

VITAL THERAPIES INC  
Form 10-K  
March 20, 2015  
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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**WASHINGTON, D.C. 20549**

**FORM 10-K**

(Mark One)

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

**For the fiscal year ended December 31, 2014**

**or**

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

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission File Number: 001-36201**

**Vital Therapies, Inc.**

**(Exact name of registrant as specified in its charter)**

**Delaware**  
**(State or other jurisdiction of**  
**incorporation or organization)**

**56-2358443**  
**(IRS Employer**  
**Identification No.)**

**15010 Avenue of Science, Suite 200, San Diego,**  
**California**

**92128**

**(Address of principal executive offices)**

**(Zip Code)**

**Registrant's telephone number, including area code: (858) 673-6840**

**Securities registered pursuant to Section 12(b) of the Act:**

**Title of Each Class**  
**Common Stock, par value \$0.0001 per share**

**Name of Each Exchange on Which Registered**  
**The NASDAQ Stock Market LLC**

**(The NASDAQ Global Market)**

**Securities registered pursuant to Section 12(g) of the Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐  
Non-accelerated filer ☒ (Do not check if a smaller reporting company) Smaller reporting company ☐  
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the  
Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting stock held by non-affiliates of the registrant, based on the closing sale price of the registrant's common stock on June 30, 2014, the last business day of the registrant's most recently completed second fiscal quarter, as reported on The NASDAQ Global Market, was approximately \$399.1 million. Shares of common stock held by each executive officer and director and by each person who owns 10% or more of the outstanding common stock, based on filings with the Securities and Exchange Commission, have been excluded from this computation since such persons may be deemed to be affiliates of the registrant. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

There were 23,993,389 shares of the registrant's common stock, \$0.0001 par value per share, outstanding as of February 27, 2015.

#### **DOCUMENTS INCORPORATED BY REFERENCE**

None.

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**Vital Therapies, Inc.**

**ANNUAL REPORT ON FORM 10-K**

**For the Fiscal Year Ended December 31, 2014**

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**Special Note Regarding Forward-Looking Statements**

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities and Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management, and are contained principally in the sections entitled Business, Risk Factors, and Management's Discussion and Analysis of Financial Condition and Results of Operations. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as anticipates, believes, could, seeks, estimates, expects, intends, may, potential, predicts, projects, should, will, would or similar expressions and the negatives of those terms.

These forward-looking statements include, among other things, statements about:

the initiation, cost, timing and results of our clinical programs for the ELAD® System;

the timing of, and our ability to obtain and maintain regulatory approvals for the ELAD System;

regulatory developments in the United States and foreign countries;

the potential market for the ELAD System;

the rate and degree of market acceptance and clinical utility of the ELAD System;

our commercialization, marketing and manufacturing capabilities and strategy;

our plans to improve the ELAD System;

our plans to explore other uses for our VTL C3A cells;

our plans to obtain funding for our operations;

the performance of third parties in connection with the development of the ELAD System, including third parties involved in our clinical trials and third-party suppliers;

the development, regulatory approval, efficacy and commercialization of competing products;

our ability to retain key scientific or management personnel;

our intellectual property position;

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;  
and

our ability to achieve and maintain effective internal control over financial reporting.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements including those described in Risk Factors and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this Annual Report. You should read this Annual Report and the documents that we reference in this Annual Report and have filed with the Securities and Exchange Commission, or SEC, as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

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**PART I**

**Item 1. Business.**

**Overview**

We are a biotherapeutic company focused on developing a cell-based therapy targeting treatment of all forms of acute liver failure. Our product candidate, the ELAD<sup>®</sup> System, is an extracorporeal bio-artificial liver therapy designed to allow the patient's own liver to regenerate to a healthy state, or to stabilize the patient until transplant. The ELAD System is the only bio-artificial liver support system containing immortal human liver-derived cells, or C3A cells, to enter Phase 3 clinical trials. We designed the ELAD System to supplement key aspects of normal liver function to improve patient survival. We estimate that at least 40,000 patients annually in the United States, or U.S., experience forms of acute liver failure, such as acute-on-chronic, surgery-induced and fulminant liver failures, for which the ELAD System may be a life-saving therapy. Outside of liver transplant, which is severely limited by the availability of organs and not available to many patients, the current standard of care for acute liver failure is primarily focused on the management of complications, which does not restore lost liver function and is associated with a high rate of mortality. The ELAD System has received orphan designation in the U.S. and Europe for the treatment of patients with acute liver failure. This designation provides tax credits for qualified clinical testing, seven years of market exclusivity in the U.S., and ten years of market exclusivity in Europe for the first orphan drug approved for a given indication. However, orphan designation does not alter the standard regulatory requirements or the process for obtaining marketing approval.

We currently have three ongoing clinical trials involving the ELAD System including our leading Phase 3 clinical trial in subjects with alcohol-induced liver decompensation, or AILD, a second Phase 3 clinical trial for subjects with severe acute alcoholic hepatitis, or SAAH, and a Phase 2 clinical trial for subjects with fulminant hepatic failure, referred to as FHF, and surgery-induced acute liver failure, referred to as SILF.

In March 2013, we initiated VTI-208, a Phase 3 randomized, controlled, open-label clinical trial with a targeted enrollment of 200 subjects with alcohol-induced liver decompensation. The primary endpoint of VTI-208 is overall survival up to at least study day ninety-one. The VTI-208 clinical trial completed enrollment in January 2015 with 203 subjects having been enrolled at 40 clinical sites in U.S., United Kingdom, or U.K., and Australia. We expect to report topline results from the VTI-208 clinical trial in the third quarter of 2015. This is a quarter later than we had previously projected due to our decision to wait until the database is locked before any analysis of the results, rather than starting the analysis after the last patient enrolled has completed up to at least the study day ninety-one survival period. After dialogue with regulatory authorities, we decided that an earlier analysis carries a risk of compromising the data and, therefore, decided to wait for database lock to be safe. If the study is statistically and clinically successful, we expect to submit a Biologics License Application, or BLA, to the U.S. Food and Drug Administration, or FDA, in the first half of 2016.

We have obtained regulatory allowance in the U.S., U.K., Germany and Spain to enroll subjects, and have commenced enrollment, in our second Phase 3 randomized, controlled, open-label clinical trial, VTI-210, in subjects with SAAH who we believe are at a substantially increased risk of mortality. We previously received regulatory guidance from the Scientific Advice Working Party, or SAWP, of the European Medicines Agency, or EMA, on VTI-210 and, based on such guidance, we modified the trial protocol to expand enrollment to SAAH diagnosed without biopsy and to stratify subjects into groups based on SAAH diagnosis either by biopsy or on clinical grounds without biopsy. Subsequently, based on the results of a third party U.K. study, we also modified the VTI-210 trial protocol to allow subject enrollment independent of steroid administration. The statistical plan for VTI-210 provides for an event-driven clinical design (a statistical plan that allows the study sample size to be adjusted according to

aggregate mortality) with a minimum of 150 subjects. The primary endpoint of VTI-210 is overall survival up to at least study day ninety-one. As of March 18, 2015, we had enrolled six subjects in VTI-210 and 18 clinical sites were open for enrollment. We currently project having database lock and topline results from the VTI-210 clinical trial in early 2017, again a quarter later than previously expected due to waiting for database lock to initiate the analysis.

The VTI-208 and VTI-210 clinical studies are designed to complement each other and to confirm study outcomes, and the studies may both be used to support product registration in the U.S. and the European Union, or EU. We designed VTI-208 with input from the FDA to support product registration in the U.S. In addition, based upon discussions with the FDA, we believe the VTI-208 clinical study, if successful from both a statistical and clinical standpoint, may support product registration in the U.S. on a stand-alone basis. However, according to the FDA, a second confirmatory clinical trial that substantiates positive results may be necessary to support a BLA. Similarly, we designed VTI-210 with input from the EMA to support product registration in the EU. Based upon our discussions with the European regulatory authority, including communications with SAWP regarding subsequent modifications to the study protocol, we also believe VTI-210 may support on a stand-alone basis, if successful from both a statistical and clinical standpoint, product registration in the EU.

We have also enrolled four subjects in VTI-212, an open-label Phase 2 study that is part of a Phase 2/3 clinical program in subjects with either fulminant hepatic failure or surgery-induced acute liver failure. We are beginning this program with a Phase 2 single-arm component enrolling 40 subjects, which may later be followed by a randomized, controlled Phase 3 component. Results from the single-arm component will be compared with historical or case-matched controls, and we currently anticipate Phase 2 data in 2016. Since FHF and SILF have high mortality rates and affect a very small number of patients for which there is currently no satisfactory therapeutic intervention available, the results from the Phase 2 single-arm component may provide support for an expedited regulatory approval pathway. However, regulatory agreement on an expedited regulatory pathway has not yet been sought and may never be granted. In the event that randomized or other Phase 3 data are necessary for approval in FHF and SILF, we expect to perform a randomized Phase 3 trial, the design of which would be finalized upon analysis of the Phase 2 component. Data from VTI-212 may also be used to support our planned marketing applications for AILD and SAAH



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The ELAD System consists of customized disposable sets and a reusable bedside unit attached to four disposable cartridges containing our human liver-derived C3A cells, or VTL C3A cells. The bedside unit is based on a cardio-pulmonary bypass machine, which we have configured for the ELAD System therapy. This bedside unit and customized disposable sets are attached to the cartridges where the patient's blood plasma is treated by our VTL C3A cells before being returned to the patient. The four ELAD cartridges collectively contain 440 grams, or approximately one pound, of VTL C3A cells from our proprietary cell bank. We employ proprietary methods designed to manufacture large quantities of these cells consistently and cost-effectively. These cells have been shown to retain many key synthetic and metabolic processes of normal human hepatocytes, the primary functional cell of the liver.

During the ELAD System therapy, blood plasma is drawn from the patient through a central venous line and then passes into the cartridges via our bedside unit. Therapy is expected to consist of a single session of continuous allogeneic cellular therapy lasting between three and ten days. As the treatment with our VTL C3A cells is not patient-specific, we avoid the costly logistical and production challenges typically associated with autologous cellular therapies.

The ELAD System has shown trends indicating the potential to increase survival rates in acute liver failure. Prior to the initiation of our ongoing Phase 3 clinical trial programs, over 145 subjects have received the ELAD System therapy, including earlier iterations of the ELAD System, in seven clinical trials and through a compassionate use program. Data from a 69-subject randomized, controlled clinical trial performed at two hospital centers in Beijing, China, primarily in subjects diagnosed with viral hepatitis, showed a statistically significant difference in 28-day and 56-day transplant-free survival rates in the ELAD System-treated group as compared with the control group using the pre-defined logrank test, a statistical test that compares the survival distributions of the two study groups. This technique is widely used in clinical trials to document the efficacy of a new treatment compared to a control treatment when the measurement is the time to event (such as the time from initial treatment to death, or to a liver transplant). Data from a subset comprising the first 49 subjects in this clinical trial revealed a statistically significant difference in 84-day survival using a more sensitive analytical technique, the Wilcoxon rank-sum test. This test is another statistical method used in the analysis of clinical trial data that compares two populations, for example, in respect to their survival times. Additionally, subsets of data in subjects with FHF and AILD from previous Phase 1 and Phase 2 clinical trials showed trends indicating that the ELAD System may increase survival rates.

Early clinical trials of the ELAD System carried out prior to the current pivotal trial program were pilot in nature and designed to identify patient populations and clinical trial designs that were appropriate and necessary to pursue in pivotal clinical studies to support regulatory approval in the U.S. and Europe. Although they demonstrated trends towards increased survival, to date none of our prior trials were designed to adequately power or demonstrate statistically significant increased survival and the FDA has noted its view that our preliminary clinical evidence, at this time, does not indicate that the ELAD System may demonstrate a substantial improvement over the current standard of care. For each of the Phase 3 clinical trials to demonstrate efficacy, a statistical plan has been generated, and the studies have been powered with a sufficient number of subjects, such that, should the survival benefits be consistent with those from prior smaller studies, the sample size will be adequate to prove efficacy within statistical criteria traditionally acceptable to the FDA. We have also designed these studies with guidance from the FDA and with the intent of minimizing bias, to the extent possible, in an open-label study design. These plans have been shared with the FDA.

Other artificial liver devices to reach late-stage clinical trials have been either acellular or contained pig cells. We believe that human liver cells are necessary to allow an artificial liver to replicate key aspects of the intricate biology of normal human liver function.

We own exclusive worldwide commercial rights to the ELAD System free of royalties. If our marketing applications are approved, we intend to commercialize the ELAD System in the U.S. and Europe with a targeted sales force. We intend to opportunistically pursue markets outside the U.S. and Europe either through direct sales or collaborations. We also believe that the ELAD System may have potential use for viral hepatitis, liver resection support and liver transplant support, although we have generated limited clinical data to support these indications.

We are currently the owner of record of five U.S. patents and over a dozen issued or allowed foreign patents, including in Europe and Australia. One granted U.S. patent claims a method of using C3A cells to treat a patient's blood and is set to expire in April 2027 unless extended further. In addition, a second U.S. patent claims an extracorporeal device configuration, which we believe to include our ELAD System, independent of cell-type used and is set to expire in May 2025, unless extended further. Moreover, if approved, the ELAD System will be eligible for 12 years of data exclusivity in the U.S. under the Biologics Price Competition and Innovation Act of 2012. Finally, orphan designation provides market exclusivity for seven years in the U.S. and ten years in Europe upon regulatory approval.

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### **Our Strategy**

Key elements of our business strategy include the following:

*Successfully complete the ELAD System's clinical development in acute liver failure.* We completed enrollment in VTI-208 for AILD in January 2015 and expect to have topline results from the VTI-208 Phase 3 trial for AILD in the second quarter of 2015. We have begun enrollment in VTI-210 for SAAH and in VTI-212 for FHF and SILF.

*Obtain regulatory approval for the ELAD System in the U.S. and Europe.* If our VTI-208 or VTI-210 Phase 3 clinical trials are statistically and clinically successful, we plan to submit a BLA to the FDA, and a Marketing Authorization Application, or an MAA, to the EMA, in 2016 or 2017 for the indications of AILD and SAAH, respectively. If the Phase 2 component of VTI-212 provides compelling evidence of the safety and efficacy of the ELAD System in FHF and SILF, we plan to seek agreement from the regulatory authorities regarding the next steps to be taken in order to enable marketing authorization, which may or may not involve an additional randomized controlled Phase 3 clinical trial either prior to or after contingent marketing approval.

