William Blair

Vital Therapies, Inc.

Tackling Acute Liver Failure: Initiating Coverage With an Outperform Rating and $28 Price Target

We are initiating coverage of Vital Therapies with an Outperform rating and a price target of $28, based on our belief that the company's extracorporeal liver-assist device (ELAD), a biologic and device combination, will become the standard of care for the treatment of acute liver failure (ALF) and achieve peak worldwide sales of over $1 billion. We note that more than 75,000 patients in the United States and Europe develop ALF annually, leading to mortality rates in the 30%-90% range. Besides liver transplant, no options exist for ALF patients to improve survival and existing treatments focus only on the management of disease complications. The ELAD system, which operates as an outside-the-body liver, is designed to allow the ALF patient's own liver to recover to a healthy, functioning state or to stabilize the patient until transplant, thereby potentially improving survival. There is little competition in this setting.

ELAD is in Phase III development with the first study to read out by mid-2015; all studies have overall survival as the primary endpoint, which, if successful, should establish ELAD as the gold standard in this setting and command premium pricing, in our opinion. The first Phase III study, VTI-208, is in alcohol-induced liver decompensation (AILD), and the second Phase III study, VTI-210, focuses on acute alcoholic hepatitis (AAH), a subset of AILD. The company also plans to initiate the Phase II/III study VTI-212 in two additional forms of ALF, fulminant hepatic failure (FHF) and surgery-induced liver failure (SILF), by year end 2014 for further label extension.

We value the Vital Therapies stock at $28 per share, based on our probability-adjusted net present value (NPV) model. We estimate worldwide sales for the ELAD system will reach $1.3 billion in the United States and Europe in 2032. Assuming a 70% probability of success, our probability-adjusted NPV model suggests a fair value for ELAD at $26 at year end 2014, with $16 attributed to the United States and $10 to Europe. Adding $2 of net cash at year end 2014, we derive our price target at $28. Potential upside to our valuation includes pricing, geographic expansion, and further label extensions.

We believe a number of catalysts will drive value in the next 12-24 months, including: 1) top-line data from the Phase III VTI-208 study in AILD patients expected in first half 2015; 2) top-line data from the Phase III VTI-210 study in AAH in early 2016; 3) top-line data from the Phase II component of the VTI-212 study in FHF and SILF in late 2015 or early 2016; and 4) potential FDA approval of the ELAD system in second half 2016.

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.

May 12, 2014
Basic Report (14-063)

Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$28.00
Symbol:	VTL (NASDAQ)
Price:	$12.34 (52-Wk.: $11–$13)
Market Value (mil.):	$255
Fiscal Year End:	December

Estimates	**2013A**	**2014E**	**2015E**
EPS FY	($3.14)	($1.97)	($1.58)
Sales (mil.)	$0	$0	$0
Valuation			
P/E	NM	NM	NM

Trading Data	
Shares Outstanding (mil.)	21.1
Float (mil.)	14.0
Average Daily Volume	138,000
Financial Data	
Total Debt/Total Capital	NM
Enterprise Value (mil.)	$221
Price/Book	NM

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Investment Overview

Liver Failure Is a Life-Threatening Condition: Acute, Acute-on-Chronic, and Chronic
The liver performs vital functions for the body, including metabolic, detoxification, synthetic, and immunological activities. Liver failure occurs when the liver is damaged beyond repair and loss of function is to such a degree that is life threatening. Liver failure is generally categorized into acute liver failure, acute-on-chronic failure, and chronic liver failure, as illustrated in exhibit 1, on page 4.

Acute liver failure (ALF) is defined as the rapid onset of liver dysfunction in a patient without underlying chronic disease. Chronic liver failure is much more common than ALF, and it occurs when the liver gradually loses its function when normal liver tissues are replaced by fibrosis, scar tissues, and cirrhosis. When acute liver failure occurs with underlying liver disease, the condition is termed acute-on-chronic liver failure.

Acute Liver Failure Is an Orphan Indication Encompassing a Broad Spectrum of Conditions With High Mortality Rates

- ***Acute liver failure and its associated high mortality rates.*** Acute liver failure (ALF) usually occurs very rapidly and could be difficult to detect. ALF encompasses a broad spectrum of conditions, and its categorization depends on the underlying status of the liver and the source of the injury. We note that despite intervention, the short-term mortality rate for ALF remains above 50%. If left untreated, the mortality rate ranges between 60% and 90% in severe cases of the disease. The timely recognition and management of patients with ALF is critical and represents high unmet need.

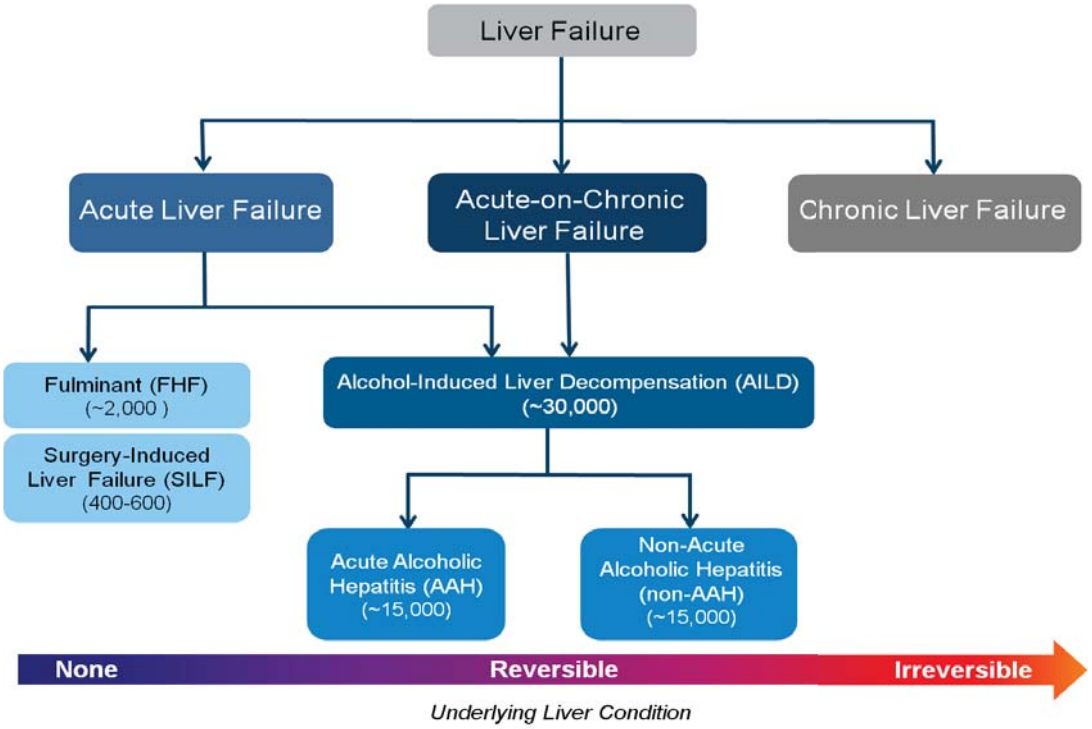
- ***Within ALF, the largest subgroup is alcohol-induced liver decompensation (AILD), a life-threatening form of ALF precipitated by recent binge ingestion of alcohol; some AILD can also be categorized as acute-on-chronic liver failure if there is clear underlying liver disease.*** AILD is typically subdivided into two subgroups: acute alcoholic hepatitis (AAH) and non-acute alcoholic hepatitis (non-AAH). Subjects with AAH have some level of pre-existing liver inflammation and enlargement as a result of long-term alcohol consumption; the changes are reversible on abstention and further exacerbated by continued alcohol use. In contrast, non-AAH occurs in subjects with stable chronic liver disease attributed to viral or autoimmune causes who experience acute liver failure because of excessive alcohol consumption. In 2011, the U.S. Department of Health and Human Services (HHS) estimated that the number of hospital admissions related to alcohol in the United States was about 99,000, with roughly 14,000 of these admissions identified as AAH as the primary diagnosis. We believe that AILD is split roughly 50-50 between AAH and non-AAH with respect to annual incidence in both the United States and Europe. We note that AAH is associated with a high mortality rate of 30% to 60%.

- ***A rarer subtype of ALF is fulminant hepatic failure (FHF),*** which is a rapid deterioration of liver functions typically associated with drug-induced (such as Tylenol) injury, viral hepatitis, or toxin-associated injury. The mortality rate associated with FHF is about 85% without a transplant; the overall short-term survival with transplantation is greater than 65%. FHF occurs in about 2,000 persons per year in the United States and in Europe each.

- ***Lastly, surgery-induced liver failure (SILF) represents another rare form of ALF.*** There are three primary forms of SILF, including 1) primary graft nonfunction, 2) small-for-size syndrome or split liver transplant, and 3) cancer resection. Each of these is generally related to surgery whereby the transplant fails or the transplant or resection results in too small of a liver to function on its own. We estimate the annual numbers of cases in the United States for primary graft nonfunction and split liver transplant ranges between 200 and 300 each. The number of SILF cases related to cancer resection, primarily from colon cancer metastases, could represent a

population of more than 10,000 cases per year. We note that roughly 45,000 colon cancer patients are diagnosed annually with metastatic disease to the liver, and despite recent advances in surgical techniques and reduced postoperative mortality, nearly two-thirds of patients are ineligible for surgical intervention because of the potential risk of SILF onset.

Exhibit 1
Vital Therapies, Inc.
Liver Failure: Various Subtypes and U.S. Incidence



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

Only Liver Transplant Has Proved to Improve Survival in ALF, but It Is Not Always an Option
Liver transplantation remains the only option to improve survival and provide long-term cure for ALF patients. However, because of the shortage of donor organs, fewer than 6,500 patients undergo transplant each year in the United States. There are 16,000 patients on the liver transplant wait list in the United States, and roughly 1,500 patients waiting on the list die each year. Similar numbers regarding liver transplants, donor organs, and annual deaths are reflected in Europe.

Importantly, a majority of ALF and acute-on-chronic liver failure patients are classified under AILD. Because six months of abstinence from alcohol is generally considered a prerequisite for inclusion on a liver transplant list, organ transplantation for AILD patients is not an option. As a result, these patients are left with no treatment options that could improve survival.

For AILD and many other ALF patients, current treatment options include the use of anti-inflammatory drugs such as corticosteroids, antioxidants such as N-acetylcysteine, and off-label pentoxifylline. These drugs focus solely on the management of disease complications, and do not address the underlying disease. Over the past several years, the use of steroids and their combination with pentoxifylline have been generally more accepted as first-line treatment for patients with ALF, particularly in Europe. In the United States, however, it is estimated that less than 25% of all treating physicians prescribe steroids on presentation of the disease in the hospital setting. In our discussions with key opinion leaders, we learned that response rates to corticosteroids in ALF patients is in the range of 20% to

30%; however, recent literature by Karhanis et al. (*Hepatology,* 2014 [59] pp. 612-21) suggests that the use of corticosteroids does not improve overall survival in various forms of ALF and might be deleterious in patients with high Model for End-Stage Liver Disease (MELD) scores. In our opinion, the use of steroids to improve response or survival for AILD remains controversial.

In summary, a significant unmet medical need exists for the treatment of ALF given the lack of available effective interventions.

The Goal of a Liver Support System for ALF Patients: Improving Survival
A few artificial liver support systems have been developed to supplement liver function while the patients are in acute liver failure, in an attempt to bridge ALF patients to recovery or to transplant. The ultimate goal of these liver support systems is to improve survival in ALF patients. For AILD patients who are not eligible for transplant, a liver support system might present the only option to improve survival. For patients who are eligible for transplant, such as FHF and SILF patients, a liver support system might be able to stabilize them while they await liver transplant.

Liver Support Systems: Artificial Versus Bioartificial
So far there are two acelluar, artificial liver devices and one celluar, bioartificial liver device containing pig cells that were evaluated in late-stage clinical trials. To date, none of these systems has succeeded in demonstrating a survival benefit in ALF patients.

- ***All artificial liver support systems failed to date.*** The acellular, artificial support systems included MARS by Gambro and the Prometheus by Fresenius. They are sorbent-based systems that filter toxic metabolites from the blood via adsorption. Both systems failed to demonstrate any survival benefit. MARS is cleared as a device in the United States for use in hepatic encephalopathy, drug overdoses, and poisoning. In Europe, both MARS and Prometheus are commercialized under CE marks as a device. We note that these devices are essentially dialysis devices for the liver.

- ***A porcine-cell-based bioartificial liver support system demonstrated survival trends in a large Phase II/III study but did not reach statistical significance.*** The cellular, bioartificial liver support system, HepatAssist by Circe Biomedical, which uses porcine cells to mimic liver function outside of the body, has shown a trend in improving survival in ALF patients, but the study did not reach statistical significance. HepatAssist is not being further developed.

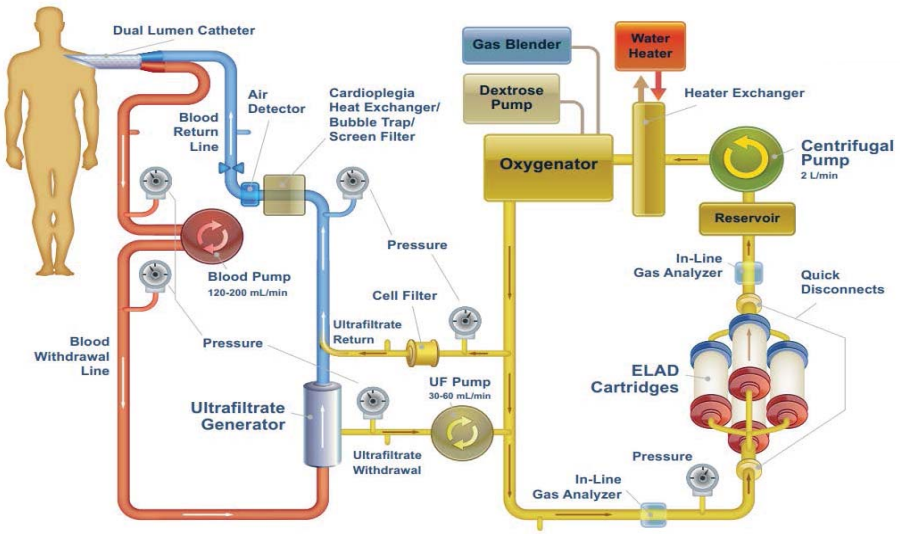
ELAD System—The First Bioartificial Liver Support System Employing Human Cells
Based in San Diego, Vital Therapies has developed the extracorporeal liver-assist device (ELAD) system as a treatment for patients with ALF.

