William Blair

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Vital Therapies, Inc.

Fourth-Quarter Financials Nonevent; VTI-208 Top-Line Data Now Expected in Third Quarter; Maintain Outperform

On Thursday, March 19, after the markets closed, Vital Therapies reported fourth quarter and full year 2014 financial results. **The company ended the quarter with $102.2 million in cash; we note that the company completed a follow-on offering early in the fourth quarter, which generated net proceeds of $33.4 million. We expect the current cash position to sustain operations through third quarter 2016. By that time, the BLA (biological license application) for ELAD in the first indication will have been filed should the study VTI-208 be successful, and the top-line data from study VTI-212 might be available as well.** The net loss for the quarter was $14.0 million, versus our estimate of $12.9 million and consensus $13.4 million. The per-share loss for the quarter was $0.59, versus our estimate of $0.54 and consensus $0.59. We updated our model as illustrated in exhibit 1.

Enrollment of VTI-208, the pivotal Phase III study in alcohol-induced liver disease (AILD), was completed in the end of January of this year, totaling 203 patients, slightly exceeding the target enrollment of 200. As the primary endpoint is overall survival at 90 days, the last patient will complete the study in the end of April. The company announced today that top-line data is now expected in third quarter 2015, as opposed to June 2015 as previously guided. Such a slight delay does not affect our valuation. Should VTI-208 be successful, the company continues to anticipate filing a BLA in first half 2016. We continue to assign a probability of success of 70% to VTI-208. Since VTI-208 is an open-label study, management had planned to begin data analysis soon after the last patient completes the study in the April/May time frame, and consequently had expected to release top-line data in June. However, upon further consideration and discussions with the FDA, the company decided to conduct data analysis after the database lock; given the last patient in was January 31, 2015, all patient data should be available by early May, and database lock should occur around early to mid-August after all the data is collected and scrubbed. As a result, we expect top-line data to be released likely in late August or early September. We believe this is the right way to go as there is always concern about conducting analyses while the full data set is being scrubbed, as it could compromise or unduly influence the analyses.

- ***VTI-208 study design.*** VTI-208 is a Phase III, randomized, open-label, multicenter, controlled study investigating the effects of ELAD (extracorporeal liver-assist device) in combination with standard therapy of the study site versus standard therapy alone in patients with AILD. The primary endpoint is overall survival at 90 days; secondary endpoints of the study include overall survival at 28 days and Model for End-Stage Liver Disease (MELD)-based time to progression. Long-term effects of ELAD will also be reported as subjects will be followed for an additional five years in an extension study. We note that the VTI-208 study is designed with 95% power to achieve statistical significance for the primary endpoint of overall survival.

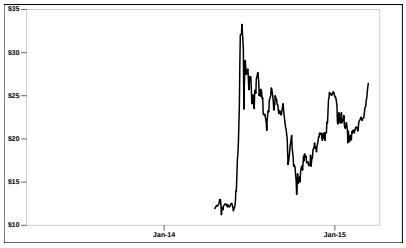
Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$40.00
Symbol:	VTL (NASDAQ)
Price:	$27.37 (52-Wk.: $11-$35)
Market Value (mil.):	$651
Fiscal Year End:	December
Long-Term EPS Growth Rate:	NA
Dividend/Yield:	None

		2013A	2014A	2015E
Estimates				
EPS	Q1	NA	A$-24.49	$-0.59
	Q2	NA	A$-0.91	$-0.61
	Q3	NA	A$-0.59	$-0.48
	Q4	NA	A$-0.59	$-0.57
	FY	$-74.86	$-3.56	$-2.25
	CY		$-3.56	$-2.25
Sales (mil.)		0	0	0
Valuation				
FY P/E		NM	NM	NM
CY P/E			NM	NM

Trading Data (FactSet)	
Shares Outstanding (mil.)	22
Float (mil.)	15
Average Daily Volume	72,015

Financial Data (FactSet)	
Long-Term Debt/Total Capital (MRQ)	0.0
Book Value Per Share (MRQ)	3.5
Return on Equity (TTM)	-45.0

Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

Vital Therapies, Inc. is a hybrid biopharmaceutical–medical technology company based in San Diego, California, focused on the development of its ELAD technology system as a treatment for patients with acute liver failure.

