

Recent Events: Ventrus initiated the first of two Phase III pivotal trials for first ever Rx treatment for hemorrhoids--top line data due 1Q 2012; a follow-on \$51.75 million public underwriting was completed in July, led by Lazard Capital Markets and Leerink-Swann.

HIGHLIGHTS

- Ventrus is developing late stage candidates targeting three widely prevalent gastrointestinal (GI) disorders – hemorrhoids, anal fissures and fecal incontinence.

- Two of the three disorders currently do not have FDA-approved prescription treatments available, and no others are currently believed to be in clinical development.

- The company's pharmaceutical candidates address three of the top ten GI disorders and offer potential US sales of \$2 billion annually. Total worldwide sales of prescription drugs for GI disorders are over \$31 billion a year.

- An estimated 12.5 million Americans suffer from hemorrhoids, four million from anal fissures, and nine million from fecal incontinence.

- Two of Ventrus' therapeutic candidates -- an ointment for hemorrhoids and a topical cream for anal fissures -- have begun Phase III pivotal trials. The third – a gel for fecal incontinence – will begin Phase IIb trials in 2012.

- Ventrus' Phase III clinical programs are characterized as 'low risk' relative to most therapeutic drug development programs. The Phase III clinical endpoints for the hemorrhoid and anal fissure candidates have been agreed to by the US FDA and have been confirmed in Phase IIb or other clinical trials. In addition, all three candidates are topical, locally active with minimal systemic absorption.

- Ventrus has an experienced management team with a proven track record in successfully developing and commercializing pharmaceutical products. CEO Russell H. Ellison, MD, MSc formerly served as VP of Medical Affairs and Chief Medical Officer at both Roche U.S. and Sanofi-Synthelabo US; VP of Clinical Development at

Ventrus Biosciences, Inc.

(Nasdaq: VTUS)

Recent Price:	\$9.00
Shares O/S:	12.4 million
Approx. MktCap:	\$114 million
Avg Daily Vol:	83,000
Fiscal Year Ends:	Dec. 31

Published: October 2011

Fibrogen, Inc., and most recently Executive Vice President of Paramount Biosciences.

- Ventrus' IPO [December 2011-\$20.5 million] and its follow-on public offering [July 2011-\$51.75 million] will fund numerous high-value inflection points coming over the next six quarters. These include three anticipated milestones for the hemorrhoid ointment: (1) initiation of Phase III trials [Q2 2011]; (2) publication of German Phase II-B results [Q4 2011]; and (3) announcement of Phase III data [Q1 2012] plus three events for the anal fissure candidate: (1) anticipated US Patent Office action on an existing filing [Q4 2011] (2) completion of Phase III enrollment [Q1-2012]; and (3) announcement of Phase III data [Q2 2012].

VEN 309

Iferanserin for Hemorrhoids

VEN 309 (Iferanserin), Ventrus' ointment for topical treatment of hemorrhoids, is a new chemical entity that targets the 5-HT_{2A} receptor and improves the flow of blood out of the dilated veins that comprise the hemorrhoid, thereby reducing bleeding, itchiness and pain. Approximately 13 million Americans suffer from hemorrhoids every year, creating the potential for more than \$1 billion in reimbursable sales annually in the US alone.

There are no FDA-approved drug treatments for this condition. Neither of the two most commonly used products

– Preparation H which is sold over the counter and Anusol HC, a prescription pharmaceutical – have any clinical data to support claims that they relieve hemorrhoidal symptoms.

Preparation H, which was originally brought to market in the late 1930s, is sold in a variety of formulations that can include combinations of shark oil, phenylephrine and hydrocortisone. Preparation H has never been subjected to double blind clinical trials to test its effectiveness versus a placebo. Every year, approximately 22 million units of Preparation H type products are sold in the US.

Anusol HC is a formulation of prescription strength hydrocortisone. It, too, has never been subjected to clinical trials for relief of hemorrhoid symptoms. Similarly, Anusol HC also poses certain safety risks related to the potential systemic absorption of steroids. Every year, approximately four million prescriptions for Anusol type products are written in the US, the majority of which are for treatment of hemorrhoids.

The development of Ventrus' VEN 309 was made possible through discovery in the mid-1990s of the role played by serotonin and the 5-HT_{2A} receptor in the formation of hemorrhoids. This discovery identified for the first time a potential drugable target for pharmaceutical treatment of hemorrhoids. VEN 309 is a powerful and highly selective antagonist to the 5HT_{2A} receptor which blocks serotonin induced venous constriction and platelet aggregation and promotes blood flow, thereby disrupting the pathology of the disease. VEN 309 is administered topically twice daily over a two-week period using disposable applicators.

The FDA has concluded that VEN 309 is ready to begin Phase III testing.

Ventrus anticipates initiating the first of two double-blind Phase III pivotal trials mid-2011. A total of 600 patients will be enrolled at 70 sites across the country for a 28-day trial. Subjects will be randomized to either a placebo ointment groups for a 14-day treatment period or to drug for 14 days or

to drug for one week followed by placebo for one week, with 14-days of follow-up for the three groups. After the double blind phase, patients will be followed in an open label phase for one year for the treatment of recurrence. The first pivotal Phase III trial data is expected to be available in the first quarter of 2012.