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.

The ELAD system is illustrated in exhibit 2, on the following page.

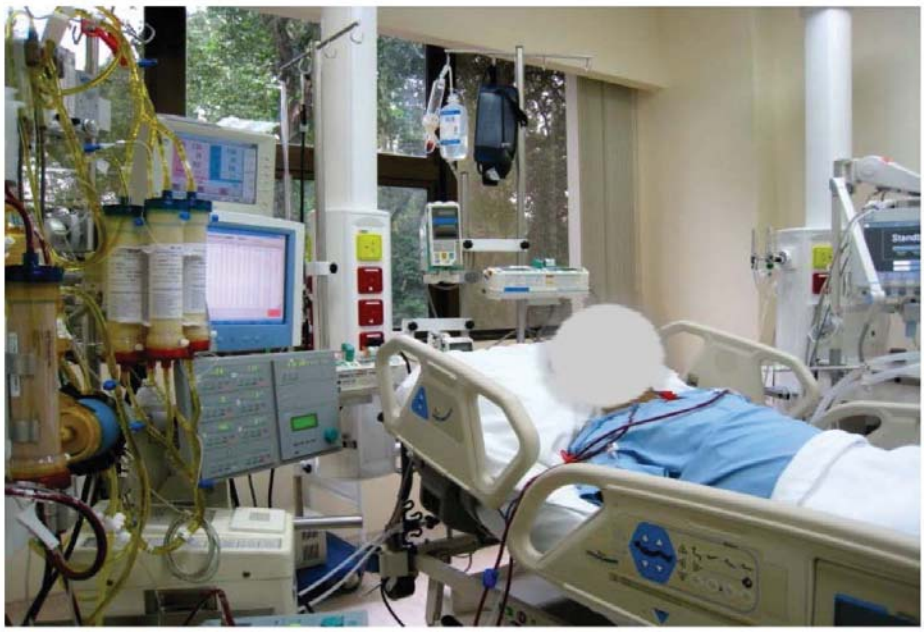
Exhibit 2
Vital Therapies, Inc.
The ELAD (Extracorporeal Liver Assist Device) System

a) Schematic of ELAD System



Source: Vital Therapies, Inc.

b) ELAD System in Use



Source: Vital Therapies, Inc.

ELAD Stands to Be the Most Promising Liver Support Biologic-Device Combo
As the liver is an active, dynamic biological system and performs more than 500 functions necessary for human life, an acellular approach that focuses on only one aspect of liver function is not sufficient to replace full liver function. We believe a cellular approach is more likely to mimic the key biological complexities of the liver and could have the necessary breadth and dynamic properties to successfully supplement liver function.

Between the two cellular approaches that reached late-stage development, we believe ELAD has a number of key advantages over HepatAssist, which leads us to believe that ELAD is the best-in-class, most promising liver support biologic-device combo developed to date.

- ***The use of human hepatocytes (liver cells) versus porcine hepatocytes.*** Human C3A cells are the closest in properties to functioning hepatocytes. There is much less concern on safety with human cells than with animal cells.

- ***Immunological risk with animal cells.*** Humans have naturally occurring antibodies against porcine antigens, and the antibodies would attack the porcine hepatocytes, causing them to lose function and die. Further, repeated treatment with porcine cells could augment immunological responses and thereby heighten risks.

- ***ELAD uses 11 times more cells than HepatAssist.*** HepatAssist contained approximately 40 grams of pig hepatocytes, while ELAD contains about one pound of human hepatocytes, which represents one-third of the average human liver mass. ELAD provides a much more substantial artificial liver mass, potentially better supplementing liver function.

- ***ELAD offers much longer duration of therapy.*** 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. One HepatAssist cartridge can only be used for six to eight hours per day and a fresh cartridge is needed every day, likely not enough treatment time for the liver to regenerate.

ELAD Is Regulated as a Biologic, Not as a Device
ELAD, a biologic-device combo, is regulated as a biologic in both the United States and Europe, unlike the aforementioned MARS and Prometheus, which are regulated as devices. Vital Therapies will file a biologics license application (BLA) with the Center for Biologics Evaluation and Research of the FDA if pivotal studies are successful; the application will also receive feedback from the Center for Devices and Radiological Health. In Europe, Vital Therapies will file a marketing authorization application (MAA) with the Committee for Advanced Therapies of the European Medicines Agency (EMA).

ELAD Clinical Development Program Covers Major Subgroups in ALF With Survival as the Primary Endpoint

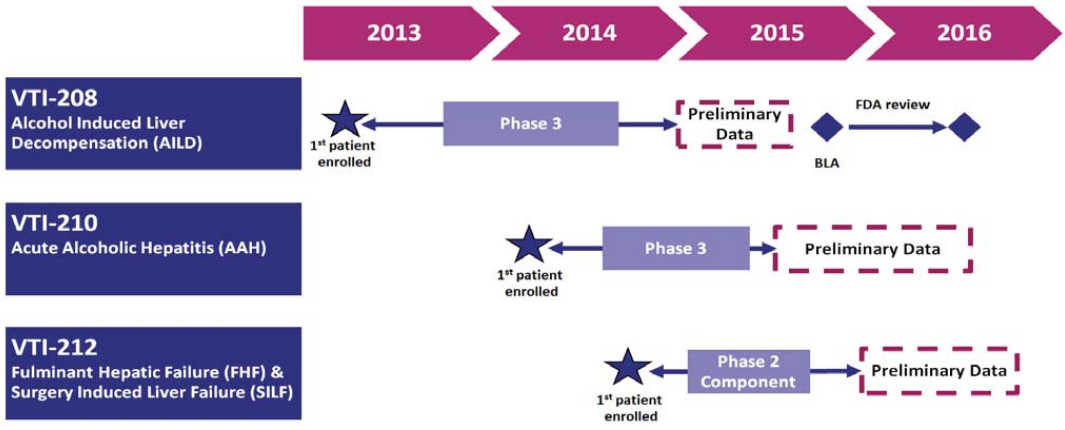
- ***The first Phase III study, VTI-208, is a randomized, open-label, multicenter, controlled study investigating the effects of ELAD in combination with standard therapy of the study site versus standard therapy alone in patients with alcohol-induced liver decompensation (AILD).*** The primary endpoint is overall survival at 90 days; secondary endpoints of the study include overall survival at 28 days and 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. As of the end of April, 100 of the 200 expected patients have been enrolled in VTI-208. We expect top-line data from the study by mid-2015. VTI-208 is primarily conducted in the United States.

- ***The second Phase III study, VTI-210, is a randomized, open-label, multicenter, controlled study investigating the effects of ELAD in AAH patients, a subset of AILD, who failed steroids.*** Initiated in April 2013, the study will enroll 120 AAH patients who have failed at least seven days but no more than nine days of steroid therapy, according to predefined criteria. The primary endpoint is overall survival at 90 days; the secondary objective 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. We anticipate complete enrollment in the study by mid-2015 and top-line data by late 2015 or early 2016. VTI-210 is primarily conducted in Europe, where steroid use in AAH patients is considered frontline therapy.

- ***Planned Phase II/III VTI-212 study in patients with FHF or SILF to start by year end 2014.*** Vital Therapies also plans to initiate the Phase II single-arm portion of the VTI-212 study by year end 2014, targeting to enroll 40 patients with FHF or SILF. The planned primary endpoint of the Phase II component 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 by late 2015 or early 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.

We illustrate the ELAD system development timeline in exhibit 3.

Exhibit 3
Vital Therapies, Inc.
Clinical and Regulatory Timelines for ELAD System



Source: Vital Therapies, Inc.

Registrational Strategy for ELAD

Vital Therapies has disclosed that the VTI-208 study alone might be sufficient for filing of the BLA in later 2015 and potential approval in the United States in 2016, should the study be successful. If additional supportive data is needed for U.S. approval, the company will submit the application incorporating results from both the VTI-208 study in AILD patients and the VTI-210 study in AAH patients in 2016.

In Europe, the VTI-210 study alone, if successful, will be sufficient for the filing of the MAA with the EMA and will support European approval. We expect submission of the MAA during 2016.

Lastly, data from the FHF and SILF indications are intended to support the filing and label expansion of the ELAD system on both continents if ELAD is first approved in the AILD or AAH settings.

We Assign the ELAD System a 70% Chance of Success Across Its Phase III Programs
While evidence to date supports ELAD being a promising treatment for various forms of ALF, we 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 had demonstrated survival trend in favor of ELAD, and that one of the three studies reached statistical significance. The studies informed powering and design for the 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 limitations.*** 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 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 the first 49 subjects, but a protocol amendment led to further enrollment of patients with less severe disease. Analyses on the two different populations led to different sets of conclusions, 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 positive signals observed from Phase II studies warrant larger studies for a definitive proof of the survival benefit, and we believe the Phase III program is well designed to achieve this goal.

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 key for success of the Phase III program: expected mortality rate of 50% and a regenerable liver.*** 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 probability of death of 40%-50% 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.*** As noted earlier, both ongoing Phase III studies (VTI-208 and VTI-210) 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%.

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.*** As discussed in detail in later sections, 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 HepatAssist bodes well for ELAD, in our opinion.*** As discussed above, the design of the HepatAssist system looks to be inferior to the ELAD system in terms of the number of cells supplied, duration of treatment, and high immunological risks. Despite all the 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 review the data in a later section and are encouraged by such data. We believe such data might bode well for ELAD, which appears to exceed the HepatAssist system in supplementing liver function in almost every aspect.

Huge Commercial Potential in an Orphan Population—a Multi-Billion-Dollar Opportunity
Given the dire need for intervention for ALF patients, we believe that the ELAD system could eventually become the standard of care for AILD patients as well as patients with FHF and SILF if the Phase III program is successful. We estimate that over 30,000 annual cases of ALF in the United States and 40,000 in Europe could eventually be eligible for treatment with the ELAD system.

If we assume a conservative market penetration for the ELAD system in the overall U.S. and European ALF market of roughly 10% to 15%, and an average wholesale price of $125,000 per treatment, we estimate the ELAD system could generate peak sales of about $1.3 billion by 2032. If the adoption rates are higher, and pricing is higher, the ELAD commercial opportunity could reach multibillion-dollar levels.

- ***Similarities to other orphan disease opportunities.*** We view the market opportunity for the ELAD system as similar to certain other orphan disease markets—for example, the cystic fibrosis market—given 1) the similar addressable patient population (about 75,000 in the United States and Europe), 2) the unmet medical need for the disease, and 3) the ability to command high pricing (we note that Vertex's Kalydeco for a subset of cystic fibrosis mutations is priced at over $300,000 annually per patient). As ELAD has the potential to demonstrate a mortality benefit, allowing patients the opportunity to live for decades once saved, in addition to providing savings for the healthcare system, it could command premium pricing given the strong pharmacoeconomic argument.

Worldwide Commercialization Strategy
Vital Therapies plans to commercialize the ELAD system on its own in both the United States and Europe. The market is highly concentrated, with an estimated 200 centers, composed of about 100 liver transplant centers and roughly 100 specialist intensive care units (ICUs) in the United States that treat ALF patients; we note that the market composition in Europe across the "big five" countries (Germany, France, United Kingdom, Spain, and Italy) is similar to that of the United States.

- ***Details of commercial rollout.*** Vital Therapies plans to launch immediately in about 40 centers each in the United States and Europe, as these centers have been conducting clinical studies on ELAD and are set up for and familiar with the system. The company estimates that about 10,000 eligible patients (roughly one-third of the addressable ALF population) already reside in this circle of centers and their referral networks. Over the ensuing 10 years, Vital Therapies plans to launch ELAD to the aforementioned 200 centers each in the United States and Europe. Outside the United States and Europe, parallel efforts will also begin in Australia, leaving Eastern Europe, the Middle East, and Asia as significant future upside opportunities for potential partners.

  The company plans to employ a commercial sales team of fewer than 100 individuals comprising account managers, pricing and reimbursement specialists, medical science liaisons, marketers, and ELAD technicians in the initial launch in the United States. We assume that at peak commercialization, the company will employ a commercial staff of about 200 individuals to cover the 200 targeted centers in the United States. The size of the sales team in Europe is expected to be smaller.

- ***Support staff upon launch, switching to ER nurses later.*** Upon commercialization, the company plans to launch with 50 dedicated specialists, or nurses, tending to the ELAD device at the various treatment centers in the United States; we assume a similar rollout of dedicated specialists for the European launch. After a few years, the company will transition from employing a specialist staff to using the given hospital's own nursing staff.

William Blair Revenue Model for ELAD Sales in the United States and Europe

We illustrate our ELAD revenue model and projections for ELAD worldwide sales in exhibits 4 and 5, on the following pages. As discussed above, the annual incidence of AILD in the United States and Europe is roughly 30,000 and 40,000, respectively; we conservatively estimate that about 75% and 50% of these patients, respectively, will be eligible for ELAD treatment. For FHF and SILF, we estimate the annual incidence in these two regions at 2,500 each, with 100% of the patients eligible for treatment. As a result, we estimate the aggregate number of patients eligible for ELAD therapy in the United States at roughly 25,250 and in Europe at 22,500 when the therapy is launched in 2016.