The company has begun enrollment into the second Phase III study VTI-210, and top-line data is now expected in early 2017, as opposed to the earlier guided late 2016. This is due to the fact that VTI-210 and VTI-208 enroll very similar patients, and the enrollment of VTI-210 will accelerate only after VTI-208 is completed. Further, due to the recent data from the STOPAH study, the design of VTI-210 has been modified as well. As of March 18, 6 patients had been enrolled into VTI-210 with 18 sites open for enrollment. By the end of the year, management expects 40 trial sites to be open and the target for full enrollment is 150 patients. VTI-210 is a randomized, open-label, multicenter, controlled study investigating the effects of ELAD in combination with standard therapy of the study site versus standard therapy alone in acute alcoholic hepatitis (AAH) patients, a subset of AILD. The study targets to enroll 150 patients, who will be stratified based on AAH diagnosis by biopsy or clinical grounds without biopsy. The VTI-210 study will be primarily conducted in Europe, and could satisfy regulatory approval if successful. The study had required that all patients take steroids as the frontline therapy for 7 to 9 days, and nonresponders would be subsequently randomized into the study. However, as discussed below, the protocol has recently been amended based on the STOPAH findings. The primary endpoint of the study is overall survival at 90 days; the secondary endpoint of the study is survival at 28 days. Similar to the VTI-208 study, the VTI-210 study is designed with 95% power to achieve statistical significance for the primary endpoint of overall survival.

- ***STOPAH data showed that steroids do not improve overall survival in AAH patients.*** Data from the unrelated STOPAH (Steroids or Pentoxifylline for Alcoholic Hepatitis) study was presented at the 2014 meeting of the American Association for the Study of Liver Diseases (AASLD; November 7-11, Boston). This study evaluated the effect of steroids and/or pentoxifylline treatment in 1,103 AAH patients throughout the United Kingdom and found that neither agent significantly improved survival at 90 days or 1 year, although there was a transient but significant improvement of overall survival from steroids at 28 days. The large data set is convincing in demonstrating lack of overall survival benefit from steroids, underscoring the large, unmet medical need for treating this population.

- ***As a result, the VTI-210 protocol has been amended.*** The VTI-210 study protocol is no longer requiring patients to receive 7 to 9 days of steroids before randomization. Patients will now receive seven days of standard of care of the provider's choice, which may or may not include steroids. Management commented that with the change enrollment may be quicker since patients who were ineligible for steroids could now be enrolled into VTI-210.

The 10th site for VTI-212, the Phase II/III study in fulminant hepatic failure (FHF) or surgery-induced liver failure (SILF) patients, is now open. Four patients have been enrolled to date. Top-line data is expected in 2016, consistent with previous guidance. The planned primary endpoint of the 40-patient, Phase II portion of the study is 28-day survival, which will be compared with historical or matched controls. We anticipate top-line data from the Phase II portion of the study in 2016. We note that results from the Phase II portion of the study might be sufficient for an expedited regulatory approval pathway; however, in the event a Phase III study is necessary for the indication, the study design would be finalized based on analysis of the Phase II component.

Background on ELAD (extracorporeal liver-assist device). The ELAD System is the first human-cell-based bioartificial liver (BAL) therapy to be evaluated in Phase III clinical development for the treatment of ALF. ELAD is an allogeneic cellular therapy system in which human-liver-derived cells, known as C3A cells, contained in a single-use disposable set of four hollow fiber cartridges, are incorporated into a reusable, customized heart-lung machine—a device typically used in open-heart surgery to support the body during the surgical procedure. The heart-lung machine provides extracorporeal circulation of the patient's blood plasma to the cartridges containing the C3A cells for a two-way exchange of toxins, metabolites, and nutrients, and then returns the plasma to the patient. The ELAD system is specifically designed to simulate liver function while the patient's liver is given an opportunity to recover its regenerative properties.

