products. Ventrus, formerly known as South Island BioSciences, Inc., was incorporated in the State of Delaware on October 7, 2005 and commenced operations in April 2007.

Basis of presentation:

The accompanying audited financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America.

The Company's primary activities since incorporation have been organizational activities, including recruiting personnel, acquiring licenses for its pharmaceutical compound pipeline, performing business and financial planning, conducting clinical and nonclinical trials, performing research and development, and raising funds through the issuance of debt and common stock.

The Company is in the development stage and has funded its operations primarily through the issuance of equity and debt. The Company expects to continue to expend substantial amounts for continued product research, development, and commercialization activities for the foreseeable future. Management believes the Company's funds are sufficient to continue operations through the U.S. Food and Drug Administration ("FDA") approval and initial launch and commercialization of diltiazem. Assuming such approval and launch, thereafter, continuation of the Company will be dependent on its ability to achieve profitable operations or obtain additional financing. There is no assurance, however, that such financing will be available or that the Company's efforts ultimately will be successful.

Capital resources:

The Company has not derived any revenue from product sales to date as our products have not been approved for sale by the FDA or any foreign regulatory agency. Since inception, the Company's operations have been financed primarily through the sale of equity securities, the proceeds from the exercise of warrants and stock options and issuance of debt. The Company has incurred losses from operations and negative cash flows since the inception and expects to continue to incur substantial losses for the next two years as it continues product development, and thereafter if its product diltiazem is not approved by the FDA and successfully launched. In July 2011, the Company raised net proceeds of approximately $47,600,000 in a secondary offering of its equity securities. In May and June 2012, the Company raised approximately $4,166,000 in an at-the-market common equity sales program. In February 2013, the Company raised approximately $20,700,000 in net proceeds in a public offering of its common stock and Series A non-voting convertible preferred stock. Management believes the Company currently has sufficient funds to meet its operating requirements and scheduled regulatory and development activities through FDA approval and initial launch and commercialization of diltiazem. Assuming such approval and launch, thereafter, if the Company cannot generate significant cash from its operations, it intends to obtain any additional funding it requires through strategic relationships, public or private equity or debt financings, or other arrangements and it cannot assure such funding will be available on reasonable terms, or at all.

Note 2 - Summary of Significant Accounting Policies:

Cash and cash equivalents:

All highly liquid investments with maturities of three months or less at the time of purchase are considered to be cash equivalents. All of the Company's cash equivalents have liquid markets and high credit ratings. The Company maintains its cash in bank deposit and other accounts, the balances of which, at times and at December 31, 2012, exceed federally insured limits.

Use of estimates:

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America 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 reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates.

Significant estimates inherent in the preparation of the accompanying financial statements include the fair value of stock options and warrants granted to employees, consultants, directors, investors, licensors, placement agents and underwriters.

Additionally, the Company provides a valuation allowance for deferred income tax assets when it is considered more likely than not that all or a portion of such deferred income tax assets will not be realized.

Computer equipment:

Computer equipment is stated at cost and depreciated using the straight-line method over the estimated useful life of the related assets of three years.

Stock-based compensation:

The Company's share-based compensation cost is measured at grant date, using the Black-Scholes option pricing model to estimate the fair value of the award, and is recognized as expense over the employee's or director's requisite service period on a straight-line basis. The Company accounts for stock options and warrants granted to non-employees on a fair value basis which is estimated using the Black-Scholes option pricing model. The initial non-cash charge to operations for non-employee options and warrants with vesting are revalued at the end of each reporting period until vested and recognized as consulting expense over the related vesting period.

Warrants issued with convertible notes:

For the purpose of valuing the warrants issued with convertible notes (See Notes 3 and 8), the Company used the Black-Scholes option pricing model utilizing the assumptions noted in those Notes. To determine the risk-free interest rate, the Company utilized the U.S. Treasury yield curve in effect at the time of grant with a term consistent with the expected term of the Company's awards. The Company estimated the expected life of the warrants is based on the full term of the warrant. The expected dividend yield reflects the Company's current and expected future policy for dividends on its common stock. The expected stock price volatility for the Company's stock was calculated by examining historical volatilities for publicly traded industry peers as the Company did not have any trading history for its common stock at the time the grants were issued.

Warrants, or any other detachable instruments issued in connection with debt financing agreement not required to be recorded at fair value, are accounted for using the relative fair value method and allocated to additional paid-in capital and recorded as a reduction in the carrying value of the related debt. This discount is amortized to interest expense from the issuance date through the maturity date of the debt using the effective interest method.

Beneficial conversion feature:

When the conversion feature of conventional convertible debt provides for a rate of conversion that is below market value, this feature is characterized as a beneficial conversion feature ("BCF"). Prior to the determination of the BCF, the proceeds from the debt instrument are first allocated between the convertible debt and any detachable free standing instruments that are included, such as common stock warrants. The Company has disclosed the contingent nature of its BCFs (See Notes 3 and 8) and has recorded their effects.