- ***Conservative market penetration for both indications.*** As illustrated in exhibit 4, we peg peak penetration of ELAD in the AILD setting at 20% in the United States and 15% in Europe. For patients with FHF or SILF, we conservatively model peak penetration of 40% and 35% in the United States and Europe, respectively. Our launch assumptions are based on similar product launches of analog hospital-based medical devices, which typically take several years to build acceptance and momentum.

- ***Pricing and reimbursement.*** We estimate the launch list price per course of therapy with the ELAD system at $125,000 in the United States at launch in 2017 with a gross-to-net discount rate of 12%. In addition, we forecast an annual 1% price increase in the United States. In Europe, we estimate a course of therapy with the ELAD system to cost $125,000 at launch in 2018; however, we include a gross-to-net discount rate of 8% with flat pricing throughout the European Union.

- ***Our revenue projection.*** We therefore derive peak sales of the ELAD system at $1.3 billion in 2032, with U.S. peak sales of $800 million and $520 million in Europe.

Exhibit 4
Vital Therapies, Inc.
William Blair Revenue Model for ELAD
(dollars in thousands)

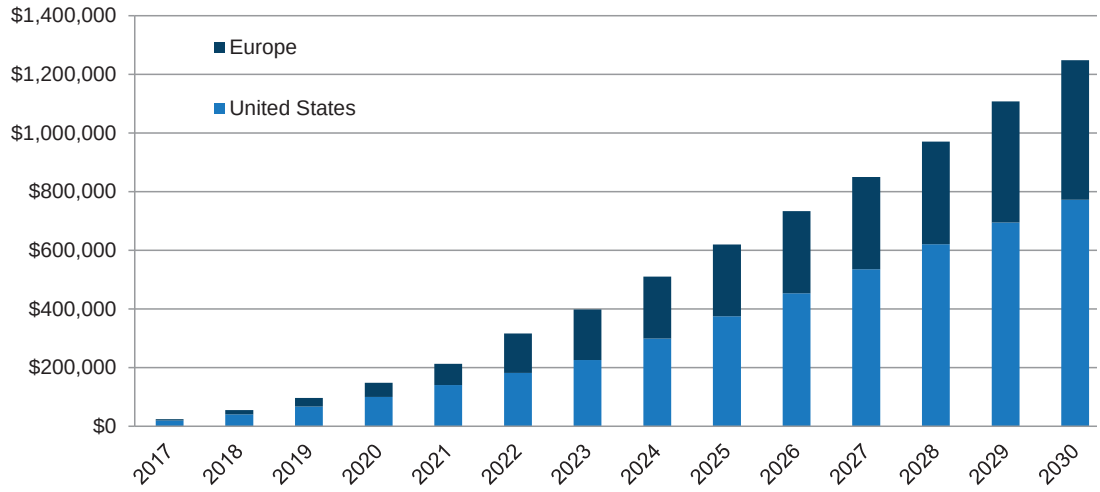
United States		2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
AILD patients		30,300	30,603	30,909	31,218	31,530	31,846	32,164	32,486	32,811	33,139	33,470	33,805	34,143	34,484	34,829	35,177	35,529
Growth Rate	*1%*																	
AILD patients - Eligible		22,725	22,952	23,182	23,414	23,648	23,884	24,123	24,364	24,608	24,854	25,103	25,354	25,607	25,863	26,122	26,383	26,647
% of eligible patients	*75%*																	
Penetration		*0%*	*1%*	*1%*	*2%*	*3%*	*4%*	*5%*	*6%*	*8%*	*10%*	*12%*	*14%*	*16%*	*18%*	*20%*	*20%*	*20%*
Treated ALD patients		**45**	**138**	**278**	**468**	**709**	**955**	**1206**	**1462**	**1969**	**2485**	**3012**	**3549**	**4097**	**4655**	**5224**	**5277**	**5329**
FHF patients		2,525	2,550	2,576	2,602	2,628	2,654	2,680	2,707	2,734	2,762	2,789	2,817	2,845	2,874	2,902	2,931	2,961
% of eligible patients	*100%*																	
Penetration		*0%*	*2%*	*4%*	*6%*	*8%*	*12%*	*16%*	*20%*	*24%*	*28%*	*32%*	*36%*	*40%*	*40%*	*40%*	*40%*	*40%*
Treated FHF patients		**-**	**51**	**103**	**156**	**210**	**318**	**429**	**541**	**656**	**773**	**893**	**1014**	**1138**	**1149**	**1161**	**1173**	**1184**
Total ELAD Treated Patients		**45**	**189**	**381**	**624**	**920**	**1274**	**1635**	**2003**	**2625**	**3259**	**3905**	**4564**	**5235**	**5805**	**6385**	**6449**	**6514**
Net Pricing per course ($)		**$106,250**	**$106,250**	**$107,313**	**$108,386**	**$109,469**	**$110,564**	**$111,670**	**$112,787**	**$113,914**	**$115,054**	**$116,204**	**$117,366**	**$118,540**	**$119,725**	**$120,922**	**$122,132**	**$123,353**
price increase	1%																	
Net ELAD sales ($)		**4,829**	**$20,051**	**$40,909**	**$67,672**	**$100,672**	**$140,839**	**$182,581**	**$225,944**	**$299,008**	**$374,917**	**$453,758**	**$535,617**	**$620,583**	**$694,986**	**$772,129**	**$787,649**	**$803,481**
% Growth				*104%*	*65%*	*49%*	*40%*	*30%*	*24%*	*32%*	*25%*	*21%*	*18%*	*16%*	*12%*	*11%*	*2%*	*2%*

EU Market		2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
AILD patients		40,000	40,400	40,804	41,212	41,624	42,040	42,461	42,885	43,314	43,747	44,185	44,627	45,073	45,524	45,979	46,439	46,903
Growth Rate	*1%*																	
AAH patients		20,000	20,200	20,402	20,606	20,812	21,020	21,230	21,443	21,657	21,874	22,092	22,313	22,537	22,762	22,989	23,219	23,452
% of eligible patients	*50%*																	
Penetration			*0%*	*1%*	*1%*	*2%*	*2%*	*4%*	*5%*	*6%*	*7%*	*8%*	*9%*	*10%*	*12%*	*14%*	*15%*	*15%*
Treated AAH patients		**-**	**40**	**102**	**206**	**312**	**420**	**849**	**1072**	**1299**	**1531**	**1767**	**2008**	**2254**	**2731**	**3219**	**3483**	**3518**
FHF patients		2,500	2,525	2,550	2,576	2,602	2,628	2,654	2,680	2,707	2,734	2,762	2,789	2,817	2,845	2,874	2,902	2,931
% of eligible patients	*100%*																	
Penetration				*1%*	*2%*	*4%*	*8%*	*12%*	*16%*	*20%*	*22%*	*24%*	*26%*	*28%*	*30%*	*32%*	*34%*	*35%*
Treated FHF patients		**-**	**-**	**26**	**52**	**104**	**210**	**318**	**429**	**541**	**602**	**663**	**725**	**789**	**854**	**920**	**987**	**1026**
Total ELAD Treated Patients		**-**	**40**	**128**	**258**	**416**	**631**	**1168**	**1501**	**1841**	**2133**	**2430**	**2733**	**3042**	**3585**	**4138**	**4470**	**4544**
Net Pricing per course ($)		**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**	**$115,000**
price increase	0%																	
Net ELAD sales ($)		**-**	**4,646**	**$14,664**	**$29,621**	**$47,868**	**$72,520**	**$134,282**	**$172,614**	**$211,698**	**$245,259**	**$279,469**	**$314,340**	**$349,879**	**$412,274**	**$475,882**	**$514,019**	**$522,530**
% Growth					*102%*	*62%*	*52%*	*85%*	*29%*	*23%*	*16%*	*14%*	*12%*	*11%*	*18%*	*15%*	*8%*	*2%*

Year	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
Total ELAD Revenue - U.S. and EU	**$4,829**	**$24,697**	**$55,573**	**$97,293**	**$148,540**	**$213,359**	**$316,863**	**$398,557**	**$510,706**	**$620,176**	**$733,228**	**$849,956**	**$970,462**	**$1,107,260**	**$1,248,012**	**$1,301,668**	**$1,326,011**

Source: William Blair & Company, L.L.C. estimates

Exhibit 5
Vital Therapies, Inc.
William Blair Estimates for U.S. and EU Sales of ELAD
(dollars in thousands)



Source: William Blair & Company, L.L.C. estimates

Considerable Upside Exists to Our Revenue Model

Our Outperform rating is centered on our belief that ELAD will become the standard of care for the treatment of ALF in both the United States and Europe. Potential sources of major upside to our revenue estimate include the following:

- ***The biggest lever is pricing.*** 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 by decades the lives of patients who are either ineligible for transplant or waitlisted for transplant, the value proposition is strong, in our opinion. A study commissioned by Vital Therapies investigated pricing through three different lenses: 1) orphan drug pricing, 2) health economics, and 3) actual reimbursement for the current standard of care; it concluded that ELAD could be priced in a range of $150,000 to $275,000 with potential upside to $350,000. If such pricing comes to fruition, our pricing assumption of $125,000 would be very conservative.

- ***Expansion from AAH to full AILD patient population in Europe could lead to an additional $300 million in peak sales on the continent.*** We assume only 50% of the AILD market in Europe to be eligible for ELAD therapy based on the Phase III VTI-210 study design, which includes only AAH patients. If the company files for an expanded label and receives approval for the ELAD system to include non-AAH AILD patients, we believe the addressable population for ELAD therapy would increase by nearly two-thirds, to about 38,000 patients.

- ***ELAD's application for marketing approval has been on file in China since 2007; approval in the United States would trigger final approval in China, the biggest market of liver disease in the world.*** Vital Therapies completed a study of ALF patients with viral hepatitis in China, and although the study was small, it reached statistical significance and was stopped early. It is generally agreed that the Chinese regulatory authorities would grant approval to ELAD if ELAD were approved in its home country. As a result, we believe that upon potential U.S. approval, ELAD could be approved in China as well, and that Vital Therapies might choose to commercialize in China with a partner. We note that a million ALF cases occur in China annually, as compared with 30,000 in the United States.

- ***Sales outside the United States, Europe, and China are further upside.*** We have included revenues only from the United States and Europe in our model. Sales outside these areas—including territories such as Eastern Europe, Australia, the Middle East, and in particular, China and other parts of Asia—would be upside to our valuation. We believe Vital Therapies will commercialize in these regions via partners.

- ***Further label extensions.*** Besides the AILD, AAH, FHF, and SILF indications that are being studied in the existing development programs, ELAD could be used in other indications as well, such as viral hepatitis, liver resection support, and liver transplant support.

Reimbursement Issues to Consider

Drug pricing and reimbursement has been a focus topic in recent years. Given ELAD's unique profile—a biologic-device combo with the ability to increase survival—it is important to delineate the reimbursement process.

As discussed above, the only option ALF patients have for a potential long-term cure is liver transplant. Unfortunately, liver transplant is limited to a small number of eligible candidates, which leaves many patients without options. As a result, there is a clear unmet medical need that ELAD can serve if ELAD definitively demonstrates improved survival in its Phase III programs. In particular, for the AILD patients for whom transplant is not an option, the value position for ELAD is strong if it significantly improves survival, given that a transplant costs more than $500,000 per procedure.

The majority of the ALF patient population is below the age of 65 and will most likely be covered by private insurance rather than Medicare or Medicaid. Private payers derive their reimbursement rate on a negotiated basis whereas Medicare goes through a committee that decides on a reimbursement price. Lastly, the Medicaid process is unique in that it is determined on a state-by-state basis. Generally, most state Medicaid programs align with Medicare while some choose to negotiate independently.

- ***Reimbursement through private payers is a negotiated process using case rates, similar to liver transplant.*** The process is as follows: 1) the company creates a dossier identifying the burden of disease and all associated costs; 2) the company identifies the top-tier accounts; 3) the company meets with payers and presents its dossier; and 4) once an agreement is reached, a comprehensive publication plan is drafted. We note that the most important step is picking the appropriate provider for the first reimbursement because it will most likely set the bar for the group.

- ***ELAD is expected to be reimbursed as an inpatient drug through a diagnosis-related group (DRG) determined by the Centers for Medicare & Medicaid Services' (CMS's) coordination and maintenance committee.*** Because ELAD is a new therapy, it will also need its own procedural code from the International Classification of Diseases, Tenth Revision (ICD-10), which can take up to a year. Once an ICD-10 code is established, the DRG is expected to be issued two to three years following approval, during which time the CMS evaluates the effectiveness of ELAD and establishes the actuarial process based on the cost experience in the first two to three years on the market. Before the DRG is set up, ELAD should be reimbursed by the new technology add-on payment (NTAP) and outlier payments. Reimbursement rates under Medicaid can be revisited on a yearly basis.

Intellectual Property for ELAD

Vital Therapies holds a method-of-use patent for treating patients' blood with C3A cells in the United States, which expires in April 2027. A second granted patent in the United States covers the extracorporeal device configuration, or bedside unit, independent of any cells employed in the circuit; this patent is set to expire in May 2025. Foreign counterparts of these and other patents have been

issued in Australia, Canada, Indonesia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea, and Taiwan, while patents are still under review in Europe, Brazil, China, India, and the Philippines. Two additional ELAD patents are pending in the U.S. Patent Office.

On the regulatory side, ELAD received orphan designation from the FDA and EMA, which provides 7 years of market exclusivity in the United States and 10 in Europe. In addition, under the Patient Protection and Affordable Care Act, ELAD will also receive 12 years of data exclusivity in the United States once it is approved, keeping potential biosimilars off the market during this period.

Aside from these patents and exclusivities, there are substantial trade secrets and know-how pertaining to the maintenance and development of C3A cells, which have been shown to be hard to duplicate. To date, no outside studies have employed immortal human hepatocytes.