*Maximize the commercial potential of the ELAD System in the U.S. and Europe.* If approved, we intend to directly commercialize the ELAD System in the U.S. and Europe with a targeted sales force focusing on liver transplant and other specialist intensive care centers. We believe that we can price the ELAD System in a range consistent with other currently marketed lifesaving therapies, such as left ventricular assist devices, orphan biologic medications for hereditary metabolic diseases, and monoclonal antibody medications for cancer.

*Opportunistically explore commercial opportunities for the ELAD System in other international markets.* We have completed a trial for the ELAD System that may be considered pivotal in China. The study predominantly enrolled subjects with viral hepatitis, and our application for marketing approval, filed in 2007, is still under review. However, we do not currently anticipate receiving approval in China prior to our receipt of FDA approval, if any, in the U.S. We plan to address the commercial opportunity in China following approval in the U.S. and Europe. We also plan to evaluate commercial opportunities in Australia, Japan, India, other Asian markets, the Middle East, Brazil, and Africa.

*Pursue development of the ELAD System in additional indications.* If the ELAD System is approved for use in treating AILD, SAAH, FHF or SILF, we anticipate pursuing the ELAD System's clinical development in viral hepatitis and bridge-to-transplant.

*Technical Improvements and New Applications.* We plan to continue our development of the ELAD System with the incorporation of technical improvements to our bedside unit, customized disposable sets, and cells. In addition, we plan to explore the development of next generation systems and other uses for VTL C3A cells, including the potential commercialization of proteins and other C3A-produced compounds.

## **Our ELAD System Product Candidate**

### ***ELAD System***

The ELAD System is a Phase 3 investigational, extracorporeal bio-artificial liver therapy designed to supplement hepatic function in order to improve survival rates among patients with acute liver failure. The ELAD System consists of a reusable bedside unit attached to four disposable cartridges, which collectively contain thousands of hollow fibers and approximately one pound of VTL C3A cells from our proprietary cell bank.

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The below figure is a schematic of the ELAD System:

During ELAD System therapy, blood is drawn from the patient via a central venous line and then passes into the bedside unit where plasma ultrafiltrate is isolated by an ultrafiltrate generator. The patient's plasma ultrafiltrate then passes into the four cartridges where it contacts our VTL C3A cells after passing through fibers which allow appropriate two-way transfer of toxins, metabolites and nutrients, mimicking liver function. The fibers, made of a semi-permeable membrane, permit passage of macromolecules and other substances from our VTL C3A cells to the patient's plasma ultrafiltrate. At the same time, these fibers permit the passage of toxins such as ammonia and bilirubin and nutrients such as glucose and oxygen from the plasma ultrafiltrate to our VTL C3A cells. Heparin, a widely-available anti-coagulant drug, is administered during the ELAD System therapy in some patients to prevent blood-clotting in the ultrafiltrate cartridge.

Treated plasma ultrafiltrate is then filtered, reconstituted with blood cells and returned to the patient via the central venous line. Meanwhile, the bedside unit monitors and adjusts glucose and oxygen concentrations in the plasma ultrafiltrate as well as temperature in order to maintain the cells' viability. Therapy is expected to consist of a single session of continuous treatment lasting between three and ten days, as determined by the treating physician.

### ***Our Proprietary VTL C3A Cell Bank***

The key to the performance of the ELAD System is our VTL C3A cell bank. The bank contains human liver-derived cells that can be grown in almost unlimited quantities, stored and shipped worldwide. These properties enable continuous patient treatment for up to ten days usually without changing the cartridges. Moreover, the immortal VTL C3A cells mimic certain functions of human liver cells and have been shown to retain many of the specific metabolic processes and pathways of hepatocytes. These functions include an active P450 enzyme system as well as the production of liver-specific proteins such as albumin, anti-thrombin III, alpha-fetoprotein, C3 complement, Factor V, transferrin, alpha-1-antichymotrypsin, alpha-1-antitrypsin, growth factors and immunomodulatory proteins.

Past attempts to develop a liver assist product based on human hepatocytes faced two problems: human hepatocytes could not be expanded in the large quantities needed for a commercial product and the cells lost their hepatocyte functions in a short time. This meant that products based on human hepatocytes were not scalable and could not provide the prolonged treatment necessary for liver support. In the late 1980s, scientists at Baylor College of Medicine in Houston set out to develop a human hepatocyte cell line that could be grown in commercial quantities, ceased cell division on filling space available, retained key hepatocyte functions and survived therapy in human blood. Baylor entered into a cooperative program with The Wistar Institute to develop a new cell line. The parties recognized that the cell properties they sought would likely be found in a tumor cell and worked with the HepG2 cell line derived from a human hepatoblastoma, a mildly metastatic human liver tumor taken from a young person. This cell line was not homogeneous and they searched for a clone of HepG2, which displayed the properties they sought. The C3A cell satisfied most of the criteria that they had specified and they began work with C3A cells in a specially-designed bedside delivery system.

The C3A cell line has been studied by independent investigators who have confirmed its hepatocyte properties, such as the presence of a functional cytochrome P450 toxin-processing enzyme system and the production of many liver-specific proteins. However, the C3A cell line does not entirely mimic the behavior of primary hepatocytes. For instance, it has not been shown to process ammonia as effectively as primary hepatocytes do and C3A produces large amounts of alpha-fetoprotein, or AFP. We believe these issues are manageable since excess ammonia can be removed

by dialysis if needed, and AFP is a non-toxic fetal analogue of albumin.

In order to better understand the performance of the VTL C3A cell line during the treatment of subjects with acute forms of liver failure, we have initiated a program of research to assess the types of proteins produced by the cells during cell culture, and at different times during treatment. Preliminary results from these studies suggest that the cells express a broad spectrum of cytochrome P450 enzymes not only during culture but also during patient treatment, and that the types and amounts of the enzymes produced can vary presumably in response to the exposure of the cells to the patient's plasma ultrafiltrate. Furthermore, initial experiments suggest that the production of proteins by the C3A cells can be measured in the plasma ultrafiltrate and are associated with increases in the levels of these proteins in the blood of liver failure patients. The reproducibility of these data need to be confirmed.

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We are also evaluating the characteristics of the C3A cells using electron microscopy to see how they change during treatment. Preliminary data suggest that the cells can remain metabolically active throughout the course of treatment and have the ability to organize themselves into structures that have characteristics similar to those found in the normal liver. The functional significance of these structures, if any, is yet to be determined.

We have customized the now-publicly available C3A cell line we originally acquired from Baylor University to create a proprietary VTL C3A cell bank for use in the ELAD System, which we culture and expand through proprietary techniques. This cell bank represents a well-characterized stock of original cells that have been subjected to rigorous testing for viruses, pathogens and other contaminants in order to allow them to be used in humans. This bank contains enough cells to enable our clinical development and commercialization. We own this VTL C3A cell bank exclusively and on a royalty-free basis. In addition, we have developed proprietary methods for growing, storing and optimizing the function of these cells.

The ELAD System therapy is not patient specific and our VTL C3A cells, which are derived from a single source, are used to treat all patients. This process is known as allogeneic cellular therapy. In contrast, autologous cellular therapy uses a patient's own cells, which are manipulated in individual production batches, a costly and complex process. As a result, the production and logistics of treatment with our VTL C3A cells does not face the challenges commonly associated with autologous cellular therapies.

Our proprietary VTL C3A cell bank is stored in three separate locations around the world for security purposes and is used as the basis for growing approximately one pound of cells needed for each patient at our production facility in San Diego, California.

### ***Differentiating Factors of the ELAD System***

Unlike other potential therapies developed for acute liver failure in the past, we believe the ELAD System has a unique combination of attributes:

*Biologically active.* The ELAD System is a biologically active system that is designed to replicate many liver functions. The functional unit of the liver, the hepatocyte, is thought to be responsible for 500 or more biologic processes necessary for human life. Moreover, many processes of the liver occur at ever-fluctuating rates in response to the liver's constantly changing biologic environment. As a result, we believe that an acellular solution to liver failure is unlikely to effectively replace lost liver function. We believe that a cellular approach, capable of replicating key biologic processes performed by a human hepatocyte, is best able to provide the requisite flexibility and breadth of function to sufficiently supplement liver function and improve survival in patients with acute liver failure.

*Human cellular therapy.* The ELAD System is based on human cells which confer a considerable advantage over non-human, animal-based cell therapies. Given the widespread availability of animal tissues, much work has been done on the use of animal liver cells, often derived from pigs, to treat humans with liver failure. While immunological risk is always present in cellular therapy, the use of non-human animal tissues presents greater immunological risk compared to human cellular therapy. Humans possess naturally occurring antibodies that react with antigens on porcine cell surfaces. These antibodies can mount an immediate attack in the presence of porcine cells, causing these cells to rapidly lose function and die. Moreover, repeated treatments with a porcine cell may cause subsequent immune responses to become

increasingly severe. The infusion of porcine enzymes into a patient's blood stream also poses immunologic risk. We are not aware of any FDA-approved, non-human animal-based cellular therapy for use in patients.

*Immortal human liver-derived C3A cells.* Our VTL C3A cells used in the ELAD System are derived from a human hepatoblastoma and are immortal. They can be expanded and can survive a session of up to ten days of ELAD System therapy, usually without needing to be replaced during treatment. Hepatocytes are the main cell in the liver and deteriorate rapidly when removed from the body. Hepatocytes cannot be grown outside the body as they de-differentiate and die in a short period of time. The inability to expand makes hepatocytes unsuitable for a liver assist device which requires large amounts of hepatocytes.

*Commercially scalable.* We have developed a process to grow our VTL C3A cell line in our facility in San Diego, California that is designed for scalable production. Each patient set of four cartridges contains a total of about one pound of cells and is grown in a production process that takes about six weeks. The process is carefully controlled and is performed under ultra-clean conditions to avoid contamination in our cGMP-compliant production plant. The process is scalable by modular units.

*Minimal manipulation needed by site.* Prior to shipment, the ELAD cartridges are put into a dormant state and can survive up to 60 hours before being used for treatment. When the hospital receives the cartridges, they are unpacked by our ELAD System specialists on site, placed on the bedside unit, flushed with saline and are ready to be used for patient therapy. Our VTL C3A cells can remain alive for the duration of anticipated patient therapy and the ELAD cartridges do not usually need to be replaced, thus enhancing ease-of-use and reducing cost of goods.



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**Liver Failure**

The liver performs a wide variety of vital life functions including metabolic, regulatory, detoxification and synthetic activities. The primary liver cell, the hepatocyte, is thought to be responsible for approximately 500 or more specific biologic processes. In addition, the liver also serves as a reservoir for immune cells which clear the blood of pathogens. As a result, the liver's failure to perform its normal role can have devastating or fatal consequences. Causes of liver failure are numerous, and the condition is typically described in terms of rapidity of onset. The two main categories are acute liver failure and chronic liver failure. In 2013 liver disease represented the twelfth leading cause of death in the U.S. In China, where viral hepatitis is endemic, liver and liver-related disease represented the fourth leading cause of death in 2011 and over 1 million cases of liver failure are estimated to occur each year in urban areas alone.

***Acute Liver Failure***

Acute liver failure refers to the rapid onset of liver dysfunction in a patient without chronic liver disease. The most common early features include yellowing of the skin and eyes, mental status changes and bleeding. Acute liver failure may occur from a variety of causes such as acute flares of viral hepatitis, paracetamol or acetaminophen overdose, surgical interventions, idiosyncratic drug reactions and excessive alcohol intake. Despite improvements in intensive care management, mortality continues to be unacceptably high. Most acute liver failure patients, except active drinkers of alcohol, are considered suitable for liver transplant. When acute liver failure occurs in the presence of underlying liver disease, such as with AILD, the condition is sometimes referred to as acute-on-chronic liver failure. Other forms of acute liver failure include FHF and SILF.

***Alcohol-Induced Liver Decompensation***

AILD is a life-threatening form of acute liver failure precipitated by the recent ingestion of alcohol. AILD can occur with or without chronic underlying liver disease and can manifest itself in several clinical patterns depending on the acute response of the liver to alcohol's toxic effect. One common and well-recognized form of AILD is SAAH, which is characterized by inflammation and enlargement of the liver. Most subjects with SAAH are thought to have some underlying chronic changes to the liver as a result of longer-term alcohol use, although these changes may be reversible on abstinence. Because of the frequency with which the AILD population has been found to have some degree of pre-existing liver disease, this condition is also often referred to as acute-on-chronic liver failure, or acute-on-chronic hepatitis.

A second form of AILD, which we refer to as non-SAAH AILD, occurs in subjects with underlying stable chronic liver disease who suffer from an episode of acute liver failure due to excessive consumption of alcohol. Current standard of care for AILD is defined by the treating facility and typically includes the use of anti-inflammatory drugs, such as corticosteroids, and the treatment of secondary complications such as bleeding, kidney failure and hepatic coma and may include admission to an intensive care unit. Since abstinence from alcohol for six months is generally considered a pre-requisite for inclusion on a liver transplant list, organ transplantation is usually not available for these patients.

The Department of Health and Human Services in the U.S. estimates that for 2012 the number of hospital admissions related to SAAH in the U.S. was approximately 95,000, with approximately 14,000 of these admissions identifying SAAH as the primary diagnosis. In addition, approximately 305,000 hospital admissions occurred in 2012 related to alcoholic cirrhosis, alcohol liver damage not-otherwise-specified or alcoholic fatty liver, with approximately 48,000 hospital admissions identifying these conditions as the primary diagnosis. We believe that a subset of these patients have a form of non-SAAH AILD that may be treatable with the ELAD System. Incidence rates for both SAAH and

non-SAAH AILD appear to be similar in Europe.

*Fulminant Hepatic Failure*

A second form of acute liver failure is FHF, a relatively rare condition characterized by a rapid deterioration of liver function with altered mental state and coagulopathy in individuals without known pre-existing liver disease. The most frequent causes include drug or toxin-induced liver injury, viral hepatitis, autoimmune disease and hypoperfusion. Two thousand cases of FHF are estimated to occur in the U.S. each year. The standard of care includes liver transplantation, although these patients tend to progress very rapidly and may succumb to their disease before a suitable organ is made available. We believe the ELAD System may provide patients with a bridge-to-transplant, or potentially, recovery without transplantation.