Research and development:

Research and development expenses include personnel and facility-related expenses, third party contracted services including clinical trial costs, manufacturing and process development costs, research costs and other consulting services. Research and development costs are expensed as incurred. In instances where the Company enters into agreements with third parties for clinical trials, manufacturing and process development, research and other consulting activities, costs are expensed as services are performed. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables.

The Company's accruals for clinical trials are based on estimates of the services received and pursuant to contracts with the respective clinical trial centers and clinical research organizations. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients, and the completion of portions of the clinical trial or similar conditions. The objective of the Company's accrual policy is to match the recording of expenses in its financial statements to the actual services received. As such, expense accruals related to clinical trials are recognized based on the estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract.

Income taxes:

The Company's income tax expense consists of current and deferred income tax expense or benefit. Current income tax expense or benefit is the amount of income taxes expected to be payable or refundable for the current year. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to temporary differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established when it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company has adopted the provisions that tax positions must meet a "more-likely-than-not" recognition threshold to be recognized. The Company has no unrecognized tax benefits recorded for the years ended December 31, 2012 and 2011. When an accrual for interest and penalties is required, interest and penalties will be recognized in tax expense. The Company files income tax returns in the U.S. federal jurisdiction and in New York. There are currently no federal income tax examinations in process. The 2009 through 2012 tax years remain subject to examination by the Internal Revenue Service and other taxing authorities for U.S. federal and state/local tax purposes. The Company does, however, have prior year net operating losses dating back to 2007, which are subject to examination.

Loss per common share:

Basic net loss per common share excludes dilution and is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per common share reflects the potential dilution that could occur if securities or other contracts to issue common stock were exercised or converted into common stock or resulted in the issuance of common stock that then shared in the earnings of the entity unless inclusion of such shares would be anti-dilutive. Since the Company has only incurred losses, basic and diluted net loss per share is the same. The number of potentially dilutive securities (options, warrants and convertible instruments) excluded from the diluted loss per share calculation at December 31, 2012, 2011 and 2010 was 2,755,142, 3,002,898 and 2,093,064, respectively.

Note 3 - Related Party Transactions:

The following are descriptions of the Company's related party transactions that have been entered into, modified, terminated, or were still in effect in 2012.

Paramount BioSciences, LLC and Affiliates:

*Paramount Corporate Development, LLC***:**

From April 2007 through August 31, 2008, the Company had a contractual arrangement with Paramount Corporate Development, LLC ("Paramount"), an affiliate of Dr. Lindsay A. Rosenwald, M.D., formerly a significant investor in and stockholder of the Company. During this period, the Company incurred $425,000 under this arrangement. As of December 31, 2012 and 2011, the Company had $100,000 outstanding under this arrangement, which is included in accounts payable.

Notes payable to Paramount Credit Partners, LLC:

During 2009, the Company issued four separate 10% promissory notes (collectively, the "PCP Notes") to Paramount Credit Partners, LLC ("PCP"), an entity whose managing member is Dr. Rosenwald. The PCP Notes consisted of notes in the aggregate principal amount of $1,573,000. The Company repaid the notes in full in July 2011, and the remaining debt discount was fully charged to interest expense.

As part of the note financing, PCP received five-year warrants ("PCP Warrants") to purchase 104,867 shares of common stock at an exercise price of $6.60. The Company allocated proceeds of $480,049 from the sale of the PCP Notes to the warrants at the time of issuance, which was recorded as a debt discount and amortized to interest expense over the term of the PCP Notes.

On December 22, 2010, in connection with the completion of the IPO and pursuant to the terms of the warrants held by the purchasers of the convertible notes issued in 2010 (the "2010 Notes"), the above related party holders of 2010 Notes were issued 182,703 warrants with a per share exercise price of $6.60. Each of these warrants will expire on February 26, 2015. The Company valued these warrants at $915,118 using the Black-Scholes option pricing model, and the Company expensed the entire amount as interest expense in 2010.

Line of Credit:

On December 3, 2008, the Company, Parmount Biosciences ("PBS") and various other private pharmaceutical companies in which Dr. Rosenwald is a significant investor and stockholder, entered into a loan agreement with Bank of America, N.A. for a line of credit of $2,000,000. As of December 31, 2009, the amount borrowed by the Company under the Bank of America, N.A. line of credit was $320,000. In November 2010, the Company paid off the Bank of America, N.A. line of credit with proceeds from a promissory note issued to Israel Discount Bank of New York ("Israel Discount Bank").

On September 23, 2010, the Company borrowed $800,000 and on November 5, 2010 borrowed an additional $420,000 from Israel Discount Bank. The loans were personally guaranteed by Dr. Rosenwald. In consideration for the guarantees, the Company entered into a letter agreement with Dr. Rosenwald whereby Dr. Rosenwald has the right to attend meetings of the Company's board of directors and to appoint two directors to the board. Dr. Rosenwald ceased attending board meetings in May 2011 and never exercised his right to appoint these directors and this agreement was terminated in February 2012.

The Company repaid the Israel Discount Bank promissory notes in full in January 2011.