Valuation: 12-Month Price Target of $28

In building a probability-adjusted NPV model, we estimate the peak sales of a given drug candidate, its probability of advancing to the next stage of development and eventually reaching the market, and a company's share of revenue and expenses depending on the commercialization plan and/or structure of partnerships, if any. We then calculate the cash flows after adjusting all revenues and expenses with respective cumulative probabilities for each stage. The cash flows are then discounted back using an industry-specific weighted average cost of capital (WACC) of 12% to arrive at a probability-adjusted NPV for each drug candidate. Once we determine the NPV for each candidate, we add net cash and other costs, which include expenses not directly associated with the development of the clinical candidates, to arrive at a fair value estimate for a stock.

In exhibit 6, we summarize our sum-of-the-parts valuation for Vital Therapies. As discussed above, we assign a 70% probability for ELAD to reach the market and estimate peak sales for ELAD in the United States and Europe at $1.3 billion. We value ELAD at $16 per share in the United States and $10 per share in Europe. Adding $2 net cash at the end of 2014, we derive our price target of $28.

Exhibit 6
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	$803,481	Phase III	H2:2016	70%	100%	$340,573	$15.59	55.0%
ELAD system—European Union	$522,530	Phase III	H1:2017	70%	100%	$232,990	$10.66	37.6%
Subtotal						**$573,563**	**$26.25**	**92.6%**
Net Cash at Year-end 2014						$54,592	$2.50	8.8%
Net Present Value of additional Gain (Loss)*						($8,929)	($0.41)	(1.4%)
Sum-of-Parts Fair Value						**$619,227**	**$28.34**	**100.0%**

* Includes costs not directly related to programs above
Sources: Company reports and William Blair & Company, L.L.C. estimates

Key Catalysts Driving Value in the Next 12-24 Months

In exhibit 7, we summarize key upcoming events for Vital Therapies; highlighted rows indicate potential stock-moving catalysts. Over the next 12-24 months, we expect 1) top-line data from the Phase III VTI-208 study in AILD patients in first half 2015; 2) the submission of the BLA to the FDA by year end 2015; 3) top-line data from the Phase III VTI-208 study in severe AAH, a subset of AILD, anticipated in late 2015 or early 2016; 4) top-line data from the Phase II component of the VTI-212 study in FHF and SILF in 2016; and 5) potential FDA approval of the ELAD system by second half 2016.

Exhibit 7
Vital Therapies, Inc.
Clinical Development Timeline and Milestones

Biologic/ Device	ELAD (Extracorporeal Liver Assist Device) System
Indication	**Acute Liver Failure**
Class	**Human-cell-based bioartificial liver support system**
Partner	
Q1:13	Initiation of Phase III VTI-208 study in AILD (March)
Q2:13	
Q3:13	
Q4:13	
Q1:14	
Q2:14	Enroll first patient in Phase III VTI-210 in AAH
Q3:14	
Q4:14	Complete enrollment of Phase III VTI-208 study; Enroll first patient in Phase II component of VTI-212 study in FHF and SILF
Q1:15	Top-line data from Phase III VTI-208 study; Complete enrollment of Phase III VTI-210 study
Q2:15	
Q3:15	Potential submission of ELAD BLA and MAA for the treatment of AILD
Q4:15	
H1:16	Top-line data from Phase III VTII-210 study in AAH; Top-line data from Phase II VTI-212 study in FHF and SILF
H2:16	Potential FDA approval and commercial launch of ELAD in the U.S.
H1:17	
H2:17	Potential EMA approval and European launch of ELAD

Highlighted cells: events likely to affect the stock price
Sources: Company reports and William Blair & Company, L.L.C. estimates

Experienced Management Team

Vital Therapies is led by an experienced management team whose executives have successful track records. In exhibit 8, we summarize the key experience of the top executives.

Exhibit 8
Vital Therapies, Inc.
Management Team

Management	Position	Previous Experience
Terry Winters, Ph.D.	Co-Chairman and Chief Executive Officer	Special Limited Partner of Valley Ventures (concurrently) General Partner of Columbine Venture Funds Vice President of DS Ventures Director of CollaGenex Pharmaceuticals, Inc. Director of Orthologic Corp. Director of Clinuvel Pharmaceuticals
Robert A. Ashley, M.A.	Chief Technical Officer, Executive Vice President	President and Chief Executive Officer of AmpliMed Corp. Senior Vice President of Commercial Development at CollaGenex Pharmaceuticals, Inc.
Duane Nash, M.D., J.D., M.B.A.	Chief Business Officer, Executive Vice President	Vice President/Life Sciences Analyst at Wedbush PacGrow Board of directors of Akebia Therapeutics, Inc. Board of directors of Aerpio Therapeutics, Inc. Attorney at Davis Polk & Wardell LLP
Michael V. Swanson, M.B.A.	Chief Financial Officer	Chief Financial Officer of Amira Pharmaceuticals, Inc. Senior Vice President, Finance and Chief Financial Officer at Prometheus Laboratories Inc. Senior Vice President and Chief Financial Officer of Advanced Tissue Sciences, Inc. Director of Finance of the Fisher Scientific Group, Inc.
Andrew Henry	Vice President of Clinical Operations	Senior Director of Global Clinical Operational Strategy and Senior Director of Clinical Trial Management at MedImmune Senior Director at Schering-Plough Oncology and Novartis Oncology
Andrea Loewen	Vice President of Regulatory Affairs and Quality	Head of Regulatory Affairs for the Shire Regenerative Medicine business Regulatory Affairs at Biogen and Baxter Healthcare
Richard Murawski	Vice President of Manufacturing	Manufacturing at Cytogen, Baxter Healthcare, and Favrille
Aron P. Stern, M.B.A.	Chief Administration Officer	Chief Financial Officer of Protein Polymer Technologies, Inc. Chief Financial Officer of VitaGen, Inc.

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

Key Risks to Our Outperform Rating and Price Target

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 biologic-device combination requiring approval from 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 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.

Understanding Liver Failure

The Functions of the Liver

The liver is the largest internal organ in the body, comprising thousands of lobules, which contain several different types of liver cells. Hepatocytes represent the functional part of the liver, composing 80% of its volume. Hepatocytes perform a multitude of functions, including synthetic, metabolic, and excretory functions.

Overall, the liver performs more than 500 vital functions. The liver supports protein metabolism; processes fats and carbohydrates (sugars); produces cholesterol, triglycerides, and bile; and produces plasma proteins. It acts as the principal site of detoxification, processes poisonous ammonia into urea, regulates blood clotting, and plays a role in fighting infections via the production of immune factors and through the filtration of bacteria, fungi, and viruses from the bloodstream.

Liver Disease and Liver Failure

Unlike other organs, the liver has the distinct ability to regenerate itself if injured. However, if the injury persists, there might not be an opportunity for the liver to recover, leaving it vulnerable to long-term, irreversible damage. Liver injury is generally the result of a viral infection (i.e., hepatitis A, hepatitis B, and hepatitis C) or excessive exposure to poisons or drugs, including alcohol. In the early stages of liver disease, the liver becomes inflamed as a result of infection and tries to repair itself from injury. If the inflammation persists, scarring could result, eventually replacing healthy liver tissue. This process, known as fibrosis, can ultimately prevent blood from flowing through the liver, preventing normal liver function and regeneration. If left untreated, cirrhosis might ensue—a stage whereby the damage is irreversible—ultimately leading to liver failure.

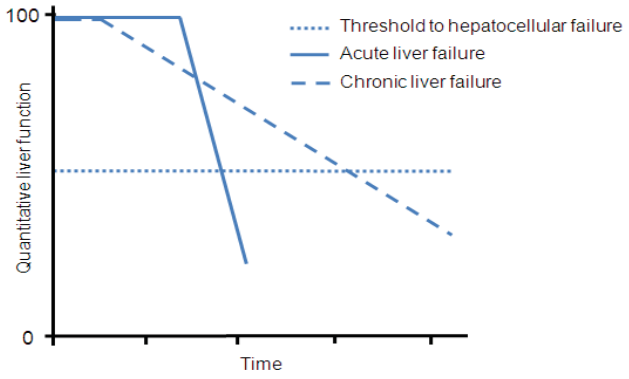
Acute Liver Failure Versus Chronic Liver Failure

Liver failure is classified into two main forms: acute liver failure (ALF) or chronic liver failure (CLF). Specifically, ALF refers to an acute decline of liver function over a period of hours or days following an insult to the liver, either directly (alcohol- and drug-induced) or indirectly (sepsis), in a patient with no underlying disease or previously well-compensated chronic liver disease. When acute liver failure occurs with underlying liver disease, the condition is also termed acute-on-chronic liver failure. By comparison, CLF occurs in decompensated patients because of progressive deterioration attributed to widespread fibrosis or cirrhosis. The main differences between ALF and CLF are the potential for recovery, the occurrence or absence of a precipitating event, and the potential evolution toward multi-organ failure.

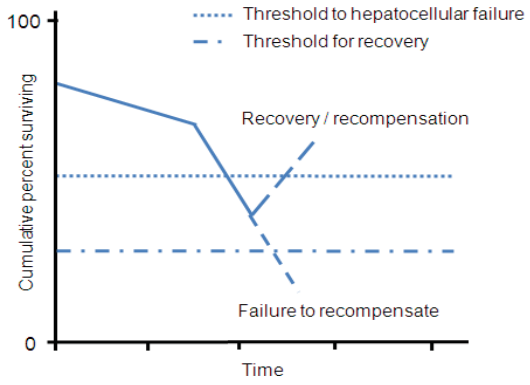
We illustrate the differences between acute and chronic liver failures, with respect to the principal of threshold for recovery, in exhibit 9.

Exhibit 9
Vital Therapies, Inc.
Threshold to Recovery for Liver Failure

a) Quantitative Liver Function: Acute Versus Chronic



b) Survival Based on Threshold for Recovery



Sources: Adapted from Jalan et al. *(Jour of Hepatology* 2012 [57] pp.1336-48); and William Blair & Company, L.L.C.

Background on Acute Liver Failure

Acute liver failure (ALF) is typically characterized by acute liver injury, hepatic encephalopathy, and an elevated prothrombin time/international normalized ratio (used to measure the clotting tendency of blood) in patients with well-compensated livers but without underlying liver disease. The most common early features of the disease include jaundice (yellowing of the skin and eyes), mental status changes, and bleeding. Despite currently available interventions, the short-term mortality rate for ALF remains above 50%. If left untreated, the mortality rate ranges between 60% and 90% in severe cases of the disease. As a result, the timely recognition and management of patients with ALF is critical.

Acute Liver Failure Encompasses a Broad Spectrum

Acute liver failure encompasses a broad spectrum that depends on the underlying liver condition and the source of the injury. There are three main forms of ALF: 1) alcohol-induced liver decompensation (AILD), 2) fulminant hepatic failure (FHF), and 3) surgery-induced liver failure (SILF).

Alcohol-induced liver decompensation. The biggest subgroup of ALF is alcohol-induced liver decompensation (AILD), a life-threatening injury triggered by alcohol that occurs with and without underlying liver disease. Moreover, there are two subgroups: acute alcoholic hepatitis (AAH) and non-acute alcoholic hepatitis (non-AAH). Subjects with AAH have pre-existing liver disease attributed to heavy alcohol consumption, which is further exacerbated by continued alcohol use, leaving a small window for liver regeneration. By contrast, non-AAH occurs in subjects with stable chronic liver disease attributed to viral or autoimmune issue who experience acute liver failure as a result of excessive alcohol consumption. In these patients, the underlying disease might stem from reactivation of hepatitis B or hepatitis C, fungal infection (e.g., spirochetal, protozoal, or helminthic), bacterial infection, or a parasitic infection that invades the liver from other sites. Interestingly, the prevalence of infection is correlated with geography. Alcohol and drugs constitute the majority of the acute insults in the Western Hemisphere, while infectious etiologies predominate in the Eastern Hemisphere.

- *Acute alcoholic hepatitis (AAH):* Alcohol is the major cause of liver cirrhosis in the Western world, accounting for about 44% of the 26,000 cirrhotic deaths each year in the United States. It is estimated that 90%-100% of heavy drinkers present with fatty liver but only 10%-30%

progress to alcohol-induced hepatitis, while 8%-20% develop hepatitis. There are three forms of alcohol liver disease: 1) alcoholic fatty liver (steatosis), 2) acute alcoholic hepatitis (AAH), and 3) alcoholic cirrhosis.

Of the three forms of disease, steatosis is the mildest form of disease; patients present with fatty liver but with normal liver function. Further, abstinence from alcohol consumption generally results in liver regeneration. By contrast, AAH is not as transient as steatosis, partly because of the years of drinking (estimated at 15 to 20 years) associated with the disease. In AAH, hepatocytes undergo necrosis and are accompanied by degeneration. As a result, AAH is associated with a high mortality rate (30% to 60%) with patients quickly deteriorating on hospital admission, but in all patients with alcoholic hepatitis the overall 30-day mortality rate is about 15%. AAH is the precursor to cirrhosis, the most severe form of the disease, where survival is 60%-70% at one year and 35%-50% at five years.

In 2011 in the United States, there were roughly 99,000 hospital admissions related to AAH, and of those, 30,000 are believed to be addressable by ELAD. Generally, the subjects are in their 40s with high mortality rates. Further, these patients are not eligible for transplants because a transplant would require six months of abstinence from alcohol.

- *Non-acute alcoholic hepatitis (non-AAH):* Outside the Western world, hepatitis plays a bigger role in acute liver failure. Alcoholic cirrhosis constitutes 50%-70% of all the underlying liver diseases of acute-on-chronic liver failure (ACLF) in the West and hepatitis B-related cirrhosis constitutes about 10%-15% of all the cases. By contrast, hepatitis B constitutes 70% and alcohol only about 15% of all the etiologies of ACLF in most Asian countries. Given these numbers, hepatitis serological testing is recommended for viral infection regardless of whether another assumed etiology is identified. A closer look at the various forms of hepatitis suggests that infrequent hepatitis A and B are the leading forms, with hepatitis B reactivation the primary source of cases in the United States. Although hepatitis C is the second-largest type of hepatitis, research suggests that hepatitis C alone does not result in acute liver failure. By comparison, hepatitis E is a significant cause of liver failure in areas where the disease is widespread, such as Russia, Mexico, India, and Pakistan.

