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VTUS RESEARCH REPORT:

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COMPANY OVERVIEW:

Ventrus BioSciences Inc. (VTUS) is a development-stage specialty pharmaceutical company currently focused on the development of gastrointestinal products, including infections of the gastrointestinal system. Out of the four product candidates the company has in-licensed, VTUS is actively developing only two of them right now. These candidates include VEN 307, a diltiazem cream for the relief of pain associated with anal fissures, and VEN 310 for use as a colonic delivery mechanism, which is a pH sensitive system to deliver bacteria, complex proteins, viral antigens, small molecules and other treatments to the gastrointestinal tract. In addition, VTUS intends to in-license or acquire other development stage and pre-clinical compounds and biologics.

In June 2012, the company ceased all activity related to one of their other product candidates, VEN 309, after its phase III clinical trial for patients with hemorrhoidal disease did not meet its endpoints. Additionally, VTUS has also said that at this time it is not actively pursuing the development of its fourth product candidate, VEN 308, a phenylephrine gel for the treatment of fecal incontinence associated with ileal pouch anal anastomosis (IPAA).

MARKET AND COMPETITION:

Gastrointestinal or gastroenterology is the branch of medicine related to the gastrointestinal tract (see: stomach and intestines) and the accessory organs of digestion from the mouth to the anus. Overall, the market for gastrointestinal products is fairly large with considerable progress having been made over the years in several areas such as gastroesophageal reflux, peptic ulcer disease and inflammatory bowel disease (IBD). However, many major gastrointestinal disorders offer few medical treatment options while some still lack treatments altogether. It is here that VTUS believes it can make some strides.

Although not a huge market, it is estimated there are approximately 1.1 million office visits per year for anal fissures in the United States[1], while the British Medical Journal *Best Practice* estimates that the incidence of anal fissures in adults is around 1 in 350.[2] Despite these figures, there is currently only one drug that has received US Food and Drug Administration (FDA) approval for the treatment of pain associated with anal fissures and that is Rectiv, which is a prescription nitroglycerin ointment. Although Rectiv is effective in reducing pain, an oft-cited side effect is moderate to severe headaches stemming from the drug's active ingredient – nitroglycerin.

Meanwhile, through the company's in-license with Therabiome, LLC, VTUS is developing VEN 310, which is a pH sensitive system used to deliver bacteria, complex proteins, viral antigens and small molecules to the gastrointestinal tract. The development of this intellectual property will be used in gastrointestinal dysbiosis, including C. difficile associated diarrhea (CDAD), irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) among others; auto-immune disorders and autism, including those controlled by bacteria or viruses; and orally delivered vaccines, including viral and bacterial. Ventrus believes that it can capture a portion of this bacterial therapy market designed to treat some of these

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illnesses such as CDAD and IBD. For example, any potential treatment options, including some oral vaccines, may require an effective delivery mechanism targeted to the colon or terminal ileum.

Lastly, while the company is currently not actively pursuing the development of VEN 308 (phenylephrine gel) for the treatment of fecal incontinence associated with ileal pouch anal anastomosis (IPAA) – a surgical treatment for patients with ulcerative colitis – this also represents a very small market size. Although it is estimated that about 2.2% of US adults suffer from fecal incontinence, only about 50,000 to 100,000 people suffer from IPAA-related fecal incontinence in the US.[3] As a result, VTUS has been granted orphan drug status by the FDA for the treatment of this affliction. Further, there are currently no FDA-approved drugs on the market with most physicians recommending diet modification, sitz baths, over-the-counter (OTC) antidiarrheal medication, and sometimes surgery.

RE-ALLOCATION OF RESOURCES AND PAST FAILURES:

The company's decision to not actively pursue the development of VEN 308 can be viewed as both a positive and a negative. On the one hand, it might make sense to continue development of a drug that has received orphan status. However, on the other hand, the expenses involved in performing trials and additional research and development (R&D) might be better spent on other drug candidates such as VEN 307 and VEN 310.

As such, VTUS has stated that assuming sufficient resources in the future, they expect to conduct a phase IIb trial in IPAA patients with one or two phase III trials to follow pending positive results. It should also be noted that VEN 308 is currently covered by a patent that will expire in December 2017, which although is more than three years away, might provide an impetus for VTUS to move forward with the drug trials.