Placement Agent:

In connection with the offering of the 2010 Notes and related warrants, National Securities Corporation ("National") and the Company entered into a placement agency agreement, pursuant to which the Company paid National cash fees of $671,592. In addition, the Company issued National warrants to purchase an aggregate of 89,000 shares of common stock, with an exercise price of $7.50. In addition, the Company paid National's outside counsel $32,500 for its services as placement agent counsel. Dr. Lindsay A. Rosenwald beneficially owns, indirectly, a controlling interest in the parent holding company of National.

In connection with the Company's IPO, National, Rodman & Renshaw ("Rodman") and the Company entered into an underwriting agreement, pursuant to which the Company paid National and Rodman cash fees of $1,662,400. In addition, the Company issued to each of National and Rodman warrants to purchase an aggregate of 98,600 shares of common stock with an exercise price of $7.50.

Note 4 - Income Taxes:

There was no current or deferred income tax provision for the years ended December 31, 2012, 2011 and 2010.

The Company's deferred tax assets as of December 31 consist of the following:

	2012	2011
Net operating loss	$ 23,792,000	$ 15,372,000
Stock-based compensation	5,808,000	4,396,000
In-Process Research & Development	5,014,000	5,520,000
Research and development credits	783,000	977,000
Totals	35,397,000	26,265,000
Less: valuation allowance	(35,397,000)	(26,265,000)
	$ -	$ -

A valuation allowance is provided when it is more likely than not that some portion or all of the deferred tax assets will not be realized. The net increase in the total valuation allowance for the years ended December 31, 2012 and 2011 was $9,132,000 and $16,473,000, respectively. The tax benefit assumed the Federal statutory tax rate of 34% and a state and local tax rate of 11% and has been fully offset by the aforementioned valuation allowance.

At December 31, 2012, the Company had potentially utilizable gross Federal net operating loss carry-forwards of approximately $55,00,000, State net operating loss carry-forwards of approximately $48,000,000 and research and development credit carry forward of approximately $783,000, all of which expire between 2027 and 2031.

An ownership change under Internal Revenue Code ("IRC") Section 382 is likely to have occurred due to common stock issued in the IPO and debt conversions in December 2010. Due to the change in ownership provisions of the IRC, the availability of the Company's net operating loss carry forwards may be subject to annual limitations against taxable income in future periods, which could substantially limit the eventual utilization of such carry forwards. The Company has not analyzed the historical or potential impact of its equity financings on beneficial ownership and therefore no determination has been made whether the net operating loss carry forward is subject to any IRC Section 382 limitation. To the extent there is a limitation, there would be a reduction in the deferred tax asset with an offsetting reduction in the valuation allowance.

	2012	2011
Statutory Federal tax rate	(34)%	(34)%
Statutory state and local income taxes (net of Federal)	(7)%	(7)%
Effect of valuation allowance	41%	41%
Effective tax rate	0%	0%

Note 5 - Commitments:

Employment agreements:

The Company's Chief Executive Officer has an employment agreement which provides for a base salary of $375,000 per year, a guaranteed bonus of $75,000 per year and an annual performance-based bonus of up to 50% of his base salary. The agreement also provides incentive bonuses of $250,000 and $500,000 in the event that the Company's market capitalization exceeds specified levels. The first threshold was met and the $250,000 bonus was paid in the third quarter of 2011. The second threshold has not yet occurred.

The Chief Financial Officer has an employment agreement which provides for a base salary of $250,000 per year. The agreement also provides incentive bonuses of $250,000 and $500,000 in the event that the Company's market capitalization exceeds specified levels. The first threshold was met and the $250,000 bonus was paid in the third quarter of 2011. The second threshold has not yet occurred.

On August 24, 2011, the above agreements were amended to provide that if the second market capitalization threshold is attained, the bonus of $500,000 will be paid in a combination of shares of the Company's common stock worth $300,000 and $200,000 in cash. The number of the shares of common stock each would receive was determined by the closing price of the Company's common stock as reported on NASDAQ on August 24, 2011 ($9.85), which could result in 30,457 shares being issued to each of Chief Executive Officer and Chief Financial Officer if the second market capitalization threshold is attained. As of December 31, 2012, the second market capitalization threshold has not been attained. In addition, the amendment to the Chief Financial Officer's agreement provides that he will be eligible for an incentive cash bonus in the discretion of the Company's Compensation Committee of up to 25% of his base salary.

Note 6 - Stockholders' Transactions:

Common Stock Transactions:

During March and April 2007, the Company issued 368,012 shares of common stock to its founders for $4,564, or $0.0124 per share.

During May and June 2007, the Company issued 9,677 shares of common stock to its employees for $120, or $0.0124 per share. During August 2007, the Company issued 18,401 shares of common stock at $0.0124 per share in accordance with the license agreement between the Company and S.L.A. Pharma (see note 7). During 2007, the Company recorded $228 of stock-based research and development expense in connection with this license.

During June through September 2008, the Company issued 18,977 shares of common stock and 3,796 warrants at $60.39 per unit (consisting of a share of common stock with 20% warrant coverage) in connection with a private placement financing at $60.39 per unit. Each warrant has a seven-year term and an exercise price of $66.46. The Company raised $929,457 of net proceeds.