Fulminant hepatic failure. Fulminant hepatic failure (FHF) is a rare form of ALF with an estimated incidence of about 2,000 cases per year in the United States. FHF is attributed to roughly 6% of all liver failure deaths and accounts for roughly 11%-13% of all liver transplants among adults. FHF is characterized by the development of severe liver injury with impaired synthetic capacity and encephalopathy in patients with a previously normal liver or at least well-compensated liver disease.

In adult patients in the United States, most cases of ALF are related to acetaminophen (e.g., Tylenol) poisoning, severe liver injury from other drugs, viral hepatitis, and shock liver, with other, often undefined etiologies making up the remaining cases. Patients typically present with nonspecific symptoms, including fatigue, malaise, anorexia, nausea, abdominal pain, fever, and jaundice. Progression of symptoms leads to the development of encephalopathy and/or coma, typically preceded by coagulopathy and followed by multisystem organ failure.

To date, liver transplantation is the only effective mode of treatment of FHF. Moreover, transplantation is recommended regardless of etiology and should be considered if patients register an international normalized ratio that reaches 4. A system such as ELAD could help support the patient's liver until a suitable donor is available for liver transplantation.

Surgery-induced liver failure. Surgery-induced liver failure (SILF) is another rare form of acute liver failure that presents in three forms: 1) primary graft nonfunction, 2) small-for-size syndrome or split liver transplant, and 3) cancer resection. Each of these is generally related to surgery whereby

the transplant fails or the transplant or resection results in too small of a liver to function on its own. This type of acute liver failure is unique in that it is not associated with an underlying disease and instead just requires enough time to allow the liver to grow. ELAD might be the only option for these patients to bridge to recovery by providing a few days of outside-the-body liver support.

We estimate the annual numbers of cases in the United States for primary graft nonfunction and split liver transplant ranges between 200 and 300 each. The number of SILF cases related to cancer resection, primarily from colon cancer metastases, could represent a population of more than 10,000 cases per year. We note that annually roughly 45,000 colon cancer patients are diagnosed with metastatic disease to the liver, and despite recent advances in surgical techniques and reduced postoperative mortality, nearly two-thirds of patients are ineligible for surgical intervention—a select proportion them because of the potential risk of SILF onset.

All Other Liver Support Systems Failed in ALF So Far

While liver transplantation is the best treatment for salvaging patients with ALF, as noted earlier, it is not always possible because of donor shortage and eligibility requirements related to age, alcohol, and drug use. As a result, over the past few decades, several companies have tried to design systems to mimic the function of the liver to address the existing unmet medical need associated with ALF. We summarize several of these attempts, including the ELAD system, in the following sections.

Goal of Liver Support Systems
The overall goal of a support device for ALF is to temporarily replace the patient's acutely failing liver to: 1) allow time for recovery of the patient's native liver or 2) bridge the patient to liver transplantation, thereby improving survival.

Subtypes of Liver Support Systems: Artificial Versus Bioartificial
Liver support systems are typically segmented in two categories: artificial and bioartificial systems. Artificial support systems are sorbent-based systems that provide detoxification support without the use of cellular material, whereas bioartificial systems use cellular material, primarily hepatocytes (whether human or of other mammalian origin), to mimic several of the native liver's synthetic functions in addition to detoxification. These hepatocytes are typically used in cartridges in extracorporeal circuits, either with or without sorbent columns.

Review of Support Systems Previously Evaluated in ALF
Artificial support systems previously investigated in ALF patients include Gambro's MARS and Fresenius's Prometheus, while several bioartificial systems have been clinically tested, including Circe Biomedical's HepatAssist, which uses porcine hepatocytes, and Vital Therapies' ELAD system, which uses human hepatocytes. We describe the MARS, Prometheus, and HepatAssist systems below. To our knowledge, no other liver support systems are in clinical trials.

- ***Molecular adsorbents recirculating system (MARS) from Gambro*:** Developed by Gambro, MARS is a two-circuit artificial support system devised to bridge ALF patients to transplantation. The unit removes endogenous albumin-bound toxins, (e.g., bilirubin, bile acids, and aromatic toxins) that accumulate and result in liver failure. In addition to toxin filtration, it reduces the number of pro-inflammatory cytokines TNF-α, IL-10, and IL-6 that might perpetuate the liver damage and extend the inflammatory cascade to other organs. The MARS support system passes blood through a hollow-fiber dialysis module where it is filtered through an albumin-impregnated polysulfone membrane (MARS Flux dialyzer). As blood passes through the membrane, the toxins are released on contact with the membrane according to the concentration gradient and are carried to the other side of the membrane. On the other side of the

membrane, a toxin-enriched albumin solution is passed through a countercurrent buffered exchange where the toxins are cleared through diffusion. The solution is then further purified on line from albumin-bound toxins by the incorporation of unspecific adsorbents, which results in "recycled" albumin.

- ***Prometheus from Fresenius*:** The Prometheus system passes blood through its AlbuFlow column, which is made of polysulfone hollow fibers and is permeable to albumin, thus leaving behind red blood cells and large proteins. The plasma then passes, unlike the MARS system, through two absorbers—a column with neutral resin (prometh01) and a second column with an anion-exchange resin adsorber (prometh02). The bound toxins are captured by direct contact with the high-affinity adsorbing material, with native albumin returning to the circuit. The plasma is returned to the AlbuFlow, where it is rejoined by blood cells that were removed earlier. Lastly, the blood is dialyzed to remove the remaining water-soluble toxins, and the filtered blood is then reintroduced to the patient.

- ***HepatAssist from Circe Biomedical*:** The HepatAssist device works in a three-step process. First, the large proteins and blood cells are separated from the blood, leaving the plasma. The plasma then passes through a charcoal filter, which removes bacteria and particulate matter, followed by an oxygenator. Lastly, the plasma enters the bioreactor, which houses cryopreserved porcine hepatocytes that further filter the plasma. Afterward, the treated plasma and blood cells are reconstituted and returned to the patient.

All Previous Liver Support Systems Failed So Far

Late-stage studies evaluating the MARS, Prometheus, and HepatAssist systems in ALF patients have all failed to show an improvement in overall survival.

- ***MARS and Prometheus fail to demonstrate significant survival benefit in ALF patients.*** Phase III studies evaluating both the MARS and Prometheus systems in ALF patients failed to show an improvement in overall survival. In the Phase III RELIEF study, which evaluated MARS versus the standard therapy, the 28-day transplant-free survival rate in the intent-to-treat (ITT) population was 60.7% for MARS versus 58.9% (p=0.79). In the randomized study evaluating the Prometheus liver support system, the ITT analyses demonstrated a day 28 survival rate of 66% for the Prometheus group, compared with 63% for the control group (p=0.70).

- ***HepatAssist cell-based system also misses survival endpoint but demonstrates trend, offering hope to the bioartificial approach and the ELAD system.*** Lastly, for the Phase II/III study evaluating the HepatAssist in 147 FHF and subfulminant hepatic failure (SHF) patients, the 30-day survival rates were 73% for the HepatAssist arm versus 59% in the control arm (p=0.10). We note that despite the failure, the HepatAssist demonstrated a trend toward 30-day survival, providing rationale for the use of bioartificial approaches to the treatment of ALF and a potential positive read-through, in our opinion, for use of the ELAD system as a treatment option for ALF patients. We illustrate the Kaplan-Meier curves for overall survival from the MARS, Prometheus, and HepatAssist studies in parts a-c of exhibit 10.

Small-Molecule Treatments Have Yet to Demonstrate Proof of Concept

- ***Pentoxifylline and prednisone combo failed to demonstrate survival benefit.*** Along with steroids, pentoxifylline is often used off-label to manage symptoms associated with acute liver failure; penoxifylline is currently approved for the treatment of patients with intermittent claudication on the basis of chronic occlusive arterial disease of the limbs. We note that treatment with penoxifylline has been shown to improve the flow properties of blood by decreasing its viscosity.

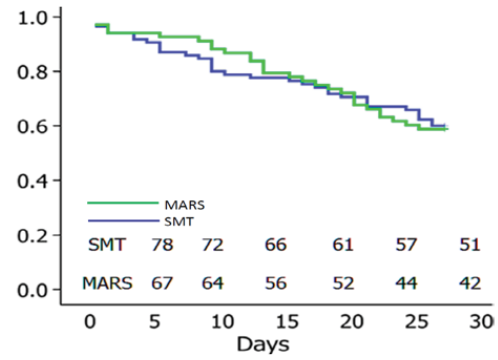
The randomized, double-blind Phase III CorpentoxHAA study evaluated the effectiveness of pentoxifylline in combination with prednisolone compared with prednisolone alone in heavy drinkers with severe biopsy-proven alcoholic hepatitis. Patients enrolled in the study were randomized to receive either the combination of 40 mg of prednisolone daily and 400 mg of pentoxifylline three times a day (n=133) or 40 mg of prednisolone alone (n=137) for 28 days. The primary endpoint of the study was six-month survival; secondary endpoints included response to therapy.

Based on an intent-to-treat analysis, six-month survival was 69.9% for the combination group versus 69.2% for the prednisolone-only group (p =0.91). We illustrate the overlapping survival curves in part d of exhibit 10. In summary, the study suggests a four-week treatment with pentoxifylline and prednisolone, compared with prednisolone alone, did not result in improved survival at six months. Therefore, the lack of difference in survival does not support the combination of the two agents for the treatment of severe alcoholic hepatitis.

- ***Proof-of-concept data for novel small-molecule approaches has yet to be established.*** Emriscan from Conatus, OCR-002 from Ocera, and cardiotrophin-1 from Digna are in clinical development for the treatment of ALF. All of the aforementioned agents have yet to demonstrate definitive improvement in overall survival in ALF patients and we await additional data from these programs to better assess their strategic position versus the ELAD system.

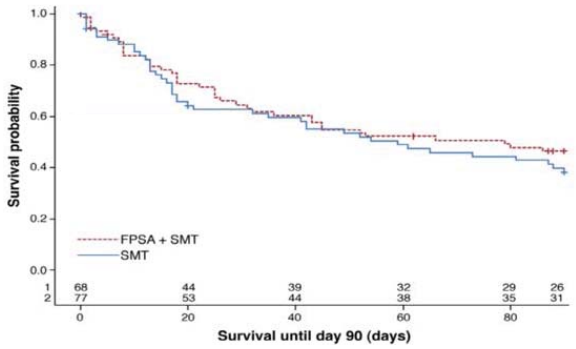
Exhibit 10
Vital Therapies, Inc.
Kaplan-Meier Curves for Overall Survival
From MARS, Prometheus, and HepaMate Liver Support Systems

a) Gambro's MARS: No Improvement in 30-Day Survival



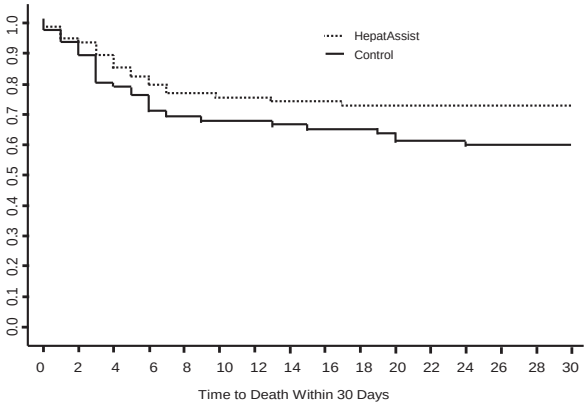
Sources: Adapted from Banares et al. *(Hepatology,* 2012;100:1-10) and William Blair & Company, L.L.C.

b) Fresenius' Prometheus: No Improvement in 90-Day Survival



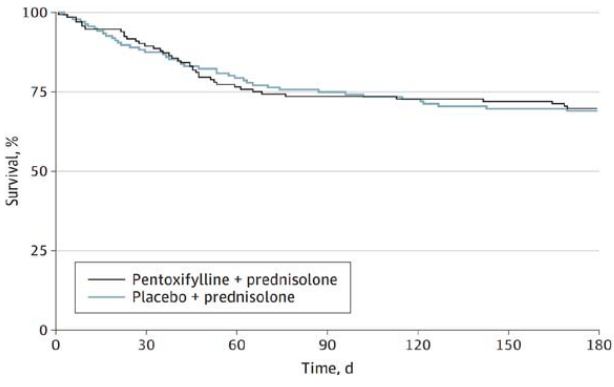
Sources: Adapted from Kribben et al. *(Gastroenterology,* 2012;142:782-789) and William Blair & Company, L.L.C.

c) Circe Biomedical's HepatAssist: Trend in 30-Day Survival



Sources: Adapted from Demetriou et al. *(Annals of Surgery,* 2004; 239:660-70), and William Blair & Company, L.L.C.

d) Pentoxifylline + Prednisolone: No Improvement in 90-Day Survival



Sources: Adapted from Mathurin et al. (*JAMA,* 2013;310[10]:1033-41) and William Blair & Company, L.L.C.

ELAD Poised to Be the First Bioartificial Therapy for ALF

C3A Cells Are a Major Differentiator of ELAD
The C3A cells are the key distinguishing feature of ELAD, setting this system apart from other bioartificial liver systems that have primarily focused on the use of porcine hepatocytes. The long-lasting and consistent performance of the C3A cells is the key to ELAD's potential efficacy. In addition, we note that the use of C3A cells in conjunction with the ELAD system is not patient-specific, making it an allogeneic cellular therapy.

What Differentiates ELAD From Previous Bioartificial Liver Support Systems?
As the liver is an active and dynamic biological system and performs more than 500 functions necessary for human life, an acellular approach that focuses on only one aspect of the liver function is not sufficient to replace the full liver function. We believe a cellular approach is more likely to mimic the key biological complexities of the liver and could have the necessary breadth and dynamic properties to successfully supplement liver function.