Meanwhile, following a failed phase III trial for VEN 309, the company decided its resources would be better allocated toward the planned completion of VEN 307, and as a result ceased all activity related to VEN 309. Considering VTUS spent over $43 million trying to develop VEN 309 – which amounts to almost 40% of the company's total accumulated deficit of $116 million as of March 31, 2014 – this represents a very large and expensive failure for the company.

Unfortunately for VTUS, this may be a sign of things to come regarding VEN 307 and the upcoming FDA meeting on June 19th to discuss its new drug application (NDA) for dolizem (diltiazem hydrochloride cream). Despite announcing positive results from its first phase III trial for VEN 307 in May 2012, the company recently announced in February 2014 that a second phase III trial showed no significant difference between VEN 307 and the placebo.

Going back to the "positive" data from May 2012, it can be seen that although the pain endpoints were met and showed improvement compared to the placebo, adverse events (i.e. side effects) were similar for all three treatment arms (4% diltiazem, 2% diltiazem and the placebo). Gastrointestinal disorders were the most common adverse event with reports of headaches that were similar in all three arms (14.7% of 4% diltiazem, 12.3% of 2% diltiazem and 14.2% of placebo).[4]

Considering the primary motivation for VTUS to develop VEN 307 was to minimize this side effect of moderate and severe headaches in patients using Rectiv, this data, along with that released in February

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2014, does not bode well for the company's upcoming meeting with the FDA and the future of their drug candidate. After seeing shares of VTUS fall 63% following the news from February 2014, the outcome of the FDA meeting this week will certainly move shares dramatically one way or the other.

ROYALTY AGREEMENTS:

Even if VTUS is successful in their pursuits, future profits will be hamstrung by the royalty agreements that are in place with their in-licensing partners.

First, in the event that VEN 307 and/or VEN 308 are commercialized, VTUS is obligated to pay S.L.A. Pharma (SLA) annual royalties based upon the net sales of the product(s). In addition, the company is also required to make payments to SLA up to an aggregate amount of $20 million upon the achievement of various milestones related to regulatory events.

In addition, VTUS is subject to a similar agreement with Therabiome regarding VEN 310. Not only is the company solely responsible for all R&D activities with respect to any product it develops under the license, VTUS must also pay Therabiome clinical and regulatory milestones for each product or therapy advanced from the platform, depending on whether the milestone occurs before the filing of the first NDA for a product or after the first, second or third NDA filings as shown below.

Task	Payment			
	Prior to First NDA Filing	After First NDA Filing	After Second NDA Filing	After Third NDA Filing
Upon the filing of an IND with the FDA:	$ 100,000	$ 110,000	$ 120,000	$ 130,000
Upon the filing of an IND equivalent with the ex-U.S. Regulatory Authorities:	See Exhibit B	110% of amount paid Prior to First NDA Filing	120% of amount paid Prior to First NDA Filing	130% of amount paid Prior to First NDA Filing
First dose first patient – human Phase I Clinical Trial	$ 250,000	$ 275,000	$ 300,000	$ 325,000
First dose first patient – human Phase II Clinical Trial	$ 500,000	$ 550,000	$ 600,000	$ 650,000
First dose first patient – human Phase III Clinical Trial	$ 750,000	$ 825,000	$ 900,000	$ 975,000
Upon filing of an NDA or BLA with the FDA:	$ 1,000,000	$ 1,100,00	$ 1,200,000	$ 1,300,000
Upon marketing approval by the FDA:	$ 3,000,000	$ 3,000,000	$ 3,000,000	$ 3,000,000
Upon marketing approval by the ex-U.S.:	See Exhibit B	See Exhibit B	See Exhibit B	See Exhibit B
Upon approval of a supplemental NDA (sNDA) for a new Indication, in the U.S.:	$ 1,000,000	$ 1,000,000	$ 1,000,000	$ 1,000,000

Source: VTUS Form 10-K, 31 December 2013, "License and Collaboration Agreement"

Further, as with SLA, the company must also pay Therabiome royalties on annual net sales of the product(s) in the low- to mid-single digit percentage once annual net sales exceed two certain thresholds, plus a one-time cash payment upon reaching each threshold.[5]

As a result of these agreements, and as indicated in their annual report, having to make these milestone and other payments will actually make it less profitable for the company to develop their drug candidates than if they owned the technology themselves. Not to mention the fact that if VTUS were to breach any of their in-licensing terms, it would result in the loss of their rights to the drug candidates altogether.