During July 2008, the Company issued 29,861 shares of common stock and 6,151 warrants at $60.39 per unit (consisting of a share of common stock with 20% warrant coverage) to related parties in connection with the conversion of amounts outstanding under certain promissory notes (see Note 3). Each warrant has a seven-year term and an exercise price of $66.46. The warrants had a fair value of $340,860 and were expensed on issuance since the promissory notes were converted.

The fair value of the warrants granted, mentioned in the preceding paragraph, was based on the following assumptions:

Risk-free interest rate	3.89%
Expected volatility	128.18%
Expected life of warrants	5 years
Expected dividend yield	0%

During December 2009, the Company issued 2,016 shares of common stock to S.L.A. Pharma pursuant to an amendment to the license agreement between the Company and S.L.A. Pharma, and 403 shares of common stock to a vendor, each at a value of $12.40 per share, recording an expense of $25,000 and $5,000 to research and development expense, respectively.

In connection with the Company's IPO, all of the issued and outstanding convertible notes issued in 2007 and 2010 converted into shares of common stock pursuant to the terms of those notes. All principal and accrued interest on the 2007 and 2010 convertible notes converted at per share price of $4.20, which was 70% of the public offering price of $6.00 per share in the IPO, resulting in an aggregate of 1,642,802 shares of common stock issued upon conversion of the 2007 convertible notes and an aggregate of 1,421,834 shares of common stock issued upon conversion of the 2010 convertible notes. Also in connection with the IPO, and pursuant to their terms, the promissory notes issued to PBS and Capretti Grandi LLC, were converted at a per share price of $4.20, which was 70% of the public offering price of $6.00 per share in the IPO, resulting in an aggregate of 269,449 shares of common stock issued upon conversion of these notes.

On December 22, 2010, the Company issued 2,900,000 shares of its common stock in an IPO at $6.00 per share and received net proceeds of $15,184,344, after deduction of underwriting discounts, commissions and other expenses related to the IPO.

Pursuant to the terms of the license agreement between the Company and S.L.A Pharma, the Company was obligated to issue to S.L.A. Pharma that number of additional shares of common stock so that, when added to the 18,401 shares initially issued, the new and old shares had an estimated fair market value equal to $500,000 (based on the price per share paid in the financing). The closing of the Company's IPO triggered this obligation. As a result, the Company issued 64,933 shares of its common stock to S.L.A. Pharma on December 22, 2010. The Company valued the stock issuance to S.L.A. Parma at $389,597 and expensed the full amount to research and development expense as of December 31, 2010.

On January 7, 2011, the Company issued 435,000 shares of its common stock to fulfill the over-allotment option that it granted to the underwriters as part of the IPO and raised net proceeds of $2,420,776.

During the twelve months ended December 31, 2011, the Company issued an aggregate of 50,034 shares of common stock pursuant to the exercise of warrants with an average exercise price of $5.77.

On July 19, 2011, the Company issued 5,175,000 shares of its common stock in an underwritten public offering and raised net proceeds of $47,568,047.

The Company filed a shelf registration statement with the Securities and Exchange Commission, which became effective on February 10, 2012, under which it may offer shares of its common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of $100,000,000. As part of the shelf registration statement, the Company included a prospectus for a possible at-the-market common equity sales program for the sale of up to $20,000,000 of common stock. In May and June 2012, the Company sold an aggregate of 354,700 shares under this program, resulting in net proceeds of approximately $4,166,000, or $11.7452 per share. As of December 31, 2012, an aggregate of approximately $95,500,000 worth of securities is available under the shelf registration statement out of which approximately $15,500,000 of common stock is available for the at-the-market common equity sales program.

See Note 9 for transactions subsequent to December 31, 2012.

Common Stock Options and Warrants:

Stock Options:

In 2007, the Company established a stock incentive plan (the "2007 Plan") under which incentive stock and/or options could be granted to officers, directors, consultants and key employees of the Company for the purchase of up to 483,871 shares of the Company's common stock. The options could have a maximum term of ten years, vest over a period to be determined by the Company's Board of Directors and have an exercise price at or above fair market value on the date of grant.

There were no options issued under the 2007 Plan in 2008 or 2009.

On May 11, 2010, the Company granted options to purchase 2,016 shares of its common stock to a director under the 2007 Plan with an exercise price of $6.00. The Company valued these options at $9,714 and expensed the full amount on the grant date since the options were fully vested.

The Company terminated the 2007 Plan in July 2010, but the 2,016 options granted under the 2007 Plan remain outstanding.

In August 2010, the Company's stockholders approved the 2010 Equity Incentive Plan (the "2010 Plan"). In May 2011, the Company's stockholders approved an amendment to the 2010 Plan to increase the shares reserved for issuance from 2,467,200 to 3,967,200 shares of the Company's common stock. The 2010 Plan authorizes the Company to issue equity incentive awards in the form of shares, options or other awards based on Ventrus common stock as part of an overall compensation package to provide performance-based compensation to attract and retain qualified personnel.