Among the two cellular approaches that reached late-stage development, we believe ELAD has a number of key advantages over HepatAssist, which leads us to believe that ELAD is the best-in-class and most promising liver support biologic-device combo developed to date.

- ***The use of human hepatocytes (liver cells) versus porcine hepatocytes.*** Human C3A cells are the closest in properties to functioning hepatocytes. There is much less concern on safety with human cells than with animal cells.

- ***Immunological risk with animal cells.*** Humans have naturally occurring antibodies against porcine antigens, and the antibodies would attack the porcine hepatocytes, causing them to lose function and die. Further, repeated treatment with porcine cells could augment immunological responses and thereby heighten risks.

- ***ELAD uses 11 times more cells than HepatAssist.*** HepatAssist contained approximately 40 grams of pig hepatocytes, while ELAD contains about one pound of human hepatocytes, which represents one-third of the average human liver mass. ELAD provides a much more substantial artificial liver mass, potentially better supplementing liver function.

- ***ELAD offers much longer duration of therapy.*** 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. One HepatAssist cartridge can only be used for six to eight hours per day and a fresh cartridge is needed every day, likely not enough treatment time for the liver to regenerate.

The Power of C3A Cells: The Most Competent Liver Support System
ELAD is the only system to incorporate immortalized human hepatocytes. The C3A cells were derived from the HpeG2 hepatocellular carcinoma cell line, and possess a nontumorigenic epithelial morphology and are highly scalable in cultivation systems, resulting in a seemingly endless supply of commercial material for ELAD cartridges. We note that once assembled into the bioreactor, C3A cells have a shipping duration of up to 60 hours and can be maintained for 50 days in storage.

Most importantly, the cells perform a number of liver-specific functions and produce a variety of major plasma proteins typically produced in the liver. Several key features of the C3A cells include:

- ***Active, functional, cytochrome P-450 enzyme system:*** The C3A cell line has been confirmed to have key hepatocyte properties, such as the presence of a functional cytochrome P450, which is involved in the metabolism of many compounds while producing many liver-specific proteins.

- ***Ability to synthesize major liver proteins while processing toxins and metabolites:*** As the plasma passes through the membrane, it limits the passage of larger proteins, such as immunoglobulins, or cells, such as leukocytes. In addition, the C3A cells synthesize certain liver proteins (e.g., albumin, transferrin, and factors V and VII) while processing toxins and metabolites, such as albumin, bilirubin, and sodium.

- ***However, we note that C3A cells do not entirely mimic the exact behavior of primary human hepatocytes.*** For example, C3A cells are less efficient in processing ammonia; this could be managed by dialysis of excess ammonia out of the system. In addition, C3A cells produce alpha-fetoprotein (AFP), a nontoxic fetal analog of albumin, in large amounts, but should have no negative effect on its function.

- ***The only immortalized human liver cells that are commercially scalable***. Vital Therapies possesses trade secrets and the know-how to culture and expand C3A cells for commercial use.

Major Benefits of ELAD

ELAD provides a unique value proposition that could position the system as the standard of care for ALF patients. Undoubtedly, there is tremendous unmet medical need given the limitations of steroid therapy and the limited number of transplants. We highlight the following key benefits that ELAD provides:

- ***ELAD is significantly less invasive than liver transplantation.*** First, the ELAD procedure does not require surgery. Second, the ELAD system supports the patients for a period of 3-15 days to bridge the patients to recovery or transplant, as compared with a transplant, which takes about seven months and may cost more than $500,000. Unlike transplantation, once ELAD is complete, there is no need for the use of expensive, lifelong immunosuppressants.

- ***ELAD is the only option for those ineligible for a transplant.*** As previously noted, only a limited number of patients are eligible for transplantation, and even then, the process is long and many eligible patients are left without a transplant. With respect to the current standard of care, namely steroids, there is limited success, leaving many with unresolved disease. Given the limitations of existing therapies, ELAD would serve an unmet medical need.

- ***ELAD can be done repeatedly and for long durations.*** Theoretically, a patient such as a SILF patient with too small of a liver to function can be on ELAD for several weeks, giving the liver the necessary time to grow to a functioning state. While the C3A cells are alive and have a limited life (roughly 3 to 10 days per session), the cells can easily be replaced by installing new cartridges in the system, allowing for extended use. In addition, given the ease of use, a patient can undergo two or more treatments.

Logistics and Cost of Goods for the ELAD System

- ***Manufacturing and assembly of ELAD system.*** The company manufactures and assembles the ELAD system in its facility in San Diego. As noted earlier, the ELAD system is composed of the C3A cells, the cartridges, and the ELAD bedside unit; the system contains both reusable and disposable medical device components. The production process to grow the C3A cells takes about six weeks for each patient set of four cartridges; the process is carefully controlled and performed in the company's good-manufacturing-practice (GMP)–compliant production plant. Prior to the shipment of the cartridges, the cells are placed into a dormant state in which they can survive up to 60 hours before use for treatment; the company believes it is capable of shipping the cartridges to all major cities where the ELAD system is likely to be used for the treatment of ALF. We note that once they are produced, the C3A cells have a 50-day lifespan.

The cartridges are supplied by third-party manufacturers. The bedside unit mainly consists of the Sorin heart-lung machine that is repurposed to incorporate ELAD cartridges and circuits. The cost per bedside unit is around $100,000 to $150,000.

- ***Current capacity of manufacturing site and future plans.*** Management has said that its facility has the capacity to support the manufacture of up to 600 four-cartridge treatment units per year. Once it achieves successful Phase III results, the company plans to expand its manufacturing space in San Diego, and it might also build a new manufacturing facility to meet the anticipated commercial demand for ELAD. The company believes that expanding the existing facility to support the manufacture of 4,000 treatment units would require a $10 million capital investment and roughly one year to construct and gain FDA approval. Management noted that a separate facility that could support the manufacture of 10,000 units per year would require an investment of $35 million and could be completed and approved in two to three years.

- ***Minimal on-site preparation for the ELAD system.*** After the treatment facility receives the ELAD cartridges, the cartridges are unpacked on-site by an ELAD system specialist; the units are then attached to the bedside unit and flushed with saline. Following the simple two-hour setup in the hospital, the ELAD cartridges are ready to be used for patient therapy.

- ***Cost of goods sold for the ELAD system.*** We include three major components in our assumption for cost of goods sold for the ELAD system: 1) cartridge costs of roughly $10,000 per unit (four cartridges per unit, or one treatment), 2) costs associated with dedicated specialists assigned to monitoring the ELAD system during therapy of $10,000 per treatment, and 3) associated amortization of $10,000 per treatment. Based on these assumptions, we estimate cost of goods sold of $30,000, or a cost-of-goods rate of roughly 25%, based on our assumption on a course price of $125,000. The cost of goods sold will decrease gradually as the cartridge production cost decreases with scale and as operation of the system transfers from company-hired specialists to center nursing staff.

ELAD Clinical Program

Clinical Experience with ELAD

Prior to the start of the ELAD Phase III clinical program, more than 145 patients with various forms of liver failure had received treatment with the ELAD system, including earlier iterations of the system that were based on the filtration of whole blood. A total of five randomized controlled studies were conducted, evaluating the latest configuration of the ELAD system, which involves circulating only the blood plasma through the cartridges; these studies were conducted across multiple clinical sites in the United States, Europe, and Asia. The studies also identified addressable population for ELAD and clarified inclusion and exclusion criteria for the Phase III programs. We list these completed studies as well as the continuing and proposed Phase III studies for ELAD in exhibit 11.

Exhibit 11
Vital Therapies, Inc.
ELAD System Clinical Program

Study	Phase	Dates	Study Design	Indication	Clinical Sites	Location(s)	Total Subjects Enrolled	Data Expected
VTI-208	**Phase III**	**Initiated March 2013**	**randomized, controlled**	**AILD**	**40+ (planned)**	**U.S., Europe, and Australia**	**200 (planned)**	**H1:2015**
VTI-210	**Phase III**	**Initiated April 2014**	**randomized, controlled**	**AAH**	**25+ (planned)**	**Europe and U.S.**	**120 (planned)**	**H2:2015**
VTI-212	**Phase II/III**	**Expected to begin enrollment in 2014**	**single-arm in Phase II component**	**FHF and SILF**	**15+ (planned)**	**U.S.**	**40 (planned)**	**H1:2016**
VTI-206	Phase IIb	2009 - 2011	randomized, controlled	AILD and other	26	U.S. and Europe	62	--
VTI-201	Phase IIa	2008 - 2009	randomized, controlled	AILD and other	6	U.S.	18	--
VTIC-301	pivotal	2006 - 2007	randomized, controlled	various, primarily viral hepatitis	2	China	69	--
CR-202	Phase II	2002 - 2003	randomized, controlled	FHF	8	U.S. and U.K.	19	--
PS-0698	Phase I	1999 - 2000	randomized, controlled	FHF	6	U.S. and U.K.	25	--

AILD: Alcohol-induced liver decompensation; AAH: Acute alcoholic hepatitis; FHF: Fulminant hepatic failure; SILF: Surgery-induced liver failure
Sources: Vital Therapies, Inc. and William Blair & Company, L.L.C.

Phase IIb VTI-206 Study: Survival Trends Observed in AILD Patients Only

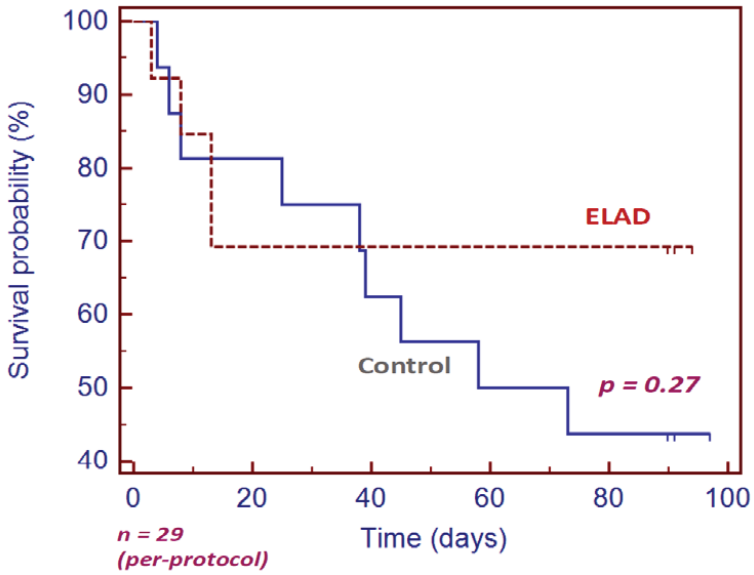
Design and inclusion criteria. Initiated in 2009, the open-label Phase IIb clinical study enrolled and randomized 62 patients with either AILD (n=37) or non-AILD (n=25) into two predefined and separately randomized cohorts. In each of the predefined cohorts, patients were randomized 1:1 to either treatment with ELAD plus standard therapy or standard therapy alone. All patients in the study had MELD scores ranging from 18 to 35. To better inform the Phase III development of ELAD, a secondary endpoint of overall survival at 90 days was adopted into the study.

DSMB recommends discontinuation of non-AILD cohort; VTI-206 terminated. In January 2011, the Data and Safety Monitoring Board (DSMB) for the study reported that only the AILD cohort had the possibility of showing any treatment effect with ELAD; the committee recommended that the non-AILD cohort be discontinued. Following discussions with the FDA, it was determined that the statistical analysis of the study would be negatively affected by the closing of the non-AILD arm, disallowing the VTI-206 study to serve as a pivotal study. As a result, the study was officially terminated in April 2011 to design a new study in AILD patients alone. Of the 25 patients enrolled in the non-AILD group, 12 patients (48%) had chronic alcoholic liver disease as their primary diagnosis.

Proof-of-concept for ELAD demonstrated in AILD patients, although signal weak. In total, 37 patients had been enrolled and randomized in the predefined AILD group, with 16 patients randomized to the ELAD arm and 21 to the control arm. After the elimination of 8 subjects under predefined criteria (baseline failure, withdrawn consent, lost to follow-up, and fewer than 72 hours of therapy), per protocol analysis of the study was based on 29 patients, with 13 ELAD and 16 control patients. Results from the subset showed a nonsignificant trend (p=0.27) in improvement in 90-day survival favoring the ELAD-treated group compared with control, with 90-day survival of 69.2% and 43.8%, respectively. The median survival for the ELAD-treated group was over 100 days, compared with

65 days for the control group. No ELAD-treated patient died following 12 days on study, and one ELAD-treated patient had a transplant at 90 days; no control patients underwent transplant. We illustrate the Kaplan-Meier survival curves in exhibit 12.

Exhibit 12
Vital Therapies, Inc.
Kaplan-Meier Curves for Overall Survival From
Phase II VTI-206 Study: Alcohol-Induced Liver Decompensation (AILD)

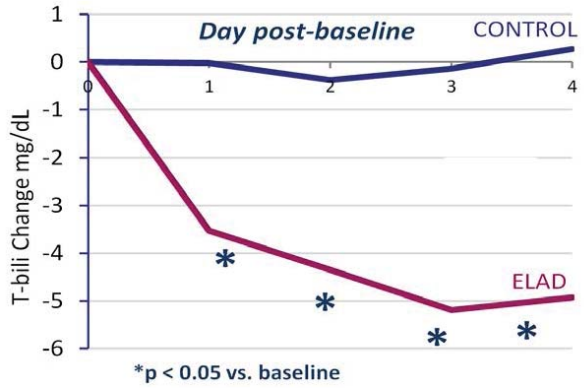


Source: Vital Therapies, Inc.

Biomarker analyses support ELAD's treatment effect in AILD patients. Several clinical laboratory measurements, including bilirubin, serum sodium, and creatinine, were also monitored in the study. Analyses of these laboratory measurements showed that patients treated with the ELAD system demonstrated positive trends that are consistent with improvement in liver function; both the change in bilirubin and the percentage change in sodium associated with the ELAD system were statistically significant compared with the control. We note that 1) bilirubin processing is a typical marker of active liver function; 2) reductions in serum sodium frequently occur in patients with liver failure; and 3) creatinine is a biomarker of kidney failure, which is often induced by liver failure. We illustrate the trends observed from these biomarkers in exhibit 13.