Also, it is important to note that all of these payments are in addition to the amounts that VTUS has already paid over the years to SLA and Therabiome, as well as to Sam Amer & Co. for VTUS' failed drug candidate, VEN 309.

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A LOOK AT THE NUMBERS:

Since inception, the company has earned no revenue from product sales and has therefore operated at a loss. Although the company's net loss over the past two years has improved somewhat – mostly due to their decrease in R&D spending following the abandonment of VEN 309 in June 2012 – VTUS' most recent quarterly loss ending March 31, 2014 stood at over -$4 million. Adding to their already large accumulated deficit, that total now sits at roughly -$116 million.

	2013	2012	2011	2010	2009
Annual Net Loss (in thousands)	($19,404)	($24,790)	($34,345)	($15,291)	($4,539)
YoY Change	*22%*	*28%*	*-125%*	*-237%*	

Source: VTUS Form 10-K, 31 December 2013

Since the company has continually operated at a loss, VTUS has funded their operations principally through debt financings prior to their initial public offering (IPO) in 2010, and through equity financings thereafter. As a result, the number of shares outstanding has increased dramatically over a short period of time.

As shown on their financial statements, as of March 31, 2014, VTUS' weighted average common shares outstanding stood at 22,094,700, which was a 30% increase year-over-year (YoY) from March 31, 2013. This YoY increase was even more dramatic in the year ended December 31, 2013 when the company's weighted average common share count stood at 19,393,486, and represented a 52% increase YoY compared to December 31, 2012.

Currently, VTUS has $23.6 million in cash and cash equivalents, which equates to $1.07 per share in cash – or about 68% of Friday's closing price of $1.58. Although that seems favorable for the time being, that number is expected to decrease significantly following the company's merger with Assembly Pharmaceuticals that is expected to close on July 10, 2014. Following the approval of VTUS shareholders, the company will issue approximately 23 million shares of common stock – just about double their existing share count – which will essentially cut their cash value per share in half and dilute existing shareholders considerably.

Furthermore, as stated in their annual report dated December 31, 2013, the company believes their existing cash position will be sufficient to fund their projected operating requirements through FDA approval of VEN 307 and its initial launch and commercialization, and into the second quarter of 2016.[6] Additionally, the strength of VTUS' balance sheet should be helped by their lack of debt and improving debt to equity (D/E) ratio, which currently stands at 0.07.

MERGER WITH ASSEMBLY PHARMACEUTICALS:

In May 2014, VTUS entered into a merger agreement with Assembly Pharmaceuticals, a privately held biopharmaceutical company that focuses on the treatment of the hepatitis B virus (HBV). The merger, among other things including a subsequent reverse merger, will be voted on at the July 10th shareholder meeting. Upon completion of the merger, the combined company will be renamed

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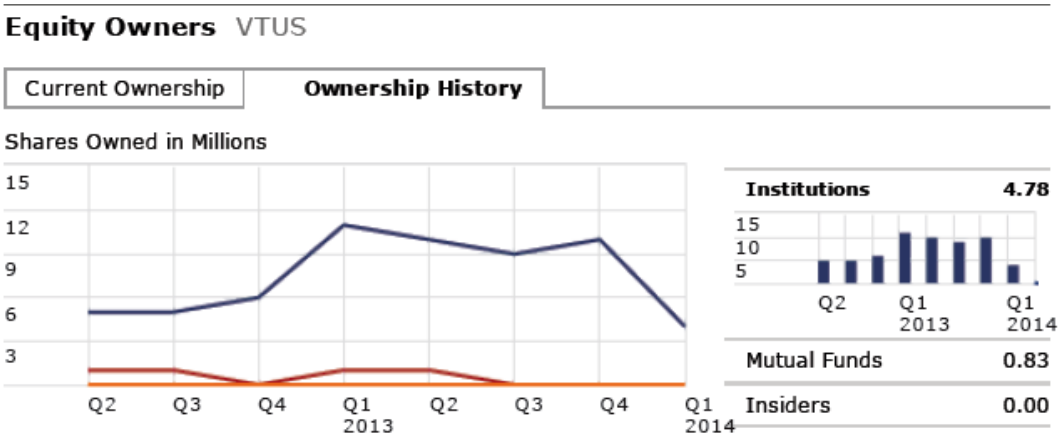
Assembly Biosciences, Inc. and its shares of common stock will trade on the Nasdaq Capital Market under the ticker ASMB.