In November 2010, the Company granted options to non-employee directors to purchase an aggregate of 160,000 shares under the 2010 Plan. In addition, under Dr. Ellison's and Mr. Barrett's respective employment agreements, in connection with the closing of the Company's IPO, the Company granted to Dr. Ellison and Mr. Barrett options under the 2010 plan to purchase shares of the Company's common stock with an exercise price of $6.00, which was equal to the initial public offering price per share, in an amount equal to 7.5% (573,599 shares) and 4.0% (305,920 shares), respectively, of the Company's fully diluted capitalization on that date.

In 2011, the Company granted options to purchase 30,000 shares to three of its directors, options to purchase an aggregate of 552,440 shares to four employees and options to purchase an aggregate of 384,240 shares to seven consultants, all pursuant to the 2010 Plan with exercise prices at or greater than the then market value of the Company's common stock ($6.00 - $15.77 per share).

In 2012, the Company granted options to purchase 35,000 shares to a new director and 228,000 options to purchase shares to eight employees which included three new employees. Additionally, the company granted options to purchase an aggregate of 162,740 shares to seven consultants all pursuant to the 2010 Plan. The exercise prices of the options granted were at the then market value of the Company's common stock ($3.60 - $10.62 per share).

A summary of the Company's option activity under its option plans and related information is as follows:

	Year Ended December 31, 2012			Year Ended December 31, 2011		
	Shares	Weighted Average Exercise Price	Aggregate Intrinsic Value	Shares	Weighted Average Exercise Price	Aggregate Intrinsic Value
Outstanding at beginning of period	2,046,455	$ 6.40	$ -	1,079,775	$ 6.01	$ -
Granted	425,740	$ 7.64	$ -	966,680	$ 6.82	$ -
Exercised	(168,240)	$ 6.11				
Forfeited	(425,480)	$ 6.64	$ -			
Outstanding at end of year	1,878,475	$ 6.72	$ -	2,046,455	$ 6.40	$ 4,092,910
Options exercisable at end of period	1,618,820	$ 6.51	$ -	1,338,896	$ 6.19	$ 2,435,852
Vested or expected to vest at December 31	1,878,475	-	-	2,046,455	-	-
Shares available on December 31 for options that may be granted	1,920,485	-	-	1,922,761	-	-

Included in the options exercised were 100,000 options exercised in a cashless exercise for 47,550 shares of common stock.

The Company expects that all outstanding unvested options will vest. The fair value of the options granted for the year ended December 31, 2012 and 2011, was based on the following assumptions:

	2012	**2011**
Risk-free interest rate	1.11%-1.32%	1.43%-3.03%
Expected volatility	76.31%-78.23%	88.05%-94.74%
Expected life of options	7 years	7 years
Expected dividend yield	0%	0%

Estimated future stock-based compensation expense relating to unvested stock options (for consultants based on the fair value at December 31, 2012) is as follows:

Years Ending December 31,	Future Stock Option Compensation Expense
2013	1,052,201
2014	509,021
2015	33,542
Total estimated future stock-based compensation expense - stock options	$ 1,594,764

The weighted average remaining contractual life of options outstanding at December 31, 2012 is approximately 7.25 years.

Stock-based compensation expensed to research and development expense for the years ended December 31, 2012, 2011 and 2010 was $846,508, $1,124,904 and $446,902, respectively. Stock-based compensation expensed to general and administrative expense for the years ended December 31, 2012, 2011 and 2010 was $2,324,585, $5,848,862, and 2,298,782 respectively.

Warrants:

During 2007, the Company granted 12,903 warrants to various consultants with an exercise price of $7.69 per share. Each warrant granted during 2007 vests equally over a three-year period and has a seven-year term. During 2008, 1,613 of these warrants were forfeited due to the consultant's relationship with the Company ending prior to the vesting period. All of the warrants that remain outstanding were fully vested at December 31, 2010.

On August 30, 2010, the Company issued a warrant to purchase 13,605 shares of its common stock with an exercise price of $1.24 per share to S.L.A. Pharma (see Note 7) pursuant to an amendment to the license agreement between the Company and S.L.A. Pharma. The warrant was fully vested at issuance and the Company recognized the full amount of $161,552 of stock-based research and development expense as of December 31, 2010. The fair value of the warrants granted and the related fair value adjustments at the end of each reporting period were based on the following assumptions:

	2007	2008	2009	2010
Risk-free interest rate	4.00%	1.55%-3.61%	1.67%-2.69%	0.75%
Expected volatility	65.55%	104.78%-219.91%	128.96%-163.74%	113.31%
Expected life of warrants (in years)	7 years	7 years	7 years	3 years
Expected dividend yield	0%	0%	0%	0%

In addition to the warrants discussed above, in connection with the Company's financings in 2007, 2008, 2009 and 2010, the Company issued warrants to investors and/or placement agents to purchase shares of common stock as well as certain consulting warrants (See Notes 3 and 8).