We maintain our Outperform rating and our price target of $40 (exhibit 2). Our Outperform rating is centered on our belief that the ELAD system will become the standard of care for the treatment of acute liver failure in both the United States and Europe, and could generate peak worldwide sales of $1.6 billion by 2032. Our probability-adjusted NPV model assumes a 70% probability of success for the ELAD system development program, and suggests a fair value for the ELAD system of $39 at year-end 2015, with $23 attributed to the United States and $16 to Europe. Adding $1 of net cash at mid-2015, we derive our price target of $40.

Potential sources of upside to our revenue estimates include: 1) pricing for ELAD therapy. Pricing consultants to Vital Therapies suggest that ELAD could be priced in the range of $150,000 to $275,000 per treatment, suggesting a potential market for ELAD of over $4.5 billion in the United States alone. We currently model pricing conservatively at $150,000. We note that the cost associated with a liver transplant is estimated to be more than $500,000. If ELAD can not only save but also prolong the lives of patients by decades who are either ineligible for transplant or waitlisted for transplant, the value

proposition for ELAD therapy would be strong, in our opinion; 2) expansion from AAH to full AILD patient population in Europe could lead to an additional $300 million in peak sales on the continent; and 3) sales outside the United States.

We believe a number of catalysts will drive value in Vital Therapies' stock over the next 12-24 months, including: 1) top-line data from the Phase III VTI-208 study in AILD patients expected third quarter 2015; 2) potential submission of the ELAD system BLA to the FDA in early 2016; 3) top-line data from the Phase II component of the VTI-212 study in FHF and SILF in 2016; 4) potential FDA approval and U.S. commercial launch of the ELAD system in late 2016 or early 2017 in AILD patients; and 5) top-line data from the Phase III VTI-210 study in AAH in early 2017.

Key risks to our Outperform rating and price target include: 1) clinical risk of the Phase III program, which was based on trends observed in previous Phase II studies; 2) regulatory risk given the FDA's concern that the Phase III VTI-208 and VTI-210 studies are open label and not blinded; 3) regulatory risk associated with a drug/device combination requiring approval from the FDA's Center for Biologics Evaluation and Research and Center for Devices and Radiological Health; 4) reimbursement risk provided that the process might be long and arduous; 5) commercialization risk if the ALF market is smaller than expected and/or difficult to penetrate; 6) manufacturing risks associated with Vital Therapies' proprietary C3A cells and cartridges; and 7) technical risk, considering that the ELAD system comprises a hybrid biologic and medical device and that a number of components of the medical device are outsourced by third parties.

While evidence to date supports ELAD as a promising treatment for various forms of ALF, we currently assign the ELAD Phase III program a 70% probability of success based on the following arguments and rationales:

1. ***Survival trends were demonstrated from three Phase II studies.*** It is encouraging that three randomized, controlled Phase II studies conducted in the United States, Europe, and China have demonstrated survival trends in favor of ELAD, and that one of the three studies reached statistical significance. The studies informed powering and design for the current Phase III studies, and also informed patient selection criteria for the Phase III program.

2. ***However, each of the three Phase II studies has its caveats.*** First, VTI-206, a randomized, controlled Phase IIb study in AILD and non-AILD subjects, was stopped early due to a lack of benefit in the non-AILD cohort. Upon termination of the study, per protocol an analysis of the AILD cohort was performed and demonstrated a survival trend. This study informed that ELAD is not effective in non-AILD patients whose livers are not readily regenerable. Second, in the FHF studies, only a post hoc meta-analysis in a subset of patients who were listed for transplant suggested a survival benefit. Lastly, VTIC-301, the Chinese study in subjects with acute flare hepatitis, was halted early due to observed efficacy in subjects. But a protocol amendment led to further enrollment of patients with less severe disease. Analyses of the two different populations led to different sets of data, and consistent statistical significance was only observed among the first 49 enrolled patients. Overall, each of the aforementioned studies and their data analyses had various degrees of limitations. Nonetheless, the signals observed warrant well-designed and well-executed Phase III studies.