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### ***Surgery-Induced Liver Failure***

Another form of acute liver failure is SILF, which is comprised of three varieties, as follows:

1. Primary Graft Non-Function, which occurs when a newly transplanted liver fails to function. This is a life threatening medical emergency, and can lead to death if a new organ does not become available quickly. We believe the ELAD System may provide patients with a bridge-to-transplant until a second liver becomes available.
2. Small-For-Size or Split Liver Transplant occurs when the transplanted liver is functioning, but may be too small to sustain the patient, either because only a small donor liver was available, or because a live person donated a portion of their liver for transplantation. We believe the ELAD System may be able to support the patient's liver function until the donated organ regenerates to a size large enough to become independent of external support. Moreover the ELAD System may also enable transplantation of smaller liver fragments than typically used, potentially expanding the available pool of donor organs.
3. Other forms of surgery-induced liver failure. Although liver resection can provide a cure for primary liver cancer, resection of too much tissue can lead to rapidly progressing liver failure. Currently, surgeons will typically only resect up to 50% of the liver in order to avoid death from liver failure. However, more extensive resections occasionally occur, and resection of smaller portions can also lead to liver failure. We believe the ELAD System may be able to support these patients and also enable surgeons to perform larger tumor resections.

We estimate that the first two categories of SILF account for several hundred patients a year in the U.S., while the third category could represent an annual population of 10,000 or more cases a year in the U.S.

### ***Chronic Liver Failure***

Chronic liver failure refers to a gradual loss of liver function and is usually characterized by the presence of widespread cirrhosis, which refers to the replacement of normal liver tissue by fibrosis, scar tissue and regenerative nodules. As normal liver is destroyed, the organ gradually fails to perform its normal metabolic, regulatory and synthetic functions. Unfortunately, damage from cirrhosis cannot be reversed and lost liver function can only be regained through transplantation. For this reason, we do not anticipate that the ELAD System will be effective for cirrhotic patients outside of the potential to bridge these patients to transplant.

### ***Limitations of Currently Available Treatment Options for Acute Liver Failure***

Given the liver's complexity, there are no simple or widely effective medical solutions to acute liver failure. The only long-term cure for acute liver failure is surgical transplantation. In 2013, according to the United Network for Organ Sharing, fewer than 6,500 liver transplants were performed in the U.S. due to an insufficient number of available donor organs. According to the United Network for Organ Sharing, the average billable charge for a liver transplant in 2011, including the one month before surgery and six months after surgery, was \$577,100. There are approximately 15,500 patients currently on the transplant waiting list and approximately 1,500 patients die while waiting each year. Similarly, there are approximately 6,000 liver transplants performed per year in Europe. Outside of transplant, current therapy is defined by the treating facility and is mostly supportive and designed to manage the symptoms and

complications associated with acute liver failure.

*Pharmaceuticals*

N-acetylcysteine is approved by the FDA for the prevention of acute liver injury following the ingestion of toxic amounts of acetaminophen. Other treatments, including steroids and pentoxifylline, are often used off-label to manage symptoms associated with acute liver failure, although steroids in particular have been shown to increase risk of potentially fatal infections. Results from the Steroids or Pentoxifylline for Alcoholic Hepatitis study, or STOPAH, were presented at the American Association for the Study of Liver Disease (AASLD) meeting in November 2014. STOPAH enrolled 1,103 subjects with alcoholic hepatitis at 65 sites in the U.K., but failed to demonstrate any significant benefit in the primary analysis of overall survival for subjects treated with either steroids, pentoxifylline or a combination of the two at one, three or twelve months, as compared with placebo. In a secondary, multivariate analysis of the data, a small benefit was observed for those subjects taking steroids at one month, although this benefit was not seen in multivariate analyses at either three months or at twelve months. Despite the availability of these treatments, the mortality rate for acute liver failure remains above approximately 40%. There are no known mechanisms for pharmacologically addressing liver failure specifically or restoring lost liver function.

**Table of Contents***Liver Support Devices*

There are no medical devices approved for liver support that have been proven to improve survival in patients with acute liver failure. Clinical trials have been conducted in recent years involving two acellular liver support devices that filter toxic metabolites from the blood. In 2004, Gambro acquired the Molecular Adsorbents Recirculation System, or MARS, a liver dialysis system. However, in 2010, a randomized, controlled clinical trial comparing MARS to standard of care among 189 subjects with AILD and other forms of liver failure failed to show any improvement in 28-day survival for subjects treated with MARS. Likewise, in 2010 a similar liver support device, Prometheus, developed by Fresenius SE & Co. KGaA, also failed to show an improvement in either 28-day or 90-day survival in a randomized, controlled trial among 145 subjects with AILD and other forms of liver failure. MARS is currently cleared as a device in the U.S. for use in hepatic encephalopathy, drug overdoses and poisoning cases. MARS and Prometheus are both commercialized in Europe under CE marks.

In 1999-2000, Circe Biomedical, Inc. ran a 171-subject randomized, controlled clinical trial in acute liver failure using a liver support device that incorporated live pig liver cells. However, the trial did not meet its 30-day survival endpoint.

**Clinical Experience with the ELAD System in Acute Liver Failure**

Prior to the initiation of our ongoing Phase 3 clinical trial program, over 145 subjects have received the ELAD System therapy, including earlier iterations of the ELAD System, at multiple clinical sites in the U.S., Europe, Asia and the Middle East in six randomized, controlled clinical trials, one single-arm trial and a compassionate-use program. Currently, we have a Phase 3 randomized, controlled clinical trial fully enrolled and a second Phase 3 clinical trial underway. We also have enrolled our first subject in a Phase 2 clinical trial of the ELAD System in subjects with FHF or SILF. Two early studies in acute liver failure were conducted using a different configuration of the ELAD System which involved circulation of whole blood to the VTL C3A cartridges rather than blood plasma. In these studies, 36 subjects were enrolled, of which 23 received the ELAD System treatment and 13 were controls. The data from these studies led to the development of the next configuration of the ELAD System utilizing blood plasma and informed the design of the next clinical trials in acute liver failure.

The following table summarizes subsequent clinical trials as well as currently planned clinical trials using the later configuration of the ELAD System involving the treatment of blood plasma:

<b>Trial</b>	<b>Date</b>	<b>Study Design</b>	<b>Indication(s)</b>	<b>Sites*</b>	<b>Location(s)</b>	<b>Total Subjects Enrolled</b>
VTI-208 (Phase 3)	Commenced March 2013	Randomized, controlled	AILD	40+	U.S., Europe, Australia	203
VTI-210 (Phase 3)	Commenced November 2014	Randomized, controlled	SAAH	40+ <i>planned</i>	U.S., Europe	150+ <i>planned</i>
VTI-212 (Phase 2/3)	Commenced June 2014	Single-arm in Phase 2 component	FHF and SILF	30+ <i>planned</i>	U.S.	40 <i>planned</i>

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VTI-206 (Phase 2b)	2009	2011	Randomized, controlled	AILD and other	26	U.S., Europe	62
Compassionate-use program	2008	2010	Single-arm	Various	6	U.S., U.K., Singapore, Saudi Arabia	16
VTI-201 (Phase 2a)	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 2)	2002	2003	Randomized, controlled	FHF	8	U.S., U.K.	19
PS-0698 (Phase 1)	1999	2000	Randomized, controlled	FHF	6	U.S., U.K.	25

\* For ongoing trials, represents numbers of clinical sites which will fluctuate throughout the trials in part based on resources and competition between trials for patients.

**Table of Contents*****The ELAD System's Clinical Development in Alcohol-Induced Liver Decompensation***

*VTI-206: Phase 2b AILD Trial.* Between 2009 and 2011, we enrolled 62 subjects in a randomized, open-label, controlled Phase 2b clinical trial of the ELAD System therapy in AILD and non-AILD subjects, which were two pre-defined and separately randomized cohorts. The clinical trial was conducted at 26 clinical sites in the U.S. and Europe. After discussions with the FDA, and to better inform our Phase 3 clinical trial, we adopted a 90-day overall survival endpoint. In each of the pre-defined cohorts, subjects were randomized in a 1:1 ratio to either the ELAD System therapy plus standard therapy, or medical treatment in accordance with the standard therapy of the institution.

In January 2011, the trial's Data Safety and Monitoring Board, or DSMB, reported that only the AILD cohort had the possibility of showing any treatment effect and therefore recommended that we discontinue the non-AILD cohort. This second cohort contained subjects with severe forms of chronic liver disease who would not be eligible for the ELAD System therapy under our Phase 3 clinical trial criteria. Discussion with our FDA reviewer indicated the statistical analysis would be affected by closing the non-AILD arm, and therefore the study would not be able to serve as a pivotal trial. It was decided to terminate VTI-206 and design a new trial in AILD subjects. There were no unexpected ELAD System-related safety issues, as the DSMB did not detect any differences in the rates of serious events between the treated and control groups. Generally, the serious adverse events reported in this study were reflective of the severity of disease and co-morbidities present in the patient population. There were 67 serious adverse events reported by 35 subjects in this study, of which 6 events were reported as possibly or probably treatment-related, and consisted of gastrointestinal bleeding (1 subject), vomiting blood (1 subject), kidney failure (1 subject), reaction to blood infection (1 subject), vaginal bleeding (1 subject) and breakdown of red blood cells (1 subject). No serious adverse events were reported as definitely treatment-related.

The trial was terminated in April 2011 when 37 subjects had been enrolled in the pre-defined AILD cohort, which resulted in 29 subjects in the per protocol analysis due to elimination of eight subjects under pre-defined criteria. This subset showed a non-significant trend ( $p=0.27$ ) toward improved 90-day survival of 69.2% in the ELAD System-treated group versus 43.8% in the control group. This trend is depicted in the figure below:

Several clinical laboratory values, including bilirubin, creatinine, and sodium, were monitored for safety in this study. We believe that these parameters are also biomarkers pertinent to our understanding of the mechanism of action of the ELAD System in these subjects. As such, we conducted a post-hoc analysis evaluating the effect of the ELAD System and standard of care versus standard of care alone on these biomarkers. These data showed subjects treated with the ELAD System demonstrated positive trends which we believe are consistent with improvements in liver function. A fourth biomarker also included in liver failure algorithms, INR, is not presented because it is transiently and artificially impacted by the administration of anti-coagulant drugs used during the ELAD System therapy. The other biomarkers are:

*Bilirubin.* Bilirubin is a degradation product of hemoglobin that is normally processed and excreted by the liver. In liver failure, bilirubin accumulates in the body and is responsible for the yellow color of jaundice. In VTI-206, the ELAD System-treated subjects experienced a statistically significant reduction in serum bilirubin levels over the five days of therapy when compared with baseline, while control subjects did not.

*Creatinine.* Serum creatinine is a biomarker of kidney function. Kidney failure frequently is induced by liver failure. In VTI-206, the ELAD System-treated subjects demonstrated a trend towards reduction in creatinine in the first six days of the trial, while control subjects did not.

*Sodium.* Sodium is an electrolyte normally found in blood in a relatively narrow concentration band. Reductions in serum sodium frequently occur in subjects with acute liver failure. In VTI-206, the ELAD System-treated subjects experienced an increase in serum sodium over the first six days, while control subjects experienced a decrease.



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The below charts depict trends of several biomarkers in VTI-206:

*VTI-201: Phase 2a AILD and Non-AILD Trial.* In preparation for VTI-206, we completed a small, randomized, open-label, controlled clinical study, enrolling 18 subjects with AILD and non-AILD, of which 16 participated in the trial. The study was intended to establish the safety of moving forward with our modified ELAD System, to define enrollment criteria for future studies in the U.S. and Europe and to assess the logistics of carrying out a large study in the U.S. and Europe. This trial was performed in 2008 and 2009, demonstrated no unexpected safety issues, and provided what we believe is preliminary evidence of the ELAD System's potential efficacy in this population. Generally, the serious adverse events reported in this study were reflective of the severity of disease and co-morbidities present in the patient population. There were 39 serious adverse events reported by 11 subjects in this study, of which only two events, reduction in the number of red blood cells (1 subject) and reduction in the number of blood platelets (1 subject), were reported as possibly treatment-related. No serious adverse events were reported as definitely treatment-related.

*Phase 3 Plan in AILD and SAAH.* We used the input we received from both the FDA and EMA since January 2011 to design VTI-208, our Phase 3 program which is primarily intended to support potential FDA approval in AILD, and VTI-210, which is primarily intended to support potential EMA approval in SAAH.

In March 2013, we enrolled the first subject in VTI-208, a 1:1 randomized, controlled, open-label pivotal trial designed to enroll 200 subjects with AILD. The VTI-208 clinical trial completed enrollment in January 2015 with 203 subjects having been enrolled at 40 clinical sites in U.S., United Kingdom, or U.K., and Australia. We expect to report topline results from the VTI-208 clinical trial in the third quarter of 2015. The study's primary endpoint is overall survival up to at least study day 91 using a Kaplan-Meier survival analysis. VTI-208's trial design is similar to that of VTI-206, although VTI-208 contains several elements designed to better focus the study on what we believe to be our addressable patient population. These changes include the addition of criteria intended to exclude subjects who are either too unstable to survive the first five days post-randomization, who have non-regenerable livers, or who have criteria suggesting that they are already recovering in the immediate pre-randomization period. Assuming a response pattern similar to the per-protocol subset analysis in VTI-206, the trial is 95% powered to reach a p-value of 0.05. A p-value of less than or equal to 0.05 means that there is at least a 95% probability that increased survival in the ELAD System treatment group is due to the ELAD System treatment and not chance.

The FDA has expressed concern that the VTI-208 study may not be adequately designed to provide convincing evidence of efficacy if there are significant differences in how the ELAD System subjects and controls are treated during the treatment period and after hospital discharge. Variations in length of hospital stay, rates of hospital re-admission, alcohol recidivism rates, nutritional support, and concomitant medications, which are not within our control, could significantly confound the study results and call into question whether any demonstrated difference in survival is due to the ELAD System or to these factors. We have developed a protocol that attempts to minimize this bias to the extent possible, including defining a protocol-specific standard of care, specifying steroid treatment, standardizing the discharge criteria for both the ELAD System and control subjects, requiring that follow-up visits are conducted by a blinded reviewer, ensuring home health care nurses and other clinical personnel are unaware of treatment assignment, educating subjects not to reveal treatment assignment to their caregivers and monitoring concomitant medications, alcohol recidivism and interaction with the health care system to provide evidence that there is no meaningful difference between the groups that could significantly confound the trial data.