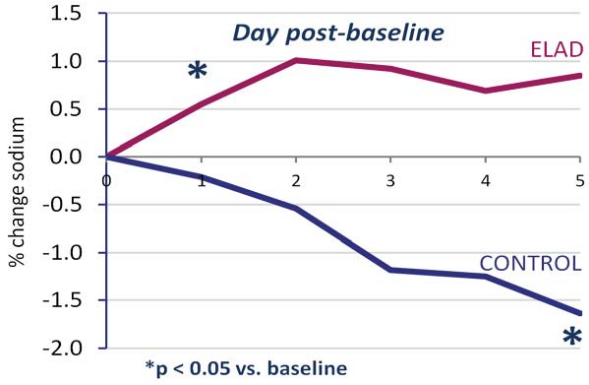
Exhibit 13
Vital Therapies, Inc.
Results From Phase II VTI-206 Study: Biomarkers

a) Change in Bilirubin



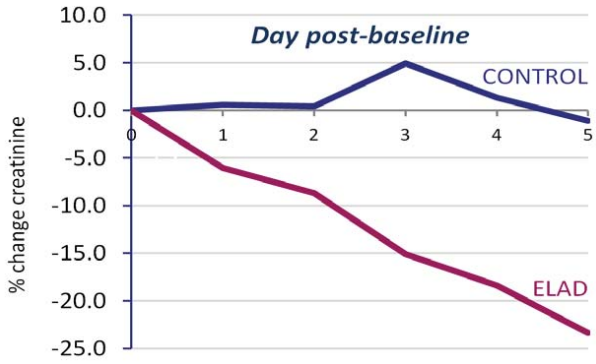
Source: Vital Therapies, Inc.

b) Percent Change in Sodium



Source: Vital Therapies, Inc.

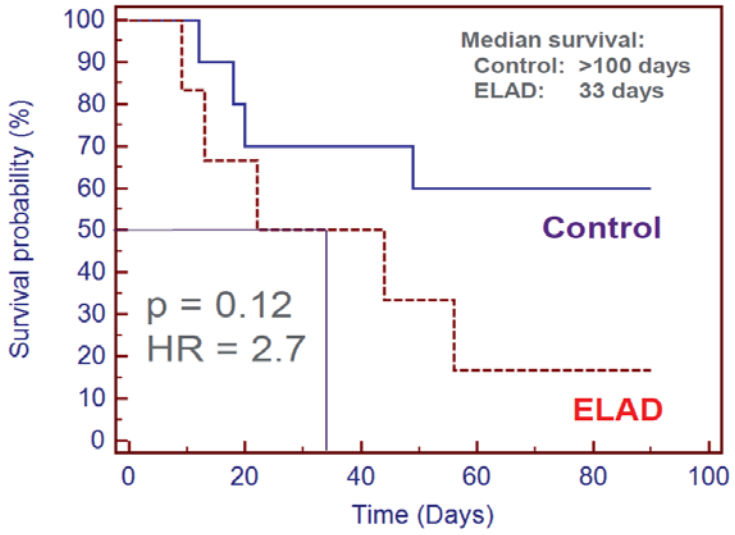
c) Percent Change in Creatinine



Source: Vital Therapies, Inc.

Differences in survival in non-AILD patients not statistically significant (exhibit 14), likely because the livers are not regenerable; non-AILD patients are excluded from Phase III studies. As previously noted, the non-AILD cohort of the study was discontinued based on the poor prospects that any treatment effect would be observed. Analysis of the 16 patients included in the per-protocol analysis for overall survival (6 patients from the ELAD-treated cohort and 10 patients in the control arm) showed no difference in 90-day survival between the two arms (p=0.12), with 17% and 60% of ELAD-treated and control patients alive at day 90, respectively. We note that the median survival for the ELAD-treated arm was 33 days, compared with over 100 days for the control arm. ELAD did not demonstrate an effect in non-AILD patients, likely because the livers of these patients are not readily regenerable. As a result, non-AILD patients are excluded from the Phase III studies. We illustrate the 90-day survival for non-AILD patients in exhibit 14, on the following page.

Exhibit 14
Vital Therapies, Inc.
Kaplan-Meier Curves for Overall Survival From
Phase II VTI-206 Study: Non-Alcohol-Induced Liver Decompensation (Non-AILD)



Source: Vital Therapies, Inc.

No unexpected safety issues; no definitive treatment-related SAEs. The DSMB did not detect any differences in the rates of serious adverse events (SAEs) between the ELAD-treated and control cohorts, and the SAEs in the study were reflective of the severity of disease and co-morbidities of the patient population. In total, there were 67 SAEs reported by 35 patients, of which 6 were reported as possibly related to ELAD, including cases of hematemesis (vomiting blood), kidney failure, bleeding, sepsis, and intravascular hemolysis.

Phase IIa VTI-201 Study: Establishing the New ELAD System

Objectives and results. Before the VTI-206 study, the company completed a small, randomized study enrolling 18 patients with AILD and non-AILD; the study was performed between 2008 and 2009. The goals of the study were to 1) establish the safety of the modified ELAD, 2) define enrollment criteria for future studies, and 3) assess the logistics of conducting a large study in the United States and Europe. The study established the ELAD system's safety while providing preliminary evidence of the ELAD system's potential efficacy in the patient population. In total, there were 39 SAEs reported by 11 patients, with only 2 events possibly treatment-related: reduction in the number of blood cells and reduction in the number of blood platelets.

Phase I PS-0698 and Phase II CR-202 Studies: Meta-Analysis Demonstrates Survival Trend in FHF

Design and inclusion criteria. The Phase I study enrolled 25 FHF subjects at six centers across the United States and the United Kingdom. The first 6 subjects were treated with ELAD and the remaining 19 were split into two groups: 1) 10 were treated with ELAD and 2) 9 were control subjects. For CR-202, another 19 FHF subjects were enrolled in the open-label Phase II study with 13 subjects treated with ELAD and the remaining 6 given standard of care. The endpoint for both studies was 30-day overall survival.

Results. In study PS-0698, patients enrolled were so severely ill that many did not survive the first few days. Some of the control subjects died within the first five days of the study as compared with some transplant subjects, who received their transplant in the same time frame. ELAD did not have any effect on outcome in this study.

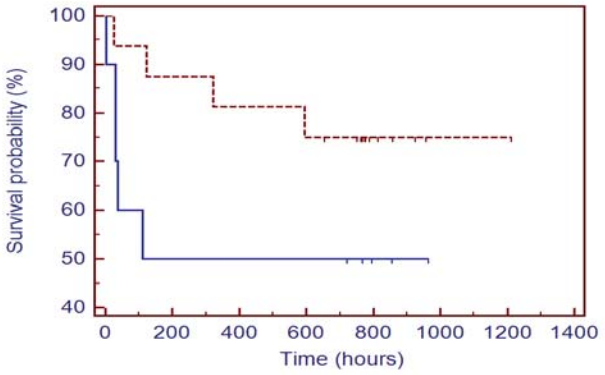
For CR-202, no intergroup differences in mortality were observed either. A higher percentage of treated subjects versus control, 54.5% versus 16.7%, received transplants. We note that neither study was designed to demonstrate a statistically significant improvement in overall survival or bridge-to-transplant/recovery (BTT/R).

Given the limitations, a post hoc meta-analysis was performed on the two studies to better understand the overall treatment effect. While ELAD did not demonstrate any benefit in survival for patients who were not listed for transplant, it demonstrated a trend in 30-day survival for patients who were listed for one. As illustrated in exhibit 15a, 30-day survival rates for ELAD-treated subjects compared with control were 75% versus 50%, respectively (p=0.12).

Further, Kaplan-Meier curves comparing success at the bridge to transplant/recovery (BTT/R) endpoint suggest an increased benefit for ELAD-treated subjects (p=0.06), as illustrated in exhibit 15b. Lastly, a chi-squared analysis of the BTT/R status of subjects at the end of the study demonstrated a statistically significant benefit favoring ELAD-treated subjects versus control subjects (p=0.03).

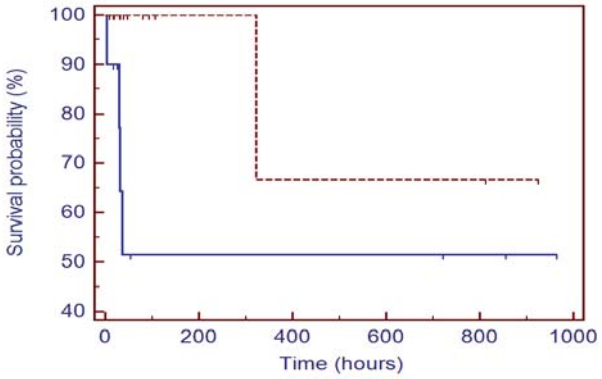
Exhibit 15
Vital Therapies, Inc.
Results of Meta-Analysis From Phase II PS-0698 and CR-202 Studies

a) Overall Survival Based on Meta-Analysis



Source: Vital Therapies, Inc.

b) Bridge-to-Transplant/Recovery (BTT/R)



Source: Vital Therapies, Inc.

Phase II VTIC-301 Study: China Study Demonstrates Significant Improvement in Survival and Robust Three- and Five-Year Follow-up Data

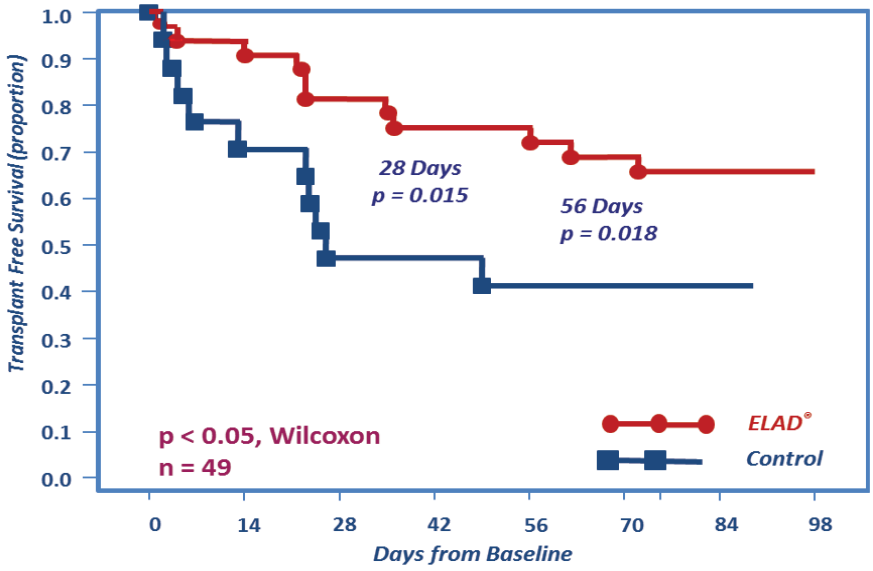
Design and inclusion criteria. The randomized, controlled, open-label Phase II study was designed to enroll 120 subjects at two Beijing hospitals, but enrollment was terminated by the ethics committee as a significant overall survival benefit was observed with the ELAD arm. The majority of enrolled patients were experiencing an acute flare-up of viral hepatitis that led to liver failure.

Eventually the study enrolled 68 patients; a key inclusion criterion was that the patients had expected a 50% chance of death by 84 days. After enrollment of the first 49 subjects, key inclusion criteria were changed, reducing the severity of disease, and in addition, a shorter ELAD treatment period was recommended. Given the revision, two separate analyses were performed. The first included the original 49-patient subset and the second included the full population comprising the 68 patients.

Results. Analysis of the first 49 subjects revealed the following: 1) there was a statistically significant difference between 28-day and 56-day survival (p=0.015 and 0.018, respectively); 2) there was a statistically significant difference in 84-day survival (p=0.049); 3) there were no unexpected safety issues; and 4) the three-year and five-year transplant-free survival benefit persisted in a statistical significant fashion. We illustrate transplant-free survival curves for the 49 subjects in the VTIC-301 study in exhibits 16 and 17, on the following page.

An analysis of the total population of 68 patients suggests the following: 1) significant differences in 28-day and 56-day survival (p=0.014 and 0.034, respectively), 2) no significant differences in 84-day survival, and 3) no unexpected safety issues. This illustrates the importance of enrolling the right patient population for the study to be successful; the patient population should be neither too sick nor too healthy.

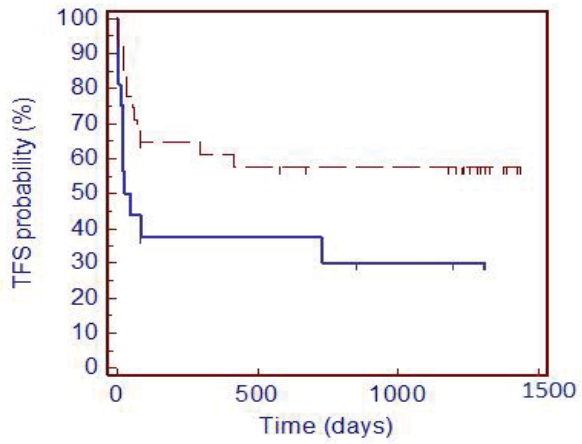
Exhibit 16
Vital Therapies, Inc.
Kaplan-Meier Curves for Transplant-Free Survival From Phase II VTIC-301 Study: Acute Flare Hepatitis



Source: Vital Therapies, Inc.