3. ***Biomarker data from Phase II studies, including improvement in bilirubin, serum sodium, and creatinine, are all pointing in the right direction.*** Bilirubin is a byproduct of hemoglobin degradation, which can accumulate and result in jaundice if it is not properly cleared and excreted by the liver. In previous Phase II studies, ELAD-treated subjects demonstrated a significant reduction in serum bilirubin levels over the five days of therapy as compared with the standard of care, indicating that the ELAD system was able to carry out the functions of a liver. Further, serum creatinine, a biomarker of kidney function, was reduced in the first six days, while the control did not reduce serum creatinine. Lastly, sodium, an electrolyte that typically decreases with acute liver failure, increased in ELAD-treated subjects over the first six days as compared with the control. Taken as a whole, these biomarkers suggest an improvement in liver function in ELAD-treated subjects.

4. ***Proper patient selection is critical for success of the Phase III program: expected mortality rate of 50% and liver is regenerable.*** The key to the success of the Phase III program is to enroll patients with an expected mortality rate of around 50% and also with regenerable livers so that ELAD can make the strongest difference in improving survival. Specifically, we point to a few of the screening criteria. Patients enrolled are required to have a MELD score of 18-35, which would include patients who are neither too healthy nor too sick; we note that a MELD score in the mid-20s predicts 40% mortality rate. They must also have a Maddrey discrimination function test score greater than 32; this test is a predictor of disease severity and mortality, and a score greater than 32 predicts a 40%-50% probability of death by 90 days. In addition, patients with cirrhotic livers are excluded, as such livers are not regenerable and ELAD would not make a difference. Further, patients who are rapidly improving or deteriorating too quickly on admission are also excluded.

5. ***Statistical powering of Phase III program is high.*** We note that the Phase III statistical plans for VTI-208 and VTI-210 are conservative based on the results from the Phase II VTI-206. Both ongoing Phase III studies are designed with 95% power to achieve statistical significance for the primary endpoint of overall survival. In other words, the studies are 95% powered to reach a p-value of 0.05 assuming 90-day survival for the control arm to be around 50% and for the ELAD arm to be 75%, with a median survival of 45 days for the control arm and 90 days for the ELAD arm.

6. ***There are a number of confounding factors due to the open-label design; a standard patient follow-up protocol has been devised to minimize potential imbalances.*** We note that there is concern regarding the ELAD Phase III programs that ELAD-treated patients would be biased to have better care and attention compared with the control group. To minimize such potential bias, a detailed patient follow-up protocol is incorporated into the Phase III studies.

7. ***The encouraging survival trend observed with Circe Biomedical's HepatAssist bodes well for ELAD, in our opinion.*** We note that the design of the porcine-cell-based BAL HepatAssist system, previously developed by Circe Biomedical, looks to be inferior to the ELAD system in terms of 1) the number of cells supplied (ELAD system uses 11 times more cells than HepatAssist); 2) the duration of treatment. ELAD can be connected to ALF patients 24/7, and the four cartridges can continue to function for up to 17 days without the need for replacement, whereas one HepatAssist cartridge can only be used for six to eight hours per day and a fresh cartridge is needed daily, which is likely not enough time for the liver to regenerate; and 3) high immunological risks (porcine [pig] versus human cells). Despite these shortcomings, HepatAssist demonstrated a survival trend in a Phase II/III study in ALF patients. In fact, a subset analysis of the study demonstrated borderline statistical significance in 30-day survival. We are encouraged by such data and believe such data might bode well for ELAD, which appears to surpass the HepatAssist system in supplementing liver function in almost every aspect.

Please see the exhibits on the following pages.

Exhibit 1
Vital Therapies, Inc.
Income Statement
(dollars in thousands)