We have obtained regulatory allowance in the U.S., U.K., Germany and Spain to begin enrolling subjects, have opened clinical sites for enrollment, and have commenced enrollment in VTI-210, a 1:1 randomized, controlled, open-label pivotal trial designed to allow for an event-driven clinical design (a statistical plan that allows the study sample size to be adjusted according to aggregate mortality) with a minimum of 150 subjects with SAAH who have failed seven days of therapy according to pre-defined criteria. The study's primary endpoint is overall survival up to at least study day 91 using a Kaplan-Meier survival analysis. Assuming a median survival of 45 days for the control group and 90 days for the ELAD System-treated group, the trial is 90% powered to reach a p-value of 0.05. As of March 18, 2015, we had enrolled six subjects in VTI-210 and 18 clinical sites were open for enrollment. We currently project having database lock and topline results from the VTI-210 clinical trial in early 2017.

**Table of Contents*****The ELAD System's Clinical Development in Fulminant Hepatic Failure***

*Phase 1 and 2 Trials of Fulminant Hepatic Failure.* Our predecessor companies, Hepatix and VitaGen, tested earlier versions of the ELAD System in four clinical trials among subjects with FHF.

*PS-0698 and CR-202.* Between May 1999 and August 2000, VitaGen enrolled 25 human subjects with FHF in an open-label, randomized Phase 1 study, titled PS-0698, at six clinical sites in the U.S. and the U.K. comparing the ELAD System therapy to medical treatment in accordance with the standard therapy of the institution. The ELAD System-treated subjects received either two or four cartridges, depending on body weight, with each cartridge containing 80 to 100 grams of VTL C3A cells. Of the 25 subjects enrolled, the first six subjects received the ELAD System therapy, with the following 19 subjects randomized to 10 ELAD System treatment (of which nine were treated) and nine controls. Between March 2002 and January 2003, VitaGen enrolled 19 human subjects with FHF in a Phase 2 open-label clinical study, titled CR-202, at eight clinical sites in the U.S., with 13 subjects randomized to the ELAD System treatment (of which 11 were treated) and six subjects randomized to standard of care. In CR-202, all the ELAD System-treated subjects received four ELAD cartridges containing 80 to 100 grams of VTL C3A cells.

Clinical study PS-0698 was designed to evaluate the safety of the ELAD System in FHF subjects. Clinical study CR-202 was designed to help inform future studies of the ELAD System in FHF. We believe the data from these preliminary studies are useful in evaluating the ELAD System's potential as a treatment for FHF.

We believe the data from study PS-0698 suggest that the principal effect of the ELAD System therapy is to allow severely ill patients with FHF to survive the first few days following study entry, so that they can receive a liver transplant. All of the control subjects who died did so within the first five days following their enrollment. All transplant subjects received their donor organs during this same time period. The ELAD System did not affect any other study variables associated with hepatic function or dysfunction. There were no serious adverse events reported that were considered by the trial investigator to be treatment-related.

In study CR-202, no intergroup differences in mortality were observed. Only two subjects, one treated and one control, died during the study. The proportion of subjects who received transplants was higher for treated subjects (54.5%) compared with control subjects (16.7%). Of the six subjects in the ELAD System group who received a transplant, three were not on the transplant list, unlike the single transplanted control who was listed. Generally, the serious adverse events reported in this study were reflective of the severity of disease and co-morbidities present in the patient population. There were 11 serious adverse events reported by seven subjects in this study. Three serious adverse events were determined by the trial investigator to be definitely treatment-related, which consisted of reduction in the number of blood platelets (1 subject), device malfunction (1 subject), and low blood pressure (1 subject). Five serious adverse events were determined by the trial investigator to be possibly or probably treatment-related, which consisted of reduction in the number of blood platelets (3 subjects), reduced body temperature (1 subject), and an increase in lactic acid (1 subject).

Neither study PS-0698 nor study CR-202 was designed to demonstrate a statistically significant improvement in overall survival or bridge-to-transplant/recovery (BTT/R). In neither case was a statistically significant improvement demonstrated. However, because inclusion criteria for these studies were similar and the endpoints were identical, we performed a post-hoc meta-analysis to explore the impact of transplant-listing on treatment outcome. While there was no evidence of an ELAD System treatment effect in the subset of subjects not listed for transplant, in the subset of subjects prospectively listed for transplant (N=26), this meta-analysis revealed positive survival trends. Moreover, as suggested by the study PS-0698 data alone, we observed additional benefit in the group treated with the ELAD System therapy in BTT/R. While BTT/R is not an acceptable regulatory endpoint, we believe that it is clinically important, and these data have helped inform the design of our Phase 3 clinical trial in FHF.

In summary this meta-analysis revealed the following:

thirty-day survival rates were 75% for the ELAD System-treated subjects and 50% for the control subjects (p=0.12);

an analysis of Kaplan-Meier curves comparing success at a BTT/R endpoint revealed additional benefits for ELAD System-treated subjects (p=0.06); and

a chi-squared analysis of the BTT/R status of subjects at the end of the study showed a statistically significant advantage for the ELAD System-treated subjects versus control subjects (p=0.03).

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The overall survival trend of the meta-analysis is demonstrated in the following Kaplan-Meier chart on the left and the bridge-to-transplant or recovery of the meta-analysis is demonstrated in the following Kaplan-Meier chart on the right:

Statistically significant differences were not observed for other outcome variables, including those related to hepatic function, in either the overall population or the subset.

*Phase 2/3 Program in Fulminant Hepatic Failure and Surgery Induced Liver Failure.* We have enrolled four subjects in VTI-212, an open-label Phase 2 study that is part of a Phase 2/3 clinical program in subjects with either FHF or SILF. We are beginning this program with a Phase 2 single-arm component enrolling a planned 40 subjects, which may later be followed by a randomized, controlled Phase 3 component. Results from the initial Phase 2 single-arm component will be compared with historical or case-matched controls, and we currently anticipate Phase 2 data in 2016.

Since FDA guidelines provide for flexibility in review of marketing applications for life-threatening conditions, such as FHF and SILF, and because these conditions affect a small number of patients, it may be possible to seek marketing approval in FHF and SILF based on results from the Phase 2 single-arm component. However, regulatory agreement on an expedited approval pathway has not yet been sought and may never be granted. In the event that randomized or other Phase 3 data are necessary for approval in FHF and SILF, we expect to perform the randomized Phase 3 portion of the program or evaluate other Phase 3 trials, the design of which would be finalized upon analysis of the Phase 2 component. Data from VTI-212 may also be used to support our planned marketing applications for AILD and SAAH.

This trial is expected to be conducted primarily in the U.S. The symptoms of FHF and SILF are similar and we currently expect to use similar inclusion criteria for either population.

### ***The ELAD System's Clinical Development in Acute Flare of Viral Hepatitis***

*VTIC-301.* Between 2006 and 2007, we enrolled 69 subjects with acute liver failure in a randomized, controlled open-label trial at two hospitals in Beijing. Inclusion criteria focused the trial's enrollment on subjects anticipated to have a 50% chance of death by 84 days, and the majority of enrolled subjects were experiencing an acute flare of viral hepatitis. The study was designed to enroll 120 subjects but was terminated early by one of the hospital's ethics committee because, in light of the results discussed below, it would have been unethical to continue to treat control subjects with standard of care alone. Endpoints included survival at 14, 28, 56 and 84 days, as analyzed using a logrank method.

A significant protocol amendment was enacted after the enrollment of the first 49 subjects, in which inclusion criteria were changed, reducing the severity of disease, and a shorter ELAD System treatment time was recommended. This change in study design resulted in far fewer deaths or transplants in the second subset of 19 ELAD System-treated and control subjects. A revised statistical plan was prepared to accommodate these differences in subject populations. Separate analyses were performed on the 49-subject subset and the full 68-subject population, and additional statistical analysis techniques were proposed, such as the use of Wilcoxon rank-sum techniques to analyze continuous variables such as survival time.

Analysis of the first 49 subjects (32 subjects randomized to be treated with the ELAD System for 3 days along with standard of care for the treating institution and 17 subjects randomized to be treated with standard of care alone) revealed the following:

significant differences in 28- and 56-day survival using the logrank test ( $p=0.015$  and  $0.026$  respectively);

significant differences in 84-day survival using the Wilcoxon test ( $p=0.049$ ) (logrank was not significant at 14 and 84 days,  $p=0.074$  and  $0.058$ , respectively); and

no unexpected safety issues.

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Generally, the serious adverse events reported in this study were reflective of the severity of disease and co-morbidities present in the patient population. There were 16 post-treatment adverse events in eight of the 32 treated subjects that the investigators reported as possibly or probably treatment related.

These efficacy results are depicted in the below Kaplan-Meier curve:

Analysis of all 68 subjects treated (44 subjects randomized to be treated with the ELAD System for one to three days along with standard of care for the treating institution and 24 subjects randomized to be treated with standard of care alone) revealed the following:

Significant differences in 28-day survival using the logrank test ( $p=0.015$ );

No significant differences in 14, 56 and 84-day survival using the logrank test; and

No unexpected safety issues.

Based on these results, it was concluded that the Wilcoxon test is a more sensitive technique to elucidate differences between groups in the ELAD System clinical trials, and that a more severely diseased population and more extended treatment times should be evaluated in future clinical studies. Future clinical trials may be analyzed using the more conservative logrank technique.

One further observation from the 49 subjects in the first part of this study was that the ELAD System can significantly decrease bilirubin levels, an important biomarker of liver function in patients with acute liver failure. The overall magnitude of the decrease in mean end of treatment total bilirubin in the ELAD group was 25.1% (17.5 to 13.1 mg/dL) compared to an increase in the control group of 36.8% (17.1 to 23.4 mg/dL). Serum sodium, another biomarker associated with survival in subjects with acute liver failure, also was significantly improved in the subjects treated with the ELAD System relative to control subjects.

These China pivotal trial data formed the basis of a submission for marketing approval to the China FDA, or CFDA, in September 2007. It should be noted that this study was not designed, and will not be used, as a pivotal trial to support approval of the ELAD System in the U.S. and Europe.

Subsequent to the completion of the VTIC-301 clinical study, an additional protocol was prepared by the treating physicians to explore the long-term survival of subjects enrolled in this study. Following the grant of informed consent, subjects enrolled in VTIC-301 were contacted and invited to return to the treating hospital for examination for recurrence of liver disease or the incidence of cancer. This study was carried out in 23 and 22 subjects, respectively, three and five years following initial randomization.

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These data from the first 49 subjects suggest that the survival benefit (statistically significant at three years and five years,  $p < 0.05$ , logrank) afforded to those subjects treated with the ELAD System is maintained over a three and five year period relative to those subjects in the control group. These trends are depicted in the Kaplan-Meier curves below:

While these follow-up analyses were not prospectively defined in the VTIC-301 protocol, we believe they provide valuable information on the long-term survival of this group of patients.

The results of VTIC-301 were submitted to the CFDA, for marketing approval in September 2007. However, a regulation enacted in 2009 prevents the approval of novel foreign medical products until they are approved in their home markets first. Our application in China is pending.

### ***Future Clinical Development Plans***

In the future, we anticipate pursuing clinical development of the ELAD System in additional indications, including bridge-to-transplant.

### **Commercialization Strategy and Organization**

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. If approved, we intend to directly commercialize the ELAD System in the U.S. and Europe with a targeted hospital sales force and to either commercialize directly or utilize a variety of types of collaboration in other markets.

### ***Sales, Marketing and Reimbursement***

Following FDA and/or EMA approval, if any, we intend to launch the ELAD System commercially in the U.S. and Europe, respectively. We expect to direct our initial sales and marketing efforts at those sites which will have participated in our Phase 3 clinical trials, which we anticipate exceed 40 in number. Subsequently, we plan to gradually expand our focus in the U.S. to approximately 100 liver-transplant centers, as well as to another 100 specialist intensive care centers with a similar penetration in Europe. We expect that our commercial infrastructure would be comprised of a targeted hospital sales force led by several experienced sales management personnel, an internal marketing and medical affairs staff, and a reimbursement support team. We currently intend to focus our initial commercial efforts on the U.S. and European markets, which we believe represent the largest and most readily addressable market opportunities for the ELAD System. In addition, we believe that Australia, China, Japan, India, other Asian markets, the Middle East, Brazil, and Africa represent significant opportunities because of the prevalence of liver disease in these geographies, and we intend to pursue the commercialization of the ELAD System in certain of these markets through collaborations.

We expect the ELAD System to be reimbursed as an in-patient drug in the U.S. For patients eligible for Medicare, who we anticipate to constitute a minority of the ELAD System-addressable patients, reimbursement to the hospital is expected to occur under a diagnosis related group, which may be eligible for a New Technology Add-on Payment and outlier payments. We have begun the process to request appropriate codes and groupings for the ELAD System therapy from the Centers for Medicare & Medicaid Services, which may take several years to complete, if successful. We have been notified by the American Medical Association (AMA) that a temporary, or Category III, Current Procedural Terminology (CPT) code for physician care oversight of an extra-corporeal liver system was accepted in



February 2015, with an effective implementation date of January 1, 2016. However, implementation of a permanent, or Category I, CPT code with a predetermined physician payment value is a lengthy process and is not expected to be complete until several years after potential marketing approval in the U.S. We also expect to work with private payors to develop appropriate case-rates for the ELAD System reimbursement in the U.S. We believe we will ultimately be able to price the ELAD System in a range consistent with other currently marketed life-saving therapies, such as left ventricular assist devices, orphan biologic medications for hereditary metabolic diseases, and monoclonal antibody medications for cancer.

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### ***Manufacturing and Supply***

Our manufacturing facility is licensed as a drug and medical device manufacturer by the California Food and Drug Bureau. This facility was recently remodeled in 2014 in order to expand manufacturing capacity to support worldwide clinical trials and early marketing demands for the ELAD System. This remodel increased manufacturing clean room, quality control laboratory, and warehouse and refrigeration space. The increased clean room space will allow modular increases in the ELAD cartridge manufacture.

At our facility, we manufacture the ELAD System, which is comprised of our proprietary VTL C3A cells, cartridges and the bedside unit. The system contains both reusable and disposable medical device components. We source certain components of the ELAD System from third-party suppliers. Most components of our ELAD System are FDA-cleared and CE marked. In a few cases, we manufacture a device or a device component ourselves. Based on discussions with the regulatory authorities, we have determined that all components will have to be submitted for approval for use with the ELAD System as part of the BLA.

### ***Training and Support***

We also expect to deploy a training and support team at the liver transplant and specialist intensive care centers that our sales and marketing team are expected to target. During the initial commercialization period, it will be essential for us to have our own trained staff present during the delivery of the ELAD System therapy. This may entail the construction and operation of training centers and will require the hiring of personnel of appropriate ability to be adequately trained.