Following the merger, VTUS will jump into the HBV market that includes more than 350 million infected people worldwide and is attributable to over 600,000 deaths each year.[7] Assembly's proprietary Core Protein Allosteric Modulators (CpAMs) can alter the activities of the HBV core protein, a unique viral protein with no human analogue that is involved in multiple stages of the HBV life cycle.[8] Ventrus and Assembly alike are both optimistic in the curative potential of CpAMs that eliminate the viral reservoir in infected individuals compared to current therapies that only suppress HBV.

Despite this optimism, it should be noted that VTUS will subsequently enter into an intensely competitive and rapidly evolving hepatitis treatment market. Further, following the recent buyout of Idenix Pharmaceuticals for their nucleotide (or "nucs") drug candidate – the supposed future of hepatitis treatments – investors should be cautious ahead of VTUS' foray into the hepatitis market via this merger.

OTHER CONCERNS:

Although VTUS' institutional stock ownership is still considerably high at around 25% of shares outstanding, it is down significantly from its highs reached back in 2013 as shown below. Among those reducing their stake is Baker Bros Advisors LLC, who decreased their holdings by over 65% and now holds less than 2% of shares outstanding.



Source: Morningstar

Lastly, VTUS is literally a small company made up of ten employees, six consultants and three contract research organizations. Not surprisingly, the company does not have nor intend to establish their own manufacturing facilities, and therefore relies on third parties to formulate and manufacture their product candidates. This opens the company up to additional risks as VTUS is dependent on these third-party manufacturers to meet their clinical and commercial needs. Moreover, the company's contract manufacturers are currently all foreign, which further increases their risk through possible shipping delays and import restrictions.

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CONCLUSION:

For the immediate future, all eyes will be on VTUS' meeting with the FDA later this week to discuss their NDA filing for VEN 307. It is likely that shares will move dramatically following the outcome of this meeting, and given the company's past experiences as well as the recent news from February 2014 concerning the drug, I am pessimistic regarding the result. In addition, the company's limited pipeline, combined with their expected royalty and milestone payments with their in-licensing partners should they be successful, cautions me to avoid this stock for the time being. Lastly, the impending merger with Assembly Pharmaceuticals will likely do more harm than good for existing shareholders given the heavy competition in the in the hepatitis treatment market, and the subsequent dilution and possible reverse merger.

Additional Information:
FDA Calendar Link: http://www.biopharmcatalyst.com/fda-calendar/

SOURCES:

[1] VTUS Form 10-K. 31 December 2013. Page 1.
[2] Wikipedia. "Anal Fissure." http://en.wikipedia.org/wiki/Anal_fissure
[3] VTUS Form 10-K. 31 December 2013. Page 11.
[4] Ventrus BioSciences. Press Release. "Ventrus Biosciences Announces Positive Results from Pivotal Phase 3 Trial of Diltiazem (VEN 307) in Patients With Anal Fissures." 14 May 2012. http://investor.ventrusbio.com/releasedetail.cfm?ReleaseID=672924
[5] VTUS Form 10-K. 31 December 2013. Page F-21.
[6] Ibid. Page 41.
[7] "Ventrus Biosciences to Merge with Assembly Pharmaceuticals." GlobeNewswire. 13 June 2014.
[8] Ibid.

financial results that are forward-looking in nature and subject to risks and uncertainties. Such forward- looking statements by definition involve risks, uncertainties and other factors, which may cause the actual results, performance or achievements of mentioned company to be materially different from the statements made herein.

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