The recurrent nature of hemorrhoids and the resulting possibility of repeated usage have led the FDA to view VEN 309 as a chronic use drug. Consequently, Ventrus must create a standard 1,500 patient safety database and conduct a standard, two-year, two-species carcinogenicity study. This resulting two-year critical path timeline to submission of a New Drug Application (NDA) will allow Ventrus to conduct its two pivotal trials in series, rather than in parallel, thereby reducing risk and capital requirements prior to release of the first trial's data.

Ventrus' Phase III clinical trials program for VEN 309 appears to pose little in the way of technical risk. FDA has recently proposed (and the company agreed to) a revised trial endpoint definition: Proportion of patients with cessation of bleeding by the end of Day 7 that persists for the remainder of the treatment period (through Day 14) which, in an analysis of a previous German Phase IIb multicenter randomized placebo controlled trial of 120 patients in 2003/2004, shows a very large difference between placebo and drug, $p < .0001$.

No safety concerns have been identified in any prior stages of the trials. Topical administration allows high concentrations of the active drug (liferanserin) locally, which is subsequently diluted and metabolized in the liver before reaching other parts of the body. Liferanserin does not cross the blood brain barrier except at doses significantly higher than those used in treatment.

Ventrus owns worldwide rights to the VEN 309 ointment. While the composition of matter patent expires in 2015, the company has filed for a new range of concentration patent using previously unpublished data indicating improved results from a 0.5 percent formulation. Approval would provide 20-year protection from generic introduction.

VEN 307 Diltiazem for Anal Fissures

VEN 307 Diltiazem cream is a topical treatment for relief of the extreme pain associated with anal fissures.

Anal fissures are small tears or cuts in the skin that lines the anus. Nearly four million Americans, 2 percent of the adult population, experience anal fissures. Although 90percent of people will heal naturally in two months,

the severe pain associated with this condition drives people to seek treatment.

The preferred treatment used by many gastroenterologists is a 2 percent custom compound of Diltiazem and cream that must be specially mixed for each patient in a pharmacy.

Diltiazem is a calcium channel blocker that relaxes the anal sphincter and reduces pain. Custom compounding poses several problems for physicians and patients. There are questions of product consistency; patients receive no insurance reimbursement; and compounds can only be obtained at hospital or specialty pharmacies.

VEN 307 will be an FDA-approved proprietary formulation of a custom pharmacy-compounded treatment currently prescribed by many gastroenterologists. Experience suggests that 95 percent of physicians typically convert to use of FDA-approved pharmaceuticals, thereby creating a potential US market of over \$500 million annually.

Diltiazem was originally approved as Cardizem® for angina and high blood pressure. Ventrus is seeking FDA-approval of VEN 307 as a repurposed drug under a

505B2 application process, with only two pivotal trials required.

At a pre-IND meeting with the FDA in August 2007, Ventrus achieved clarity on a primary endpoint of reduction in pain rather than healing. One Phase III trial was begun in November 2010 by S.L.A. Pharma AG, the European marketer of the product and the company that licensed exclusive North American rights to Ventrus. Data from this trial is anticipated to be available in the second quarter of 2012. An NDA for Ven 307 is expected to be filed with the US FDA in 2013.

VEN 308 PHENYLEPHRINE FOR FECAL INCONTINENCE

Ventrus has licensed the exclusive North American rights for VEN 308 Phenylephrine Gel for fecal incontinence associated with ileal pouch anal anastomosis (IPAA), an FDA orphan indication. IPAA is a surgical procedure used as part of colectomy which commonly results in fecal incontinence.

There are no FDA-approved drug treatments for this condition.

Ventrus plans to initiate Phase IIb dosing studies in 2012.

SUMMARY POINTS

- **Ventrus is developing late stage Rx candidates for three widely prevalent gastro-intestinal (GI) disorders – hemorrhoids, anal fissures and fecal incontinence**
- **There are no other FDA-approved prescription treatments for two of three of these disorders.**
- **The three candidates address a US market of over \$2 billion annually.**
- **Two of Ventrus' pharmaceutical products -- VEN 309 for hemorrhoids and VEN 307 for anal fissures -- have begun Phase III pivotal trials.**
- **The third – VEN 308 Phenylephrine Gel for fecal incontinence – will begin Phase IIb trials in 2012.**
- **The company's Phase III clinical trial programs presents low technical risk.**
- **Ventrus has an experienced management team with a proven track record in successfully developing and commercializing pharmaceutical products.**
- **Ventrus' has raised a total of \$71.75 million through two public financings, to fund numerous high-value inflection points coming over the next six quarters.**
- **Three key milestones in the development of Ventrus' hemorrhoid candidate are scheduled over the next six quarters, with two occurring in the first half of 2011.**

For additional information, contact:

**Redington, Inc. • CT 203 222-7399 • NY 212 926-1733 • www.redingtoninc.com
Ventrus Biosciences, Inc. • 212 554-4267 • www.ventrusbio.com**