All biopharmaceutical production activities must be conducted under current Good Manufacturing Practices, or cGMP, the standards established by the FDA for pharmaceutical and biologics production. Medical devices must be manufactured in accordance with pertinent device regulations. The equipment used in the manufacturing process is based on designs typically encountered in the production of other biotechnology products, and has been customized to tailor their use to the ELAD System production. The ELAD cartridges and bedside units are tested according to the FDA's and other applicable regulatory bodies' standards before they can be released for use in humans. All device components shipped from us to our investigational sites are subject to quality control inspection.

### ***Future Commercialization Opportunity***

The VTL C3A cells which we grow in our facility produce large quantities of proteins and other cell products, such as albumin, alpha-fetoprotein, alpha-1 antichymotrypsin, alpha-1 antitrypsin, C3 complement, anti-thrombin 3, factor V, factor VII, fibrinogen, and transferrin. Many of these compounds have known or potential industrial and/or therapeutic applications. In the future we plan to explore the commercialization potential for these compounds, although we do not expect to generate revenues in this area in the near-term.

### ***Intellectual Property***

We believe that we have a patent portfolio and substantial know-how relating to the ELAD System. Our patent portfolio includes claims directed to our ELAD System, specific clonal cells and cell-lines derived from human liver-derived C3A cells, as well as methods of growing these cells. We are currently the owner of record of five issued U.S. patents and over a dozen issued or allowed foreign patents. One granted U.S. patent claims a method of using C3A cells to treat a patient's blood and is currently set to expire in April 2027, unless extended further. In addition, a second granted U.S. patent has claims covering an extracorporeal device configuration, which we believe to include our ELAD System, independent of cell-type used is set to expire in May 2025, unless extended further. Foreign

counterparts of one or more of these patents have been issued in Australia, Canada, Indonesia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea and Taiwan and remain under review in certain other jurisdictions including Europe, Brazil, China, India and the Philippines.

We strive to protect the proprietary technology that underlies the ELAD System. We seek patent protection in the U.S. and internationally for the ELAD System, its methods of use and processes of manufacture, and any other technology to which we have rights, where available and when appropriate. We also rely on trade secrets that may be important to the development of our business.

A predecessor company initially developed the ELAD System after the technology was spun out of Baylor College of Medicine in 1990. In 2003, we acquired substantially all of the assets of the predecessor, including trade secrets, know how, clinical experience and key employees and facilities. Among those assets was a U.S. patent, which we had exclusively licensed from Baylor, which is now expired.

Our success will depend on our ability to obtain and maintain patent and other proprietary rights in commercially important technology, inventions and know-how related to our business, the validity and enforceability of our patents, and the continued confidentiality of our trade secrets as well as our ability to operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also expect to rely on continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

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We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may own or license in the future, nor can we be sure that any of our existing patents or any patents we may own or license in the future will be useful in protecting our technology. For this and more comprehensive risks related to our intellectual property, please see Risk Factors Risks Relating to Intellectual Property.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional priority application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or PTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a U.S. patent that covers an FDA-approved biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the biologic is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved biologic may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of our BLA, we expect to apply for patent term extensions.

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of our proprietary technology are based on unpatented trade secrets and know-how. This includes our methods of expanding, culturing and optimizing the performance of the human VTL C3A cell line.

Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

We seek trademark protection in the U.S. and outside of the U.S. where available and when appropriate. We have registered trademark rights in the Vital Therapies and the ELAD System marks in the U.S. and Australia.

## **Competitive Environment**

The biotherapeutic and medical device industries are highly competitive and rapidly evolving, and we face potential competition from major pharmaceutical companies, specialty pharmaceutical companies, medical device developers and biotechnology companies worldwide, many of which have longer more established operating histories, and significantly greater financial, technical, marketing, sales and distribution and other resources than us. Given the significant unmet medical need for novel therapies to treat acute liver failure, many companies, public and private

universities and research organizations are actively engaged in the discovery and research and development of potential products in this field. Several of these entities are engaged in research on cell-based approaches to acute liver failure. Although we are not aware of any ongoing human clinical trials involving potentially competitive product candidates in the U.S. or Europe, such trials could be taking place or could begin in the near future. In addition, these entities compete with us for limited resources including personnel, trial sites and potential complementary assets.

We are not aware of any company that is in human clinical trials with a human cell-based product for the treatment of patients with acute liver failure. At least four companies have conducted prior research on various human hepatocyte cell lines including Exten Industries, Hepalife Technologies, Fresenius, and Hybrid Organ GmbH. In addition, the University College London, the University of Amsterdam and its spinout Hep-Art Medical Devices, and researchers affiliated with the Mayo Clinic are actively pursuing animal research in this area and may begin clinical trials in the near future.

Several companies have also attempted to develop extracorporeal therapy based upon primary porcine hepatocytes, although ongoing research in this area is difficult to ascertain.

Two commercially available liver dialysis systems, from Gambro and Fresenius, have undergone extensive clinical development, although both have failed to show an improvement in long-term survival among patients with acute liver failure. Both rely on not only traditional dialysis circuits to remove water-soluble toxins, but also albumin dialysis circuits to remove albumin-bound molecules.

In addition, there are several drugs used to treat symptoms associated with acute liver failure, including steroids, pentoxifylline and N-acetylcysteine. These drugs, alone or in combination, are used frequently in patients with acute liver failure.

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**Government Regulation**

We operate in a highly-regulated industry that is subject to significant federal, state, local and foreign regulation. Our present and future business has been, and will continue to be, subject to a variety of laws including, the Federal Food, Drug, and Cosmetic Act, or FDC Act, and the Public Health Service Act, or PHS Act, among others. Biologics and medical devices are subject to regulation under the PHS Act and FDC Act.

***Regulation of Combination Products***

The FDA has specified a definition for the term combination product, which includes: (1) a product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (2) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (3) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (4) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various Centers by product type. Different Centers typically review drug, biologic, or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

The ELAD System is regulated as a combination biologic/device in the U.S. Based upon the proposed mechanism of action, the primary Center within the FDA responsible for its regulation is the Center for Biologics Evaluation and Research, or CBER. The CBER office responsible for review is the Office of Cellular, Tissue and Gene Therapies, and the marketing application will be a BLA. CBER will consult with the Center for Devices and Radiological Health, or CDRH, in reviewing the device components of the ELAD System.

***FDA Approval Process***

In the U.S., pharmaceutical and biological products and medical devices are subject to extensive regulation by the FDA. The FDC Act, PHS Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of these products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending license applications, warning and other letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

### ***Preclinical Studies***

Biological product development in the U.S. typically involves preclinical laboratory and animal tests. Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an investigational new drug application, or IND, along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not objected to the IND within this 30-day period, the clinical trial proposed in the IND may begin.

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***Clinical Studies***

Clinical trials involve the administration of the investigational biologic to healthy volunteers or subjects with the targeted indication, or disease, under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and good clinical practices, or GCP, an international standard meant to protect the rights and health of subjects and to define the roles of clinical trial sponsors, administrators, and monitors, as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. subjects and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. The clinical trial protocol, protocol amendments and informed consent information for subjects in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

***Disclosure of Clinical Trial Information***

Sponsors of clinical trials of investigational products are required to register on [clinicaltrials.gov](http://clinicaltrials.gov), a National Institute of Health website registry database, and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

***Marketing Approval***

Clinical trials to support BLAs, which are applications for marketing approval, are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the investigational biologic candidate into healthy human subjects, the investigational biologic is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited subject population, to determine the effectiveness of the investigational biologic for a particular indication or indications, dosage tolerance and optimum dosage, and identify common adverse effects and safety risks. In the case of product candidates for severe or life-threatening diseases such as cancer, the initial human testing is often conducted in patients rather than in healthy volunteers.

If an investigational biologic demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the investigational drug and to provide adequate information for its labeling. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy and safety of the biologic for use in a specific indication or population. A single Phase 3 clinical trial with other confirmatory evidence may be sufficient in rare instances where the study is a large multi-center trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity, or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.



After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA approval of the BLA is required before marketing of the product may begin in the U.S. The BLA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's manufacture and controls. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is subject to a substantial application fee and the manufacturer or sponsor of an approved BLA is also subject to annual product and establishment user fees.

The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs. Most such applications for standard review biologics products are reviewed within twelve months of submission; most applications for priority review biologics are reviewed within eight months of submission. Priority review for biologics is limited to those products intended to treat a serious or life-threatening disease with unmet medical need relative to the currently approved products. The review process may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

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The FDA may also refer applications for novel biologics products or biologics products that present difficult questions of safety or efficacy, to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the biologic product is manufactured. The FDA will not approve the BLA unless compliance with current good manufacturing practice, or cGMP, is satisfactory, including compliance with applicable parts of the medical device Quality System Regulation, or QSR, as defined for combination products, and the BLA contains data that provide substantial evidence that the biologic is safe, pure and potent in the indication studied. Manufacturers of biologics also must comply with the FDA's general biological product standards.

After the FDA evaluates the BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter outlines the deficiencies in the submission and may require substantial additional testing, including additional large-scale clinical testing or information in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing and distribution of the biologic with specific prescribing information for specific indications. As a condition of BLA approval, the FDA may require substantial post-approval testing and surveillance to monitor the product's safety or efficacy and may impose other conditions, including labeling restrictions, which can materially affect the product's potential market and profitability. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems or safety issues are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, device components or manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs.

***Post-Approval Requirements***

Once a BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet.

Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of a BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, Risk Evaluation and Mitigation Strategies, or REMS, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as product manufacturing, packaging and labeling procedures must continue to conform to cGMP's after approval. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the agency inspects manufacturing facilities to assess

compliance with applicable regulations such as cGMPs and the QSR. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

### ***Exclusivity and Approval of Competing Products***

#### ***Biosimilar Exclusivity***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, creates an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical study, absent a waiver. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation which are still being evaluated by the FDA.

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A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) eighteen months after the first interchangeable biosimilar is approved if there is no patent challenge, (iii) eighteen months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

*Orphan Drugs*

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug or biologic for this type of disease or condition will be recovered from sales in the U.S. for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

***Federal and State Fraud and Abuse, Privacy and Transparency Laws***

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of federal and state laws in the U.S. have been applied to restrict certain business operations and activities in the biopharmaceutical and medical device industries in recent years. These laws that may affect our ability to operate include, but are not limited to:

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return, for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, service or item for which payment is made, in whole or in part, under a federal health care program. The federal healthcare program anti-kickback statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and

practices that involve remuneration intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for a statutory exception or a regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal healthcare program anti-kickback statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, or knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim to the federal government. Recently, the civil False Claims Act has been used to assert liability on the basis of kickbacks and improper referrals, improperly reported government pricing metrics such as Medicaid Best Price or Average Manufacturer Price, improper use of supplier or provider Medicare numbers when detailing a provider of services, improper promotion of drugs or off-label uses not expressly approved by the FDA in a drug's label, and misrepresentations with respect to the services rendered or items provided. The federal criminal false claims law prohibits, among other things, at any time knowingly and willingly making, or causing to be made, any false statement or representation of a material fact for use in determining rights to a benefit or payment under a federal healthcare program.

Many states also have statutes or regulations similar to the federal fraud and abuse laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor (e.g. private payors). Sanctions under federal, and state healthcare fraud and abuse laws may include, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare program, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations.

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Additionally, the civil monetary penalties statute, which, among other things, imposes fines against any person who is determined to have presented, or caused to be presented, claims to a federal healthcare program that the person knows, or should know, is for an item or service that was not provided as claimed or is false or fraudulent. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services relating to healthcare matters. Many states have similar fraud and abuse statutes and regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, private payors. In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation by both the federal government and the states in which we conduct our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Moreover, recent healthcare reform legislation has strengthened many of these laws. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA), among other things, amends the intent requirement of the federal healthcare program anti-kickback statute to a stricter standard such that a person or entity does not need to have actual knowledge of the federal healthcare program anti-kickback statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors, it is possible that some of our business activities may not satisfy the statutory exceptions or regulatory safe harbors and we could be subject to challenge under one or more of such laws. State law equivalents to these federal laws may also apply. Such a challenge could have a material adverse effect on our business, financial condition and results of operations.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report to the Centers for Medicare & Medicaid Services, or CMS, information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals. The Physician Payments Sunshine Act provisions were recently implemented in final regulation that requires applicable manufacturers to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members, with data collection beginning on August 1, 2013. Manufacturers were required to report such data to CMS by March 31, 2014 (and by the 90th day of each subsequent calendar year). Other state laws require pharmaceutical companies to adopt and or disclose specific compliance policies to regulate the Company's interactions with healthcare professionals. Moreover, some states, such as Minnesota and Vermont, also impose an outright ban on certain gifts to physicians.

Violations of some of these laws may result in substantial fines. These laws affect our promotional activities by limiting the kinds of interactions we may have with hospitals, physicians or other potential purchasers or users of our products. Both the disclosure laws and gift bans impose additional administrative and compliance burdens on us. Although we seek to structure our interactions in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how a law will be applied in specific circumstances. If an employee were to offer an inappropriate gift to a customer, we could be subject to a claim under an applicable state law. Similarly if we fail to comply with a reporting requirement, we could be subject to penalties under applicable

federal or state laws including, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. In addition to the federal and state disclosure and gift ban laws, certain countries outside of the U.S. have similarly enacted disclosure laws for which the company in its activities may be subjected to from time to time.

***Regulation in the European Union***

Biologics and medical devices are subject to extensive regulation outside of the U.S. In the European Union, for instance, a centralized approval procedure may be used to authorize the marketing of a product in all countries of the European Union, which includes most major European markets. However, for certain products, if this procedure is not used, approval in one country of the European Union can be used to obtain approval in a second country of the European Union under two simplified application processes, either the mutual recognition procedure or the decentralized procedure. Both of these procedures rely on the principle of mutual recognition. In addition to regulatory approval, pricing and reimbursement approvals are also required in most countries.