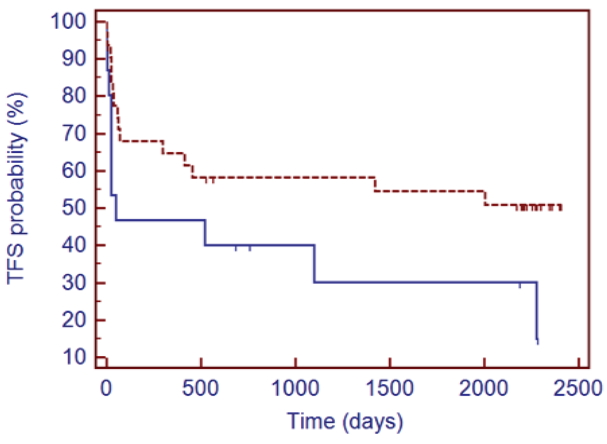
Exhibit 17
Vital Therapies, Inc.
Follow-Up Results From Phase II VTIC-301 Study: Acute Flare Hepatitis

a) Transplant-Free Survival: Three-Year Follow-up



Source: Vital Therapies, Inc.

b) Transplant-Free Survival: Five-Year Follow-up



Source: Vital Therapies, Inc.

ELAD Phase III Clinical Development Strategy

As noted earlier, Vital Therapies is enrolling two Phase III studies in patients with ALF. The first study is in patients with AILD, and the second study is in patients with AAH, a subset of AILD. In addition, the company plans to initiate a Phase II/III study to evaluate the ELAD system in patients with FHF and SILF. We review the various studies of the ELAD system clinical development program below.

Phase III VTI-208 Study Primarily in U.S. AILD Patients

The primary endpoint is overall survival through day 90 using a Kaplan-Meier survival analysis; secondary endpoints of the study include overall survival at 28 days and 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. As of the end of April, 100 of the 200 expected patients have been enrolled in VTI-208. We anticipate top-line data from the study by mid-2015.

- ***Tightening inclusion and exclusion criteria to enhance success rate.*** We note that the VTI-208 study is based on the analysis of the Phase II VTI-206 study. To increase the likelihood of success of the VTI-208 study, management incorporated several adjustments to the study protocol for the VTI-208 study. We compare and contrast the differences in inclusion and exclusion criteria for the Phase III VTI-208 and the Phase II VTI-206 studies in exhibit 18.

Exhibit 18
Vital Therapies, Inc.
Comparison of Inclusion and Exclusion Criteria From Phase III VTI-208 Study and Phase II VTI-206 Study

	VTI-208 Phase III	
	Inclusion Criteria	**Exclusion Criteria**
General Design Characteristics	Designed to select AAH/AILD patients with an expected mortality rate of 50%	Designed to avoid patients with nonregenerable liver; Designed to avoid patients who are spontaneously getting better; Designed to avoid patients who are deteriorating too quickly
New Criteria vs. VTI--206	Maddrey Discrimination Function >32 *	Liver size less than 10 cm or 750 cc; Improvement in bilirubin levels of 20% or more in past 72 hours; AST greater than 500 IU/L
Modified Criteria vs. VTI-206 †	--	Systolic blood pressure <90 mm Hg or mean arterial pressure <60 mm Hg; Hemorrhage requiring 2 units of packed red blood cells
Retained Criteria from VTI-206	MELD Score 18 - 35 **	--

* Classification that stratifies patients for risk of mortality and use of steroids—a score >32 indicates severe alcoholic hepatitis

** Scoring system for assessing the severity of chronic liver disease—a score between 30 and 39 indicates a 3-month mortality of 52.6%

† Modified from VTI-206 to provide lower barrier to exclusion

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

- ***Addressing the FDA's concerns regarding potential bias of the Phase III VTI-208 study.*** The FDA has expressed concerns regarding the open-label design of the VTI-208 study, in particular questioning whether the study would provide convincing evidence of efficacy if there are significant differences in how the ELAD system and control patients are treated during the treatment period and after hospital discharge. The agency noted that the length of hospital stay, rates of hospital re-admission, alcohol recidivism rates, nutritional support, and use of concomitant medications could significantly confound the study results and call into question whether any demonstrated difference in overall survival would be attributed to ELAD therapy or the aforementioned factors.

  As a result, the company has developed a protocol to minimize this bias and provide evidence that no meaningful difference between the groups could significantly confound the study data. Select protocol revisions include: 1) defining a protocol-specific standard of care; 2) specifying steroid treatment; 3) standardizing the discharge criteria for both patient cohorts; 4) requiring that follow-up visits be conducted by blinded reviewers; 5) ensuring home healthcare nurses and other personnel are unaware of treatment assignment; and 6) monitoring concomitant medications, alcohol recidivism, and interaction with the healthcare system.

Phase III VTI-210 Study in Steroid-Refractory Acute Alcoholic Hepatitis (AAH) Patients, Primarily in Europe

Initiated in April 2014, the study will enroll 120 AAH patients who have failed at least seven days but no more than nine days of steroid therapy, according to predefined criteria. The primary endpoint is overall survival at 90 days; the secondary objective 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. We anticipate complete enrollment in the study by mid-2015 and top-line data by late 2015 or early 2016.

Phase II/III Study in Patients With Fulminant Hepatic Failure (FHF) or Surgery-Induced Liver Failure (SILF)

Vital Therapies also plans to initiate the Phase II single-arm portion of Study VTI-212 by year end 2014, targeting to enroll 40 patients with FHF or SILF. The planned primary endpoint of the Phase II component 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 by 2015 or 2016. We note that results from the Phase II portion of the study may 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 after analysis of the Phase II component.

Exhibit 19
Vital Therapies, Inc.
Income Statement
(dollars in thousands)

	2012A	2013A	2014E					2015E	2016E
			Q1E	Q2E	Q3E	Q4E	FY:14E		
Revenues									
ELAD US revenues	$0	$0	$0	$0	$0	$0	$0	$0	$4,829
ELAD OUS revenues	-	-	-	-	-	-	-	-	-
Collaboration and licensing revenue	-	-	-	-	-	-	-	-	-
Contract and grant revenue	-	-	-	-	-	-	-	-	-
Total Revenues	-	-	-	-	-	-	-	-	4,829
Expenses									
COGS	-	-	-	-	-	-	-	-	966
R&D expense	5,097	21,787	6,536	6,863	7,206	7,566	28,171	32,745	36,487
SG&A expense	4,483	9,615	2,885	2,913	2,942	2,972	11,712	12,188	21,524
Total Operating Expenses	9,580	31,402	9,421	9,776	10,149	10,538	39,884	44,933	58,977
Operating Income	(9,580)	(31,402)	(9,421)	(9,776)	(10,149)	(10,538)	(39,884)	(44,933)	(54,148)
Interest income	4	5	4	3	5	4	16	21	46
Interest expense, net	(413)	-	-	-	-	-	-	-	-
Other (expense) income, net	7	(15)	-	-	-	-	-	-	-
Revaluation of preferred stock warrant liabilities	180	-	-	-	-	-	-	-	-
Revaluation of future purchase rights liabilities	3,101	(1,306)	-	-	-	-	-	-	-
Total Other Income (expense)	(6,701)	(32,718)	(9,417)	(9,773)	(10,144)	(10,534)	(39,868)	(44,911)	(54,102)
Pretax income/(loss)	(6,701)	(32,718)	(9,417)	(9,773)	(10,144)	(10,534)	(39,868)	(44,911)	(54,102)
Other comprehensive gain/(loss)	-	(64)	-	-	-	-	-	-	-
Accretion to redemption value of redeemable convertible preferred stock	(942)	(6,303)	-	-	-	-	-	-	-
Provision for income taxes/(income)	-	-	-	-	-	-	-	-	-
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income/(Loss)	**(7,643)**	**(39,085)**	**(9,417)**	**(9,773)**	**(10,144)**	**(10,534)**	**(39,868)**	**(44,911)**	**(54,102)**
GAAP EPS	**($17.89)**	**($3.14)**	**($0.57)**	**($0.47)**	**($0.46)**	**($0.48)**	**($1.97)**	**($1.58)**	**($1.59)**
Weighted average shares outstanding, diluted	427	10,009	16,600	20,800	21,825	21,850	20,269	28,425	34,070

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

Exhibit 20
Vital Therapies, Inc.
Balance Sheet
(dollars in thousands)

	2012A	2013A	2014E					2015E	2016E
			Q1E	Q2E	Q3E	Q4E	FY:14E		
Current assets									
Cash and cash equivalents	$4,477	$38,186	$28,894	$50,020	$40,001	$29,592	$29,592	$93,311	$213,963
Restricted Cash	355	963	1,063	1,163	1,263	1,363	1,363	1,763	2,163
Short-term investments, available-for-sale	13,996	-	-	25,000	25,000	25,000	25,000	75,000	100,000
Accounts receivable	-	-	-	-	-	-	-	-	-
Inventories, net	-	-	-	-	-	-	-	-	-
Prepaid and other current assets	-	-	-	-	-	-	-	-	-
Deferred financing costs, current portion	-	3,506	3,506	3,506	3,506	3,506	3,506	3,506	3,506
Other current assets	320	1,200	1,400	1,600	1,800	2,000	2,000	2,800	3,600
Total current assets	19,148	43,855	34,863	81,289	71,570	61,461	61,461	176,380	323,232
Property and equipment, net of accumulated depreciation	1,184	2,467	2,717	2,967	3,217	3,467	3,467	6,517	14,042
Deposits	-	-	-	-	-	-	-	-	-
Deferred financing costs, less current portion	-	-	-	-	-	-	-	-	-
Other assets	-	263	263	263	263	263	263	263	263
Total assets	**20,332**	**$46,585**	**$37,843**	**$84,519**	**$75,050**	**$65,191**	**$65,191**	**$183,160**	**$337,537**
Current liabilities		-2794							
Accounts payable	1,144	1,224	1,474	1,724	1,974	2,224	2,224	4,224	6,224
Accrued liabilities	601	3,395	3,645	3,895	4,145	4,395	4,395	6,395	8,395
Long-term debt and obligations, current portion	-	-	-	-	-	-	-	-	-
Total current liabilities	1,745	7,446	7,946	5,846	6,346	6,846	6,846	10,846	14,846
Other long-term liabilities	43	321	321	321	321	321	321	321	321
Deferred revenue, net of current	-	-	-	-	-	-	-	-	-
Loan payable, less current portion	-	-	-	-	-	-	-	-	-
Redeemable convertible preferred stock warrant liability	-	-	-	-	-	-	-	-	-
Total liabilities	**1,788**	**7,767**	**8,267**	**6,167**	**6,667**	**7,167**	**7,167**	**11,167**	**15,167**
Stockholders' equity	(7,632)	(44,657)	(53,899)	78,352	68,383	58,024	58,024	171,993	322,370
Convertible preferred stock	26,176	83,475	83,475	-	-	-	-	-	-
Total liabilities, convertible preferred and stockholders' equity	**$20,332**	**$46,585**	**$37,843**	**$84,519**	**$75,050**	**$65,191**	**$65,191**	**$183,160**	**$337,537**

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

Exhibit 21
Vital Therapies, Inc.
Statement of Cash Flows
(dollars in thousands)

	2012A	2013A	2014E	2015E	2016E
Net cash from operating activities					
Net Income (Loss)	**(6,701)**	**(32,718)**	**(39,868)**	**(44,911)**	**(54,102)**
Adjustments					
Depreciation and amortization	651	799	867	1,629	3,511
Stock-based compensation costs	144	948	350	480	720
Non-cash interest expense	382	-	-	-	-
Revaluation of preferred stock warrant liabilities	(180)	-	-	-	-
Revaluation of future purchase rights liabilities	(3,101)	1,306	-	-	-
Deferred rent	43	(16)	(15)	(15)	(15)
Gain-on sale of equipment	(7)	-	-	-	-
Other	(2)	(1)	-	-	-
Change in Operating Assets and Liabilities					
Other assets and prepaid expenses	(242)	(1,141)	(800)	(800)	(800)
Accounts payable	(219)	(91)	1,000	2,000	2,000
Accrued expenses	(12)	2,266	1,000	2,000	2,000
Net cash used in operating activities	**(9,244)**	**(28,648)**	**(37,466)**	**(39,617)**	**(46,686)**
Cash flows from investing activities					
Purchase of short-term investments	(13,992)	(2,999)	(40,000)	(75,000)	(75,000)
Sales of short-term investments	-	17,000	15,000	25,000	50,000
Proceeds from sale of equipment	20	-	-	-	-
Restricted cash	(355)	(608)	(400)	(400)	(400)
Purchase of property and equipment	(261)	(1,484)	(1,000)	(3,050)	(7,525)
Net cash used in (provided by) investing activities	**(14,588)**	**11,909**	**(26,400)**	**(53,450)**	**(32,925)**
Cash flows from financing activities					
Proceeds from debt, net of issuance costs	6,934	-	-	-	-
Deferred financing costs	-	(3,112)	(1,500)	-	-
Principal payments on term loan	(533)	-	-	-	-
Proceeds from issuance of common stock	-	-	58,374	157,920	203,040
Proceeds from issuance of preferred stock, net of issuance costs	21,100	53,195	-	-	-
Proceeds from exercise of stock options	-	135	700	960	1,440
Proceeds from early exercise of stock options	-	227	-	-	-
Net cash provided by financing activities	**27,501**	**50,445**	**57,574**	**158,880**	**204,480**
Effect of exchange rate changes on cash and cashequivalents	5	3	-	-	-
Cash balance (Beginning of Period)	**803**	**4,477**	**38,186**	**31,894**	**97,707**
Difference	3,674	33,709	(6,292)	65,813	124,869
Cash balance (End of Period)	**4,477**	**38,186**	**31,894**	**97,707**	**222,575**
Marketable securites	**-**	**-**	**22,698**	**70,604**	**91,388**
Cash balance plus marketable securities (end of period)	**4,477**	**38,186**	**54,592**	**168,311**	**313,963**

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

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DJIA:	16,550.97
S&P 500:	1,875.63
NASDAQ:	4,051.50

The prices of the common stock of other public companies mentioned in this report follow:

Conatus Pharmaceuticals Inc.	$5.32
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