A summary of the Company's warrant activity and related information is as follows:

	Year Ended December 31, 2012		Year Ended December 31, 2011		Year Ended December 31, 2010	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of period	956,443	$ 7.61	1,013,291	$ 7.58	168,885	$ 11.43
Granted	-	$ -	-	$ -	844,405	$ 6.76
Exercised	81,792	$ 7.00	56,848	$ 5.08	-	$ 6.76
Outstanding at end of year	874,651	$ 7.67	956,443	$ 7.61	1,013,290	$ 7.58
Warrants exercisable at end of period	874,651	$ 7.67	956,443	$ 7.61	1,013,290	$ 7.58

Included in the warrants exercised are 35,958 and 13,100 warrants exercised in a cashless exercise for 11,620 and 6,286 shares during the years ended December 31, 2012 and 2011 respectively. All outstanding warrants have vested and no additional expense is expected to be recorded in the future years.

Note 7 - License Agreements:

S.L.A. Pharma, AG

In March 2007, pursuant to an Exclusive License Agreement, S.L.A. Pharma, AG ("S.L.A. Pharma") granted PBS a royalty-bearing license to sell, make and use diltiazem for treatment, through topical administration, of anal fissures and phenylepherine for treatment, through topical administration, of fecal incontinence in the United States, Canada and Mexico. Pursuant to the Exclusive License Agreement, PBS was obligated to form a company to develop the technologies referenced in the Exclusive License Agreement and issue a number of shares equal to 5% of such company's outstanding common stock as of the effective date of the Exclusive License Agreement. On August 2, 2007, the Company issued 18,401 shares to S.L.A. Pharma to satisfy this obligation. In addition, the Company was obligated to issue to S.L.A. Pharma that number of additional shares of common stock so that the number of shares following specific transactions would have a fair market value equal to $500,000. On December 22, 2010, the Company issued S.L.A Pharma an additional 64,933 shares to satisfy this obligation.

In August 2007, pursuant to an Assignment and Assumption Agreement, PBS sold all of its rights in and arising out of the Exclusive License Agreement with S.L.A. Pharma to Ventrus for $1,087,876. The corresponding U.S. and foreign patents and applications for the two compounds have been licensed to Ventrus under the Assignment and Assumption Agreement (the technology referred to collectively as the "Compound Technology"). As consideration in part for the rights to the Compound Technology, an initial licensing fee of $250,000 was paid to S.L.A. Pharma and $50,000 for reimbursement of clinical development costs incurred by S.L.A. Pharma (these amounts were paid by PBS and were included in the consideration paid by the Company to PBS in connection with the Assignment and Assumption Agreement). In the event that the Compound Technology is commercialized, the Company is obligated to pay to S.L.A. Pharma annual royalties, based upon net sales of the product. In addition, the Company is required to make payments to S.L.A. Pharma up to an aggregate amount of $20 million upon the achievement of various milestones related to regulatory events. Should the Company make any improvements regarding the Compound Technology, the Company is required to grant S.L.A. Pharma licenses to use such improvements.

As compensation for S.L.A. Pharma's participation in the management and the development of the technologies, Ventrus is required to make separate payments to S.L.A. Pharma equal to $41,500 per month ("Monthly Payments") for each of diltiazem and phenylephrine. Per the agreement, Ventrus' obligation to make these monthly payments was to terminate upon a new drug application ("NDA") filing. Pursuant to amendments to the Exclusive License Agreement, the Company, as of September 30, 2010, was no longer required to make additional payments for phenylephrine. At December 31, 2012, the Company had no amounts due to S.L.A. Pharma.

The Company is also required to reimburse S.L.A. Pharma for clinical development costs associated with the technology development of the diltiazem project. The Company's total payment obligation for the diltiazem project is limited to $4,200,000. The Company made $4,200,000 of payments to S.L.A. Pharma from August 2007 through December 31, 2011.

On June 6, 2011, Ventrus further amended the Exclusive License Agreement with S.L.A. Pharma. The amendment eliminates its potential $800,000 milestone payment to S.L.A. Pharma for the development of diltiazem, previously payable upon the completion of enrollment into the Phase III clinical trial that S.L.A. Pharma is conducting in Europe. It also eliminates S.L.A. Pharma's ability to terminate the license agreement at any time, with one month's notice, in the event that Ventrus had failed to make a required payment and a third party wished to enter into a license agreement for diltiazem and phenylephrine, provided the termination would not have been effective if within that one-month period Ventrus paid all the then required payments under the agreement. Pursuant to the amendment, Ventrus must pay S.L.A. Pharma up to $1,000,000 in milestone payments, payable in four equal installments of $250,000 once specified thresholds of randomized patients are achieved in the Phase III trial for diltiazem that S.L.A. Pharma is conducting in Europe. The first two milestones were met and paid in the third quarter of 2011 and the third and fourth milestone was met and paid in the fourth quarter of 2011. Additionally, upon Ventrus' receipt of a quality controlled final study report of the Phase III trial for diltiazem in Europe, Ventrus must pay S.L.A. Pharma $400,000 in development costs for diltiazem. This report was received and the payment was made in February 2013.