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In Europe, the ELAD System is regulated as a Combination Somatic Cell Advanced Therapy Medicinal Product, or ATMP. The primary regulatory license application in Europe (a Marketing Authorization Application, or MAA) will be made to The Committee for Advanced Therapies, or CAT, and the Committee for Human Medicinal Products, or CHMP, which are the committees at the European Medicines Agency, or EMA, that are responsible for assessing the quality, safety and efficacy of ATMPs. Marketing Authorization Applications for ATMPs can only be filed using the Centralized Procedure. The CHMP and the CAT (Co)-Rapporteurs and CHMP Coordinators liaise closely together to prepare the ATMP Assessment Reports. The draft opinion prepared by the CAT is issued on any scientific assessment of ATMPs necessary to draw up the scientific opinions by the CHMP relating to granting, variation, suspension or revocation of an authorization to place ATMPs on the market in accordance with Regulation (EC) No 1394/2007 and pharmacovigilance. The CAT has also established collaborations with Notified Bodies, or NBs, in Europe in order to review the device components of combination device products, and we anticipate that the device components of our submission will be reviewed by one of those NBs. During the clinical trial phase in Europe, the company is granted authorization to conduct clinical studies through local regulatory agencies in each country, each of which has its own format and regulation for the issuance of Clinical Trial Authorizations, or CTAs. In general, it is necessary to obtain separate authorizations in each country for each clinical trial protocol from the medicines and device agencies as there is yet to be developed a procedure for dealing with combination products like the ELAD System. These authorizations have been granted by the U.K., Germany and Spain, and are being sought in other European countries though no assurance can be made that we will obtain additional authorizations. The EMA has provisions for providing companies with scientific advice through the Scientific Advice Working Party, or SAWP, and we have sought and obtained advice on our clinical development program through the SAWP process. We anticipate obtaining further guidance and advice through future interactions with the SAWP.

In other jurisdictions we anticipate that there will be different requirements for authorization for clinical trials and ultimately marketing of the ELAD System due to the complex nature of the combination of biological and device components of our ELAD System.

## ***Other Regulations***

We are also subject to numerous, federal, state, local and foreign laws and regulations relating to such matters as safe working conditions, manufacturing practices, fire hazard control, environmental protection and the disposal of hazardous and potentially hazardous substances and biological materials. We may incur significant costs to comply with such laws and their related regulations now or in the future. In addition, we are also subject to laws and regulations in foreign countries outside of the U.S. and Europe where we may seek to commercialize the ELAD System. In certain cases, these foreign laws and regulations may change at inopportune times and prevent the ELAD System's timely commercialization. For example, several years after we submitted our 2007 regulatory package in China, we were notified of a then-newly-enacted 2009 regulation which prohibits the ELAD System's approval in China until it is first approved in the U.S. As such, we now do not expect regulatory consideration of approval in China until after approvals are received in the U.S.

## **Research and Development**

We recognized \$39.5 million, \$21.8 million and \$5.1 million in research and development expenses in the years ended December 31, 2014, 2013 and 2012, respectively. For the year ended December 31, 2014, research and development expenses primarily consisted of \$30.6 million to support our clinical operations.

## **Geographic Information**

During 2014, 2013 and 2012, substantially all of our long-lived assets were located within the U.S.



## **Financial Information about Segments**

We operate in a single accounting segment. Please see Note 1 Description of Business and Basis of Financial Statements to our audited financial statements included elsewhere in this Annual Report.

## **Employees**

As of January 31, 2015, we had 96 employees, 11 of whom held Ph.D. or M.D. degrees. Of our employees, 56 were engaged in research and development, 16 in manufacturing and 24 in administration. None of our employees is represented by a labor organization or under any collective bargaining arrangement, and we have never had a work stoppage. We consider our employee relations to be good. We have also engaged numerous consultants.

## **Corporate Information and Website**

We were incorporated in California in May 2003 as Vitagen Acquisition Corp., changed our name to Vital Therapies, Inc. in June 2003, and reincorporated in Delaware in January 2004. Our principal executive offices are located at 15010 Avenue of Science, Suite 200, San Diego, CA 92128. Our telephone number is (858) 673-6840. Our website address is <http://www.vitaltherapies.com>. This Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available (free of charge) on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. Information contained on, or that can be accessed through, our website, does not constitute part of this Annual Report on Form 10-K and the inclusion of our website address in this Annual Report is an inactive textual reference only.

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Vital Therapies and ELAD are registered trademarks of Vital Therapies and the Vital Therapies logo is a trademark of Vital Therapies. Other service marks, trademarks, and tradenames referred to in this Annual Report are the property of their respective owners. Except as set forth above and solely for convenience, the trademarks and tradenames in this Annual Report are referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the beginning of the first fiscal year following the fifth anniversary of our initial public offering, or January 1, 2020, (2) the beginning of the first fiscal year after our annual gross revenue is \$1.0 billion or more, (3) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities and (4) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the JOBS Act, and references herein to emerging growth company are intended to have the meaning associated with it in the JOBS Act.

### **Item 1A. Risk Factors.**

*Investing in our common stock involves a high degree of risk. Before deciding to invest in our company or deciding to maintain or increase your investment, you should consider carefully the risks and uncertainties described below. The risks and uncertainties described below and in our other filings with the Securities Exchange Commission are not the only ones we face. If one or more of the following risks are realized, our business, financial condition and results of operations and prospects could be materially and adversely affected. In that event, the market price for our common stock could decline and you may lose your investment.*

#### **Risks Related to Our Business**

***We are a clinical-stage company with no approved products, which makes assessment of our future viability difficult.***

We are a clinical-stage company and we have no approved products or revenues from the sale of products. Our operations to date have been limited to organizing, staffing and financing our company, applying for patent rights, manufacturing on a clinical scale, undertaking clinical trials of our product candidate, and engaging in research and development. We have not yet demonstrated an ability to obtain regulatory approval, manufacture products on a commercial-scale, or conduct the sales and marketing activities necessary for successful product commercialization. As a result, there is limited information about us for investors to use when assessing our future viability and our potential to successfully develop product candidates, conduct clinical trials, manufacture our products on a commercial scale, obtain regulatory approval and profitably commercialize any approved products.

***We are totally dependent upon the success of the ELAD System, our sole product candidate.***

The ELAD® System is designed to improve survival rates of patients with acute liver failure. The ELAD System is a novel product candidate whose safety, efficacy and other attributes have not been demonstrated in well-designed, large scale, clinical trials and are not fully understood. As a cell-based therapy, the ELAD System's mechanism-of-action is complex and we cannot be certain that our currently-targeted indications of alcohol-induced liver decompensation, or AILD, severe acute alcoholic hepatitis, or SAAH, fulminant hepatic failure, referred to as FHF, and surgery-induced acute liver failure, referred to as SILF, in the U.S. and Europe, and viral hepatitis (predominantly hepatitis B) in China represent suitable applications for the ELAD System, or even ones where the ELAD System therapy can or will ultimately be shown to be safe and effective in well-designed clinical trials

necessary to support regulatory approval in any jurisdiction. For example, the U.S. Food and Drug Administration, or FDA, has expressed concern about the open-label design of study VTI-208, our pivotal study in AILD, and the need to apply a consistent standard of care and to standardize post-discharge care, both being issues that could significantly confound the study results, impact morbidity and mortality and cause the FDA or other regulatory authorities to require that we repeat clinical trials with different trial designs. Finally, even if the ELAD System is proven to be safe and effective and ultimately receives regulatory approval, there is no guarantee that its commercialization will be successful. If the ELAD System should fail at any stage in our clinical trials or at the marketing stage, our business and operating results and financial condition will be materially and adversely affected.

***We cannot give any assurance that we will successfully complete the ELAD System's clinical development, or that the ELAD System will receive regulatory approval in a timely fashion or at all.***

We must be evaluated in light of the uncertainties and complexities affecting a clinical-stage, combination product, biologic and medical device company. We have not completed clinical development for any of the ELAD System's potential indications in the U.S. or Europe where the ELAD System is regulated as a combination biologic and medical device, and a combined somatic cell Advanced Therapy Medicinal Product, respectively. We are conducting two Phase 3 clinical trials and a Phase 2/3 clinical program designed to establish the safety and efficacy of the ELAD System and to support approval in the U.S. and Europe. These clinical trials are expected to be performed in subjects with alcohol-induced liver decompensation, severe acute alcoholic hepatitis, fulminant hepatic failure and surgery-induced acute liver failure. Any additional indications we elect to pursue will require the initiation and completion of additional Phase 3 clinical trials demonstrating safety and efficacy for each such indication. For example, the FDA has noted its view that preliminary clinical evidence, at this time, does not indicate that the ELAD System may demonstrate a substantial improvement over standard of care. There is no guarantee that our clinical trials will be completed in a timely fashion or succeed. Our ability ultimately to reach profitability is critically dependent on our future success in obtaining regulatory approval for the ELAD System. However, there is no guarantee that our clinical trials will be successful, or that regulators will approve the ELAD System in a timely manner, or at all.

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***If we fail to obtain regulatory approval as anticipated in the U.S. and Europe, our business would be harmed.***

We require regulatory approval for each indication we are seeking before we can market and sell the ELAD System in a particular jurisdiction for such indication. Our ability to obtain regulatory approval of the ELAD System depends on, among other things, successful completion of clinical trials, and demonstrating efficacy with statistical significance and acceptable safety in humans. The results of our current and future clinical trials may not meet the FDA, the European Medicines Agency, or EMA, or other regulatory agencies' requirements to approve the ELAD System for marketing under any specific indication, and these regulatory agencies may otherwise determine that our manufacturing processes or facilities are insufficient to support approval. For example, the FDA has noted its view that preliminary clinical evidence, at this time, does not indicate that the ELAD System may demonstrate a substantial improvement over standard of care. As such, we may need to conduct more clinical trials than we currently anticipate and upgrade our manufacturing processes and facilities, which may require significant additional time and expense and which could delay or prevent approval. If we fail to obtain regulatory approval in a timely manner, our commercialization of the ELAD System would be delayed and our business would be harmed.

***If we are able to secure marketing approval, our commercial success will be determined by our ability to obtain acceptable pricing and reimbursement for the ELAD System therapy.***

Therapies such as the ELAD System are paid for primarily by private and government insurance, although in some markets payment may be made by private individuals and their families. Reimbursement policies and decisions for medical products is a highly bureaucratic, politicized and regulated process and includes consideration of factors such as cost effectiveness and patient benefit. There is great pressure from government and third-party payors to reduce costs. Furthermore, there are no therapies approved to restore liver function and the lack of an established reimbursement structure introduces additional uncertainty with regard to reimbursement for the ELAD System. Although we have commissioned a report from pricing study and reimbursement specialists that concluded we should target a commercial price between \$150,000 and \$275,000 for ELAD therapy in the U.S., we do not know whether this price is achievable or sustainable. We have not yet determined a target commercial price for ELAD therapy either within or outside of the U.S., but believe it may be difficult to sustain a commercial price outside of the U.S. at or above the commercial price in the U.S. We will have no control over the pricing that is set by the government or private insurers, assuming we are able to secure marketing approval for the ELAD System. In markets where payment will be made by private individuals and their families, we cannot predict if such private payors will be prepared to pay an acceptable price.

***If we are unable to implement our sales, marketing, distribution, training and support strategies or enter into agreements with third parties to perform these functions in markets outside of the U.S. and Europe, we will not be able to effectively commercialize the ELAD System and may not reach profitability.***

Our technology is new and complex, and potential customers will have limited knowledge of, or experience with, the ELAD System. In addition, we have no ELAD System-related sales and marketing experience either domestically or abroad. We have not commercialized the ELAD System anywhere and do not plan to introduce the ELAD System, if approved, into the U.S. or other foreign jurisdictions until 2017 at the earliest. Our commercial success will depend on our ability to market and receive adequate reimbursement of the ELAD System. This success will also depend on our ability to obtain and maintain adequate pricing for the ELAD System.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biologic products and medical devices. To achieve commercial success for the ELAD System, if and when we obtain marketing approval, we will need to establish a sales and marketing organization.

In the future, we expect to build a targeted sales, marketing, training and support infrastructure to market the ELAD System in the U.S. and Europe and to establish collaborations opportunistically to market, distribute and support the ELAD System outside of the U.S. and Europe. There are risks involved with establishing our own sales, marketing, distribution, training and support capabilities. For example, recruiting and training sales and marketing personnel and personnel necessary to initially provide on-site device support and later device training to end-users is expensive and time consuming and could delay any product launch. If the commercial launch of the ELAD System is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing, training and support personnel.

Factors that may inhibit our efforts to commercialize the ELAD System on our own include:

our inability to recruit, train and retain adequate numbers of effective sales, marketing, training and support personnel;

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the inability of sales personnel to obtain access to physicians, including key opinion leaders, or to persuade adequate numbers of physicians to use the ELAD System;

our inability to properly support the ELAD System therapy with our own qualified personnel at each customer site or our inability to properly train and support our customers to use the ELAD System effectively on their own;

the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive or integrated product offerings; and

unforeseen costs and expenses associated with creating an independent sales, marketing, training and support organization.

If we are unable to establish our own sales, marketing, distribution, training and support capabilities and instead enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute the ELAD System ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute the ELAD System, or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to commercialize the ELAD System effectively. If we do not establish sales, marketing, distribution, training and support capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing the ELAD System and achieving profitability, and our business would be harmed.

***We have incurred losses since our inception and expect to incur significant losses in the foreseeable future and may never become profitable. Even if we ultimately achieve profitability, it may not be sustained and we may require additional capital.***

We are a clinical-stage company and clinical development of a novel therapy is a highly speculative undertaking. We have incurred significant losses in each fiscal year since our inception, including net losses of \$47.7 million and \$32.7 million for the years ended December 31, 2014 and 2013, respectively. As of December 31, 2014, we had an accumulated deficit of \$150.8 million. We expect to spend a considerable amount of our resources on the completion of our clinical programs and the work necessary to submit and gain approval of our ELAD System, on the production of the ELAD cartridges and bedside units, on investment in production facilities, and on the commercial launch and sales and marketing of the ELAD System. We also expect to expend considerable resources on research and development to develop new and improved products and to understand the mechanism of action of the ELAD System. We do not expect to earn revenues until 2017 at the earliest, and anticipate incurring additional losses and negative cash flow from operations for at least the next several years. Even if we do achieve profitability in the future, there is no guarantee that we will be able to sustain this profitability in subsequent periods and we may need to raise additional capital.

***Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.***

As of December 31, 2014, we had net operating loss, or NOL, carryforwards of approximately \$84.8 million and \$79.4 million, net of estimated limitations caused by certain ownership changes under Section 382 of the Internal Revenue Code, for federal and state income tax purposes, respectively. In general, under Section 382, a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change NOLs to offset

future taxable income. We believe our existing NOLs are subject to limitations arising from previous ownership changes, and if we undergo any further ownership changes, our ability to utilize NOLs could be further limited. Future changes in our stock ownership, some of which are outside of our control, could also result in additional ownership changes under Section 382. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to utilize a material portion of the NOLs, even if we attain profitability.