	2012A	2013A	2014					2015E	2016E
			Q1A	Q2A	Q3A	Q4A	FY:14A	FY:15E	FY:16E
Revenues									
ELAD US revenues	$0	$0	$0	$0	$0	$0	$0	$0	$5,795
ELAD OUS revenues	-	-	-	-	-	-	-	-	-
Collaboration and licensing revenue	-	-	-	-	-	-	-	-	-
Total Revenues	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**5,795**
Expenses									
COGS	-	-	-	-	-	-	-	-	1,159
R&D expense	5,097	21,787	9,219	9,125	10,244	10,891	39,479	41,453	43,526
SG&A expense	4,483	9,615	2,657	2,513	2,566	3,127	10,863	11,949	13,144
Total Operating Expenses	9,580	31,402	11,876	11,638	12,810	14,018	50,342	53,402	57,829
Operating income	(9,580)	(31,402)	(11,876)	(11,638)	(12,810)	(14,018)	(50,342)	(53,402)	(52,034)
Interest income	4	5	-		-	-	-	33	11
Interest expense, net	(413)	-	-	-	-	-	-	-	-
Other (expense) income, net	7	(15)	-	1,471	12	64	1,547	-	-
Revaluation of preferred stock warrant liabilities	180	-	-	-	-	-	-	-	-
Revaluation of future purchase rights liabilities	3,101	(1,306)	1,128	-	-	-	1,128	-	-
Total other Income (expense)	(6,701)	(32,718)	(10,748)	(10,167)	(12,798)	(13,954)	(47,667)	(53,369)	(52,023)
Pretax income/(loss)	(6,701)	(32,718)	(10,748)	(10,167)	(12,798)	(13,954)	(47,667)	(53,369)	(52,023)
Other comprehensive gain/(loss)	-	(64)	-	-	-	-	-	-	-
Accretion to redemption value of redeemable convertible preferred stock	(942)	(6,303)	(3,070)	(6,084)	-	-	(9,154)	-	-
Provision for income taxes/(income)	-	-	-	-	-	-	-	-	-
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income/(Loss)	**(7,643)**	**(39,085)**	**(13,818)**	**(16,251)**	**(12,798)**	**(13,954)**	**(56,821)**	**(53,369)**	**(52,023)**
GAAP EPS	**($17.89)**	**($74.86)**	**($24.49)**	**($0.91)**	**($0.59)**	**($0.59)**	**($3.56)**	**($2.25)**	**($2.18)**
Weighted average shares outstanding, diluted	427	522	564	17,888	21,759	23,690	15,975	23,765	23,910

Sources: Vital Therapies, Inc., and William Blair & Company, L.L.C. estimates

Exhibit 2
Vital Therapies, Inc.
Sum-of-the-Parts Fair Value
(dollars in thousands, except shares)

Drug Candidate	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value per Share	Percentage of Fair Value
ELAD system—United States	$964,177	Phase III	H2:2016	70%	100%	$540,151	$22.69	56.6%
ELAD system—European Union	$627,036	Phase III	H1:2017	70%	100%	$382,369	$16.06	40.1%
Subtotal						**$922,520**	**$38.75**	**96.7%**
Net Cash at Year-end 2015						$49,579	$2.08	5.2%
Net Present Value of additional Gain (Loss)*						($17,857)	($0.75)	(1.9%)
Sum-of-Parts Fair Value						**$954,242**	**$40.08**	**100.0%**

* Includes costs not directly related to programs above

Sources: Vital Therapies, Inc., and William Blair & Company, L.L.C. estimates

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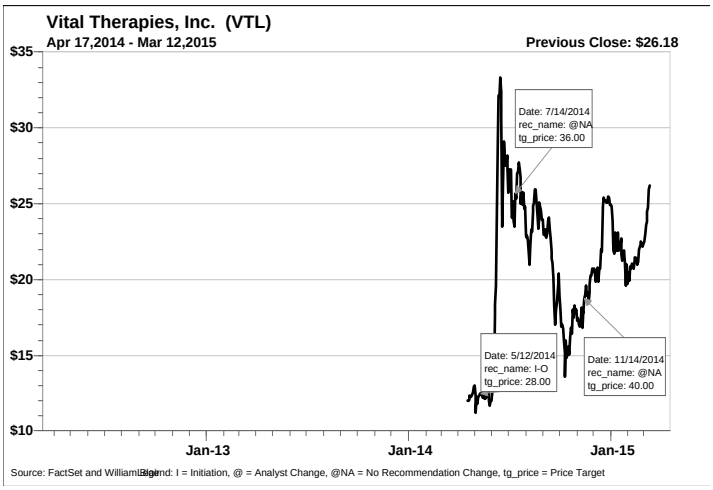
DOW JONES: 18,076.19
S&P 500: 2,099.50
NASDAQ: 4,982.83



Current Rating Distribution (as of 02/28/15)

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	65	Outperform (Buy)	16
Market Perform (Hold)	32	Market Perform (Hold)	2
Underperform (Sell)	2	Underperform (Sell)	0

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