The Company is also required to reimburse S.L.A. Pharma for clinical development costs associated with the technology development of the phenylephrine project. S.L.A. Pharma has been paid $600,000 of services for the phenylephrine project through December 31, 2011. S.L.A. Pharma did not provide Ventrus with any services for the phenylephrine project in 2011 or 2012 and management does not expect any services from SLA Pharma for the phenylephrine project in the foreseeable future.

Sam Amer and Company, Inc.

In March 2008, Ventrus entered into an exclusive worldwide license agreement with Sam Amer & Co., Inc., a California company ("Amer"), whereby Ventrus acquired certain patent rights to iferanserin for the topical treatment of any anorectal disorders. Through November 14, 2011, the Company made all contractual payments relating to the license agreement. The license agreement terminated in November 2011 upon our acquisition of all rights, title and interest to iferanserin from Amer, discussed below.

On June 5, 2011, the Company entered into an agreement with Amer to acquire all rights, title and interest to iferanserin and on November 14, 2011, closed on this transaction. The Company paid an aggregate of $12.5 million to Amer in the transaction. Because the assets purchased (1) do not meet the definition of a business combination and (2) do not have alternative future use since the assets acquired are contingent on further development and clinical risk, we determined that the entire purchase price of the asset be expensed immediately as in-process research and development.

On June 25, 2012, the Company reported that a Phase III, randomized, double-blind, placebo-controlled clinical trial of VEN 309 for the treatment of symptomatic hemorrhoids did not meet its endpoints. Based on the disappointing results of that Phase III trial and the positive results of our Phase III trial for VEN 307, reported one month earlier in May 2012, the Company has determined that its current resources would be better allocated toward the planned completion of VEN 307 development program in anal fissures. Consequently, the Company has no immediate plans to continue development of VEN 309 and has ceased all activity related to VEN 309 other than the winding down of the program.

Note 8 - Private Placements:

2007 Senior convertible notes:

During 2007 and 2008, the Company issued 8% senior convertible notes in connection with a private placement in the aggregate principal amount of $5,305,000 (the "Bridge Notes"). The Bridge Notes were originally scheduled to mature on December 20, 2008, but the Company exercised its option to extend the maturity date to December 20, 2009, at an increased interest rate of 10%. The Company subsequently obtained the consent of the note holders to an additional extension of the maturity date of the Bridge Notes to September 10, 2010 and again to December 31, 2010. The completion of the Company's IPO triggered the automatic conversion of the Bridge Notes and accrued interest into common stock at 70% conversion price of the IPO price. The Company valued the beneficial conversion feature of the 2007 Notes at $2,957,187, which was recorded as interest expense in 2010. The Company computed the conversion feature to be $2,957,187 by dividing the amount of debt and interest ($6,899,770), which is convertible into common stock by the conversion rate (70%). From this amount ($9,856,957) the amount of debt and interest ($6,899,770) was subtracted to determine the amount by which the instrument if-converted exceeds the conversion amount ($2,957,187).

In connection with the offering of the Bridge Notes, Paramount Biocapital, Inc. ("PCI") and the Company entered into a placement agency agreement dated October 9, 2007, pursuant to which the Company paid PCI and third party agents cash commissions of $243,600 and $19,250, respectively, for its services. The Company agreed to additional services by PCI during the 18-month period subsequent to March 11, 2008 which expired without any further amounts being paid. PCI is a related party to the Company since it is wholly-owned by Dr. Rosenwald.

In addition, PCI and third party agents received seven-year warrants (the "Placement Warrants"). The amount of shares and the exercise price were to be determined based on whether a qualified financing occurred on or before December 21, 2009. The qualified financing did not occur by such date and as a result the number of shares subject to the Placement Warrants is 42,782 shares, an amount equal to 10% of the principal amount of the Bridge Notes purchased, divided by $12.40, with an exercise price equal to $12.40. PCI subsequently transferred the Placement Warrants among its employees. The Company estimated the value of the Placement Warrants using the Black-Scholes option pricing model at approximately $341,000 and recorded them as deferred financing costs, which were amortized to interest expense over the term of the Bridge Notes. The fair value of the Placement Warrants granted was based on the following assumptions:

Risk-free interest rate	3.01% - 3.84%
Expected volatility	63.69% - 123.73%
Expected life of warrants	7 years
Expected dividend yield	0%

2010 Senior convertible notes:

In February, March, April and May 2010, the Company issued 8% senior convertible notes in connection with a private placement in the aggregate principal amount of $3,425,000 (the "2010 Notes"). The 2010 Notes matured on September 10, 2010. Upon the closing of a Qualified Financing (as defined below), the 2010 Notes plus any accrued but unpaid interest thereon were to convert into shares of the Company's common stock at 70% of the price at which shares of common stock are sold in the Qualified Financing (the "IPO Price"). The completion of the Company's IPO triggered the automatic conversion of the 2010 Notes. Upon conversion, the 2010 Notes were automatically cancelled.

The Company valued the beneficial conversion feature of the 2010 Notes at $1,619,687, which was recorded as interest expense after the Qualified Financing was completed. The Company computed the conversion feature to be $1,619,687 by dividing the amount of debt and interest ($3,779,269), which is convertible into common stock by the conversion rate (70%). From this amount ($5,398,956) the amount of debt and interest ($3,779,269) was subtracted to determine the amount by which the instrument if-converted exceeds the conversion amount ($1,619,687).