***Our internal computer systems, or those used by our clinical investigators, contract research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of development programs for the ELAD System.***

We rely on information technology systems to keep financial records, maintain laboratory and corporate records, communicate with staff and external parties and operate other critical functions. Despite the implementation of security measures, our internal computer systems and those used by our clinical investigators, contract research organizations, or CROs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. The techniques that could be used by criminal elements or foreign governments to attack these computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. Activities in China may be particularly at risk. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. While, to our knowledge, we have not experienced any such system failure, theft of information, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our clinical development activities. For example, the loss of clinical trial data from ongoing or future clinical trials could result in delays in regulatory approval efforts and significantly increase costs to recover or reproduce the data. To the extent that any disruption, theft of information, or security breach were to result in a loss of or damage to data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the clinical development and the future development of the ELAD System could be delayed.

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***We have limited experience in conducting pivotal clinical trials used to support regulatory approval and our prior clinical trials of the ELAD System did not demonstrate a statistically significant improvement in survival, the primary endpoint that is needed to support regulatory approval.***

We are currently undertaking our first pivotal clinical trials for the ELAD System. While the endpoints and populations for the pivotal trials are derived from results of initial studies and medical literature, in none of those prior studies have we demonstrated an effect in the population and on the endpoints prospectively described in the study plan. The pivotal trials are primarily based on trends derived from post-hoc, retrospective analyses of data subsets. Our prior clinical trials of the ELAD System in AILD were not powered to, and did not, demonstrate statistically significant improvement over standard of care in the primary endpoint of 90-day survival. Similarly, our prior clinical trials of the ELAD System in FHF did not demonstrate statistically significant improvement in the primary endpoint of 28-day survival. The lack of statistical significance could be attributed to various factors including the lack of power to demonstrate significance, the design of the studies or the lack of an ELAD System treatment benefit. Although we did complete a pivotal clinical program in acute liver failure (principally hepatitis) in China in 2007, the underlying clinical trial was terminated early by the lead hospital due to achievement of safety and efficacy goals and a determination that it was unethical to continue. We are now in the process of conducting two Phase 3 clinical programs including the U.S. and Europe. We have not previously completed a pivotal clinical trial program of the size and complexity of our current planned pivotal programs and we cannot provide any guarantee that we will successfully complete such a program. If this pivotal program is completed, there can be no assurance that the data generated can be used to support marketing approval for any indication in the U.S. or Europe. If our Phase 3 clinical trials do not achieve statistical significance for the primary endpoint, we will not receive marketing approval and we will not be able to commercialize the ELAD System.

***The results of previous clinical trials may not be predictive of future results.***

Positive results from our prior clinical trials, including either statistical significance in some endpoints or trends towards statistical significance in other endpoints, should not be relied upon as evidence that our current or future clinical trials will necessarily succeed. While we believe that we have learned valuable lessons from the results of prior trials and have attempted to use these lessons to guide our design of current and future clinical trials, there can be no guarantee that these lessons are correct or that we will effectively incorporate them into the design of current and future clinical trials. For example, our primary endpoint in VTI-208, 90-day survival, is based on the results of a subset of subjects in VTI-206. Though that subset showed a trend toward increased survival up to at least study day ninety-one, it consisted of only 29 subjects. The FDA has noted its belief that this preliminary clinical evidence does not indicate that our product may demonstrate a substantial improvement over standard of care. We cannot provide any guarantee that our current and future clinical trials will provide statistically significant data sufficient to support regulatory approval.

***If we fail to select appropriate subjects for our Phase 3 clinical trials or if these subjects do not progress as expected, it will be difficult for us to demonstrate the statistically significant efficacy of the ELAD System therapy necessary to gain approval.***

We have designed VTI-208 and VTI-210 in accordance with input provided by regulatory authorities that we must demonstrate a statistically significant improvement in a survival endpoint. VTI-208 and VTI-210 will include concurrent control subjects in a 1:1 ratio with treated subjects and all subjects will be included in the statistical analysis. Also, each study is designed to enroll subjects with an expected death rate between 50% and 75% in 30 to 90 days without the ELAD System therapy. It is necessary to select subjects with these death rates in order to be able to



determine whether the ELAD System has an effect on treated subjects with a manageable number of subjects in the clinical trial. We monitor certain baseline characteristics of the subjects we are enrolling in our studies (such as age and mean model for end-stage liver disease, or MELD, score) to assess that the population characteristics are similar to those from prior studies in which death rates were in the target range. Although subjects enrolled in VTI-208 have similar ages and MELD scores to AILD subjects enrolled in VTI-206, there is no assurance that this will continue to be the case or that these parameters are sufficient to predict survival. Moreover, if we do not succeed in selecting appropriate subjects or if the subjects we select do not progress as expected, we may not be able to demonstrate statistically significant efficacy of the ELAD System therapy to gain approval.

***Random variation or changes in standard of care could cause our clinical trials to be delayed and/or fail.***

Regulatory authorities worldwide have adopted the standard that, to gain marketing approval, clinical trials should produce a result that has less than a 5% probability of being due to random variation. There is no assurance that any of our clinical trials will meet that standard. In addition, we have designed all of our clinical trials to be judged by a survival primary endpoint, which may be difficult to achieve for many reasons, including unanticipated survival rates of control subjects due to random variations, deficiencies in our exclusion and inclusion criteria, and the standard of care of the subjects, which may vary from site to site and country to country and is continuously evolving. For example, FDA has expressed concern that the VTI-208 study may not be adequately designed to provide convincing evidence of efficacy if there are significant differences in how the ELAD System subjects and controls are treated during the treatment period and after hospital discharge. Variations in length of hospital stay, rates of hospital re-admission, alcohol recidivism rates, nutritional support, and concomitant medications, which are not within our control, could significantly confound the study results and call into question whether any difference in survival is due to the ELAD System or to these factors. Moreover, evolution in the standard of care for the treatment of patients with acute forms of liver failure could make our trials difficult to enroll and interpret. For instance, in consideration of the STOPAH study, we modified the VTI-210 trial protocol to allow subject enrollment independent of steroid administration. STOPAH failed to demonstrate any significant benefit in the primary analysis of overall survival for subjects treated with either steroids, pentoxifylline or a combination of the two at one, three or 12 months, as compared with placebo. Any of these factors, which are beyond our control, could materially and adversely affect the results of our Phase 3 clinical trials and prevent us from gaining regulatory approval of our ELAD System therapy. In addition, even if the results of our clinical programs are positive, our inability to control or adequately account for these factors between treatment arms could cause the FDA or other regulatory authorities to determine that the results are not adequate to support marketing approval.

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***The ELAD System treatment could result in significant clinical risks to the patient, including death.***

The ELAD System therapy is targeted towards very sick patients who are likely to die if left untreated. Patients in acute liver failure quickly develop failure of other organs including lungs, kidney, brain, and blood coagulation systems. Patients who receive the ELAD System therapy may die due to other serious health problems even if the ELAD System is effective.

All extracorporeal therapy systems cause a decline in blood platelets, which can lead to coagulation problems and uncontrolled bleeding because platelets are critical to the formation of blood clots. Patients with acute liver failure generally have serious blood clotting problems since the liver produces most of the body's blood clotting proteins. These patients therefore have wide variations in their ability to coagulate their blood. To minimize blood clotting issues during ELAD treatment, some patients require an infusion of small amounts of anti-coagulant therapy, which can aggravate bleeding. Because every patient is different, the need for anti-coagulant therapy is not predictable and must be established during therapy, a process that can affect the course of the therapy. The risk of uncontrolled bleeding may be addressed during the ELAD System therapy by administering platelet transfusions to patients whose platelets drop below a safe level or by administering blood coagulation factors. However, there have been cases of uncontrolled bleeding during and after the ELAD System therapy. Additionally, some patients have abnormal red blood cells, which have weakened cell walls subject to rupture by physical force, a process known as hemolysis. The physical force exerted on the red blood cells by the ultrafiltrate generator in the ELAD System line can, in some cases, be enough to cause hemolysis which, if not arrested, can be fatal. The incidence of hemolysis was approximately 2% in the acute liver failure patients enrolled in our prior clinical trials.

Human liver-derived C3A cells have been shown in animal studies to have the capacity to grow into a tumor mass under certain conditions. Although this has not been seen in the subjects treated with the ELAD System to date, it is possible that some VTL C3A cells could escape from the ELAD cartridges and cause tumors in patients or produce substances that could lead to the development of malignant tumors. These or other adverse events, even those that are currently unforeseen, could significantly affect our development and commercialization efforts, cause the regulatory authorities to place our clinical trials on hold or to refuse to grant or maintain the marketing approval or result in withdrawal of the ELAD System from the market.

***Ethical considerations require us to conduct open-label clinical trials of the ELAD System where control subjects do not receive a sham treatment and this could introduce unacceptable bias into our trial results.***

We are not conducting any of our clinical trials with a sham control extracorporeal circuit that includes empty cartridges. This is due to the potential harm that the extracorporeal circuit can cause to control subjects without the potential for any benefit, which makes it unethical to subject the controls to a sham. Although regulatory agencies agree that, due to the nature of the ELAD System therapy, it is not possible to conduct a blinded study, they have expressed concern that the open-label nature of the study may introduce significant bias in the treatment of the ELAD System or control subjects, since the study subject, physicians and caregivers know who has, and has not received the ELAD System therapy. We have developed a protocol that attempts to minimize this bias to the extent possible, including defining a protocol-specific standard of care, specifying steroid treatment, standardizing the discharge criteria for both the ELAD System and control subjects, requiring that follow-up visits are conducted by a blinded reviewer, ensuring home healthcare nurses and other clinical personnel are unaware of treatment assignment, educating subjects not to reveal treatment assignment to their caregivers and monitoring concomitant medications, alcohol recidivism and interaction with the healthcare system to provide evidence that there is no meaningful difference between the groups that could significantly confound the trial data. However, there is no guarantee that bias will not enter into the trial, affect the results or cause regulatory agencies to refuse marketing approval of the ELAD System.



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***If we encounter difficulties enrolling subjects in our clinical trials, our clinical trials could be delayed or otherwise adversely affected.***

Clinical trials for the ELAD System require us to identify and enroll a large number of subjects that meet all of the entry criteria set forth in our protocols, including having the disease under investigation. We may not be able to enroll a sufficient number of subjects who meet our protocol requirements in a timely manner. Subject enrollment is affected by numerous factors, many of which fall outside our control, including:

timeliness of contracting with clinical trial sites, and obtaining approval of the trial by the institutional review boards, or IRBs, at each site;

lack of a sufficient number of subjects who meet the enrollment criteria for our clinical trials;

perceived risks and benefits of the product candidate under study;

availability of competing therapies and clinical trials;

efforts to facilitate timely enrollment in clinical trials;

scheduling conflicts with participating clinicians; and

proximity and availability of clinical trial sites for prospective subjects.

Additionally, even if we are able to identify an appropriate subject population for a clinical trial, there can be no assurance that the subjects will complete the study.

If we have difficulty enrolling a sufficient number of subjects to conduct our clinical trials as planned or if enrolled subjects fail to complete the study or comply with our protocols, particularly with regard to follow-up appointments, the completion of our clinical trials will be delayed and our business would be harmed.

***We may face delays in completing our clinical trials, and we may be required to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with applicable regulatory requirements, the results are negative or inconclusive, or the clinical trials are not well-designed or executed as expected.***

Our current and future clinical trials must be conducted in accordance with regulations governing clinical studies, and are subject to oversight by the FDA, foreign governmental agencies, ethics committees and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials may require large numbers of test subjects. Changes in regulatory requirements may occur at any time and we may need to amend clinical trial protocols to reflect such changes. In addition, we may voluntarily amend our protocols, as we did for VTI-210. Amendments may require us to resubmit our clinical trial protocols to ethics committees or IRBs for reexamination, which may impact the costs, timing or successful completion of the underlying trial.

Our current and future clinical trials may require amendment or be delayed, unsuccessful or terminated as a result of many factors, including:

delays or failures in designing an appropriate clinical trial protocol with sufficient statistical power and in reaching agreement on trial design with investigators and regulatory authorities;

delays or failure in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

delays or failure by CROs, investigators and clinical trial sites in ensuring the proper and timely conduct of our clinical trials;

delays or failure by us in manufacturing sufficient quantities of the ELAD System pursuant to required quality standards for use in our clinical trials and by third-party manufacturers in supplying necessary and suitable components for the system;

delays or failure in transporting the ELAD System to clinical trial sites with sufficient rapidity to enable treatment to begin early enough to have an opportunity for clinical benefit;

delays or failure in completing data analysis and achieving primary and secondary endpoints;

regulators or clinical site ethics committees or IRBs may suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or concerns about patient safety;

we may suspend or terminate our clinical trials if we believe the ELAD System is exposing the participating subjects to unacceptable health risks or for other reasons;

subjects may not complete our clinical trials due to safety issues, adverse events, inconvenience or other reasons;

subjects in our clinical trials may die or suffer other adverse events for reasons that may be either related or unrelated to the ELAD System, particularly given the critically ill nature of these subjects;

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we may have difficulty in maintaining contact with subjects after treatment, preventing us from collecting the data required by our study protocol; and

final analysis of the data of our clinical trials may conclude that the ELAD System lacks sufficient clinical efficacy or presents unacceptable safety risks.

Should any of our clinical trials fail to provide evidence of safety and efficacy sufficient to satisfy the requirements of the regulatory authorities, the ELAD System will not be approved. If we experience delays in the completion of, or termination of, any clinical trial of the ELAD System, the commercial prospects of the ELAD System will be harmed, and our ability to generate revenues will be delayed or eliminated. In addition, any delays in completing our clinical trials will increase our costs, slow down our development and approval process and delay or jeopardize our ability to commercialize the ELAD System. Any of these occurrences may harm our business, financial condition and prospects significantly.

## **Risks Related to Regulatory Matters**

### ***The FDA regulatory approval process is complex, time-consuming and unpredictable.***

In the U.S., the ELAD System is regulated as a combination biologic and medical device. Before the ELAD System can be marketed in the U.S., we must submit and the FDA must approve a Biologic License Application, or a BLA. In addition, the device components of the ELAD System must be found acceptable as part of the BLA. Because the ELAD System is a novel therapy involving a combination biologic and medical device, the regulatory review process is complex, time-consuming and unpredictable. As a result, our development costs, timelines and approvals are not readily predictable.

The time required to obtain approval by the FDA to market a new therapy is unpredictable but typically takes many years and depends upon many factors, including the substantial discretion of the regulatory authorities.