Each 2010 Noteholder holds a warrant to purchase that number of shares of the Company's common stock equal to 50% of the principal amount of the 2010 Notes purchased by it divided by the IPO Price at a per share exercise price equal to 110% of the IPO Price, subject to adjustment. Each of these warrants will expire and no longer be exercisable after February 26, 2015. In connection with the Company's IPO, the number of shares of common stock issuable pursuant to these warrants is an aggregate of 285,417 shares with an exercise price of $6.60 per share. The Company valued these warrants at $1,429,590 using the Black-Scholes option pricing model and has expensed such amount as of December 31, 2010. The fair value of the warrants granted was based on the following assumptions:

Risk-free interest rate	2.02%
Expected volatility	124%
Expected life of warrants	5 years
Expected dividend yield	0%

On February 26, 2010, a 2010 Note in the aggregate principal amount of $2,192,433 and related warrant were issued to PBS for the cancellation of certain debt (as discussed in Note 3 above), which is not included in the $3,425,000 of aggregate principal amount of 2010 Notes issued in the private placement. Including such converted debt, the total aggregate principal amount of 2010 Notes was $5,617,433. In connection with the Company's IPO, these 2010 Notes converted into an aggregate of 1,421,834 shares of common stock. Upon conversion, these 2010 Notes were automatically cancelled.

Note 9. Selected Quarterly Financial Data (Unaudited)

	Quarters Ended			
	March 31	June 30	September 30	December 31
2012				
Net loss	$ (8,173,876)	$ (7,470,048)	$ (5,355,397)	$ (3,791,109)
Basic and diluted net loss per common share [1]	$ (0.66)	$ (0.59)	$ (0.41)	$ (0.29)
2011				
Net loss	$ (2,722,478)	$ (6,961,511)	$ (5,801,381)	$ (18,859,360)
Basic and diluted net loss per common share [1]	$ (0.38)	$ (0.97)	$ (0.50)	$ (1.52)

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amounts because of differences on the weighted-average common shares outstanding during each period principally due to the effect of the Company issuing shares of its common stock during the year.

Note 10- Subsequent Event

On February 4, 2013, the Company sold an aggregate of 5,800,000 shares of its common stock and 220,000 shares of its Series A non-voting convertible preferred stock in a public offering, resulting in net proceeds of approximately $18,710,000. The common stock was sold at a per share price of $2.50 and the Series A preferred stock was sold at a per share price of $25.00. Each shares of Series A preferred stock converts into 10 shares of common stock. On February 7, 2013, the Company sold an aggregate of 870,000 shares of it's common stock pursuant to the exercise by the underwriter of its over-allotment option, resulting in net proceeds of approximately $2,044,500. All of the shares of common stock and Series A preferred stock were sold under the shelf registration statement.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements of Ventrus Biosciences, Inc. (a development stage company) on Form S-3 (No. 333-179259) and Form S-8 (No. 333-173613) of our reports dated March 14, 2013, on our audits of the financial statements as of December 31 2012 and 2011, and for each of the years in the three-year period ended December 31, 2012 and for the period from October 7, 2005 (inception) to December 31, 2012, and the effectiveness of Ventrus Biosciences, Inc.'s internal control over financial reporting as of December 31, 2012, which reports are included in this Annual Report on Form 10-K to be filed on or about March 15, 2013. We also consent to the reference to our firm under the caption "Experts" in the Registration Statement on Form S-3.

/s/ EisnerAmper LLP

New York, New York

March 14, 2013

Exhibit 31.1

CERTIFICATION OF THE CHIEF EXECUTIVE OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Russell H. Ellison, certify that:

(1) I have reviewed this annual report on Form 10-K for the year ended December 31, 2012 of Ventrus Biosciences, 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 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 the 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 the 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 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 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.

Dated: March 18, 2013

Russell H. Ellison

Russell H. Ellison
Chief Executive Officer (Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David J. Barrett, certify that:

(1) I have reviewed this annual report on Form 10-K for the year ended December 31, 2012 of Ventrus Biosciences, 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 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 the 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 the 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 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.

Dated: March 18, 2013

/s/ David J. Barrett
David J. Barrett
Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION OF THE CHIEF EXECUTIVE OFFICER
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 Ventrus Biosciences, Inc. (the "Company") for the fiscal year ended December 31, 2012, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Russell H. Ellison, Chief Executive Officer (Principal 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) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 18, 2013

/s/ Russell H. Ellison
Russell H. Ellison
Chief Executive Officer (Principal Executive Officer)

Exhibit 32.2

CERTIFICATION OF THE CHIEF EXECUTIVE OFFICER
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 Ventrus Biosciences, Inc. (the "Company") for the fiscal year ended December 31, 2012, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, David J. Barrett, Chief Financial Officer (Principal Financial and Accounting 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) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 18, 2013

/s/ David J. Barrett
David J. Barrett
Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)