The ELAD System could fail to receive regulatory approval for many reasons, including the following:

the FDA may disagree with the design or implementation of our clinical trials or study endpoints. For example, it has expressed concern about the open-label design and multiplicity of confounding variables, including the need for delineating the standard of care that both treatment and controls will receive during our studies;

we may be unable to demonstrate to the satisfaction of the FDA that the ELAD System is safe and effective for its proposed indications or that the ELAD System provides significant clinical benefits;

the results of our clinical trials may not meet the level of statistical significance required by the FDA for approval or may not support approval of a label that could command a price sufficient for us to be profitable;

the FDA may disagree with our interpretation of data from preclinical studies or clinical trials. For example, the FDA has stated there are insufficient preclinical and clinical data to determine whether the ELAD

System has the potential to provide a clinically meaningful improvement in liver function;

the opportunity for bias in the clinical trials as a result of the open-label design may not be adequately handled and may cause our trial to fail;

the ELAD System may be subject to an FDA advisory committee review, which is triggered by an FDA request, which is solely within the FDA's discretion, which may result in unexpected delays or hurdles to approval;

the FDA may determine that the manufacturing processes at our facilities or facilities of third party manufacturers with which we contract for clinical and commercial supplies are inadequate;

even if VTI-208 is successful in demonstrating a statistically significant improvement over standard of care, in light of the fact that certain confounding factors may be viewed by the FDA as limiting the persuasiveness of the study results, a single Phase 3 clinical trial may not be sufficient to provide the substantial evidence of effectiveness necessary to support regulatory approval, and therefore we may need more than one Phase 3 clinical trial to secure regulatory approval;

the FDA has commented that even if one of our Phase 3 clinical trials, including VTI-208, is a statistical and clinical success, a second confirmatory trial that substantiates positive results may be necessary to support a BLA; and

the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

The FDA has expressed concern that the VTI-208 study may not be adequately designed to provide convincing evidence of efficacy if there are significant differences in how the ELAD System subjects and control subjects are treated during the study and after discharge from the hospital. Differences in length of hospital stay, rates of hospital re-admission, alcohol recidivism rates, nutritional support, and concomitant medications could significantly confound the study results.

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In addition, even if we were to obtain approval, the FDA may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve the ELAD System with a label that does not include the labeling claims necessary or desirable for successful commercialization of the ELAD System. Any of the above could materially harm the ELAD System's commercial prospects.

***The regulatory approval processes of foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable.***

Outside the U.S., our ability to market the ELAD System is contingent upon receiving marketing authorizations from appropriate regulatory authorities. If our clinical programs are successful, we currently anticipate submitting applications for marketing authorization to the EMA in the European Union. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country and we may be unable to meet such requirements. If the regulatory authority is satisfied that adequate evidence of safety, efficacy, and quality has been presented, a marketing authorization will be granted. The foreign regulatory approval process involves all of the risks associated with FDA approval.

***Even if the ELAD System receives regulatory approval, we will be subject to ongoing regulatory requirements and may face regulatory or enforcement action.***

If any ELAD System product receives regulatory approval, we will be subject to significant ongoing regulation by the FDA and other regulatory authorities, including regulation of our manufacturing operations, and any third-party manufacturing operations for compliance with applicable current Good Manufacturing Practices, or cGMP, and/or Quality System Regulation, or QSR, post-approval clinical data, adverse event reporting and complaint handling, and advertising and promotional activities. Failure to comply with regulatory requirements may subject us to sanctions. These may include warning letters, adverse publicity, civil and criminal penalties, injunctions, product seizures or detention, and refusal to approve pending product marketing applications.

## **Risks Related to the Medical Device Components of the ELAD System**

***If we or our third-party manufacturers fail to comply with the Quality System Regulation in the U.S. or Medical Device Directives and Standards in Europe, our business would suffer.***

We are required to demonstrate and maintain compliance with applicable regulations for the manufacturing of combination biologic products, including specified parts of the QSR and European Medical Device Directives, or MDD. Our third-party medical device manufacturers, are required to demonstrate and maintain compliance with the QSR and MDD. The QSR and MDD are complex regulatory schemes that cover the methods and documentation of the design, testing, control, manufacturing, labeling, quality assurance, packaging, storage and shipping of the ELAD System. Regulatory agencies enforce the QSR and MDD through periodic inspections. Prior to approval of the ELAD System, our manufacturing facility will be subject to a preapproval inspection to determine compliance with the applicable regulations, including cGMPs, parts of the QSR, the European drug cGMP regulations, and the MDD. In addition, our third-party medical device component manufacturers will be subject to a preapproval inspection to determine compliance with QSR and MDD requirements. Our failure, or the failure of our third-party manufacturers, to pass a preapproval inspection, or take satisfactory and prompt corrective action in response to an adverse inspection, could prevent or significantly delay approval of the ELAD System.

***The ELAD System bedside unit is based on a cardio-pulmonary bypass system that has been replaced with an updated system, and regulatory authorities may not view the systems as interchangeable.***



The ELAD System bedside unit was originally based exclusively on the Sorin Stöckert Perfusion System S3 Double Head Pump Module, a medical device indicated for use during cardio-pulmonary bypass surgery. Our prior clinical trials have been carried out using an ELAD System bedside unit based on Sorin's S3 system. However, Sorin stopped selling the S3 system and replaced it with an updated S5 system. We have carried out testing of an ELAD System bedside unit based on the S5 and we believe that the S3 and S5 systems are equivalent and interchangeable from a clinical and regulatory perspective. We have submitted information to both the U.S. and the European regulatory authorities to support equivalence. Both the S3 and S5 systems are being used in our ongoing clinical trials. There can be no assurance that regulatory authorities will view the S3 and S5 systems interchangeably, or that Sorin will cooperate with us or provide us with the documentation necessary for inclusion in our BLA submission, which will be required to obtain regulatory approval of our ELAD System. If regulatory authorities do not view the S3 and S5 systems as equivalent, or Sorin fails to provide the information necessary for inclusion in our regulatory filings, approval of our ELAD System may be significantly delayed or prevented.

***One of the ELAD System component suppliers is subject to an FDA consent decree which, if not lifted, would force us to find another supplier for these components.***

One of the components of the ELAD System bedside unit is manufactured by Terumo Cardiovascular Systems, or Terumo. In March 2011, Terumo entered into a consent decree with the FDA which limits its ability to ship products from certain of its manufacturing facilities including the one that manufactures the component we use. We have signed a Certificate of Medical Necessity that allows us to continue to use those components we already own while Terumo works to resolve the issues associated with the consent decree. Once the consent decree is lifted Terumo has indicated that it will resume shipping of this component. Should Terumo not be able to fulfill the requirements of the consent decree, we will have to source these components from an alternative supplier. There is no guarantee that Terumo will be able to fulfill the requirements of the consent decree, or that an alternative supplier can be found or will agree to acceptable terms.

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***Changes in any of the device components could affect our ability to complete our clinical trials and to obtain and maintain approval and commercialization efforts.***

The device components of the ELAD System will be reviewed as part of the BLA for the ELAD System. If the manufacturers of those components make modifications, discontinue supplying or are unable to supply sufficient quantities of such components during our clinical testing or after any approval, or if we elect to change a component, we will need to perform validation testing and obtain FDA and other regulatory approval prior to using the modified or replacement component. For example, one of our suppliers had an issue sourcing a raw material that is used in manufacturing of tubing which is a component of the ELAD System. If we had not been able to obtain sufficient quantities of this tubing on a timely basis, we would have had to delay enrollment in our clinical trials until additional supplies became available or we would have been required to validate an alternative tubing to use, which could have delayed our clinical trials and increased our costs. If FDA or any other regulatory body fails to approve use of those modified or replacement devices takes significant enforcement action against the manufacturer or if we are unable to validate a replacement component, we would not be able to complete our clinical trials or, in the future, we might not be able to market or could have to suspend marketing of the ELAD System in certain jurisdictions.

***We may be unable to demonstrate that devices cleared for different uses may be safe and effectively used in the ELAD System.***

Most device components of the ELAD System have been previously cleared for use by the FDA or other regulatory authorities. However, in some instances, we will be using the components outside the scope of their cleared indications. Other device components have no regulatory approvals. We may need to conduct additional testing to bridge the differences between the cleared indications for use and the proposed use in the ELAD System in order to obtain approval, or we could be required to obtain separate clearance for one or more of the components used in the ELAD System. The failure to provide adequate bridging information or to obtain separate clearance of these device components for use in the ELAD System, if required, could delay or prevent approval of the ELAD System.

## **Risks Related to the Cellular Component of ELAD System and Related Components**

***If we fail to comply with cGMPs our business will suffer.***

We are required to demonstrate and maintain compliance with cGMPs. The cGMPs describe the methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a biologic to assure the biologic meets the requirements for safety, and has the quality, purity, and potency characteristics that it purports or is represented to possess. Regulatory agencies enforce these requirements through periodic inspections. Prior to approval of the ELAD System, our manufacturing facilities will be subject to a preapproval inspection to determine compliance with U.S. and European cGMPs and applicable QSR and MDD requirements. Our failure to pass such an inspection, or take satisfactory and prompt corrective action in response to an adverse inspection, could prevent or significantly delay approval of the ELAD System.

***We rely on third party suppliers, and in some instances, a single third party supplier, for critical components of the ELAD System and these suppliers could cease to manufacture the components, go out of business or otherwise not perform as anticipated.***

While the growing of our VTL C3A cells is under our control, the manufacture of all of the other parts and components of the ELAD System are undertaken by third party suppliers. We currently rely on a single source of supply for many critical components, including components of the ELAD System bedside unit, the ultrafiltrate generator cartridges, the media we use to grow and ship our VTL C3A cells, the cartridges in which our VTL C3A

cells are grown and the bioreactors that have been developed to grow and store the ELAD cartridges. We are currently investigating additional sources of supply for these components to support future clinical development and, ultimately, commercialization of the ELAD System. If we were to fail to develop additional sources of supply, and a single source of supply of a critical component of the ELAD System were to become unavailable, our ability to continue clinical development or to initiate commercialization of the ELAD System would be severely compromised. In addition, we rely on third party suppliers for the safety of products of human and animal origin that are incorporated in the ELAD System production process and these suppliers could cease to manufacture the components, inadequately test these components, go out of business or otherwise not perform as anticipated. We do not have long-term agreements with our suppliers, and we purchase components on a purchase order basis. For components that are not readily available from other sources, we are subject to the risks that our suppliers will raise their prices or impose other terms or conditions that are less favorable or unacceptable to us.

For instance, newborn calf serum, which is a component of the cell growth media, is used in the manufacture of the ELAD System. It is obtained from an outside supplier. We are wholly reliant on the guarantee of our supplier that the calf serum used in our manufacturing procedures is free of transmitted animal viruses and other pathogens. Should the source of supply become infected, or the supplier become unable to continue to supply calf serum of the quality necessary to support human use, or the regulations change such that the calf serum cannot be used for human use, we would have to find alternative sources of supply and manufacturing methods, for which there is no guarantee of success.

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Human albumin and Trypsin-EDTA are also used in the manufacture of our ELAD System and are each provided by a single supplier. In addition, while these products are tested to be free of contamination by the supplier, we cannot guarantee that will continue to be the case.

***If our facility becomes inoperable, we will be unable to continue manufacturing our product candidate and as a result, our business will be harmed until we are able to secure a new facility.***

We manufacture and assemble the ELAD System at our facility in San Diego, California. No other manufacturing or assembly facilities are currently available to us, and any additional manufacturing or assembly facilities that we use will need to be approved by regulatory authorities prior to our use. Our facility and the equipment we use to manufacture the ELAD System would be costly to replace and could require substantial lead-time to repair or replace. The facility may be harmed or rendered inoperable by natural or man-made disasters, including fire, earthquakes, flooding and power outages, which may render it difficult or impossible for us to perform our research, development and manufacturing for some period of time. The inability to perform our research, development and manufacturing activities, combined with our limited inventory of reserve raw materials and manufactured supplies, may result in the delay of clinical trials or, if approved for sale, the loss of customers, or harm our reputation, and we may be unable to reestablish relationships with those customers in the future. Although we possess insurance for damage to our property and the disruption of our business, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all.

***We may be unable to manage our anticipated manufacturing growth to support our clinical development activities and long-term commercial demand for the ELAD System.***

In order to support our ongoing clinical programs, we will need to increase production of our ELAD System. Similarly, if and when the ELAD System is approved for sale, we will need to expand our manufacturing space in San Diego and build new manufacturing facilities to meet anticipated demand for the ELAD System in the U.S. and abroad. These activities involve significant expense, including the construction of new clean rooms and bioreactors, the movement and installation of key manufacturing equipment and the modification of manufacturing processes. In addition, we must also notify, and in some cases obtain approval from, the FDA and other regulatory authorities of any changes or modifications to our manufacturing facilities and processes, and there can be no assurance that they will authorize us to proceed. If we are not able to expand our manufacturing capacity to meet future demand, our business would be harmed.

Further, our anticipated growth will place additional strain on our organization, employees and third-party suppliers, resulting in an increased need for us to carefully monitor quality. Any failure by us to manage our growth effectively could have an adverse effect on our ability to achieve our development and commercialization goals.

***We forecast the requirements for components and materials used in the ELAD System, and if our forecasts are incorrect, we may experience delays in shipments or increased inventory costs.***

We keep limited materials, components and finished product on hand. To manage our manufacturing operations with our suppliers, we forecast anticipated product orders and material requirements to predict our future inventory needs and to enter into purchase orders on the basis of these requirements. Our limited historical experience may not provide us with enough data to accurately predict future demand. If our business expands, our demand for components and materials would increase and our suppliers may be unable to meet our demand. Many of our components are medical devices, which have fixed future expiration dates. If we overestimate our component and material requirements, we will have excess inventory, which may have to be disposed of if it exceeds approved expiration dates, which would increase our expenses. If we underestimate our component and material requirements, we may have inadequate

inventory, which could interrupt, delay or prevent delivery of the ELAD System to our customers. Any of these occurrences would negatively affect our financial performance and the level of satisfaction our customers have with our business.

***We may not be able to grow our VTL C3A cells reliably and cost-effectively.***

Operations with human cells, even a stable, immortal cell line such as the VTL C3A cells used in the ELAD System, can be subject to conditions and influences that we may not be able to control. Although our VTL C3A cells are stored at three separate locations in the U.S. and the U.K., it is possible that all three locations could be destroyed and we will lose all or a portion of our cell banks. It is also possible that the cells will simply cease to function. While we take precautions to prevent this from happening, the ELAD System employs new technologies and we could encounter unforeseen complications. To date, we have only produced the small number of the ELAD cartridges required to support our clinical trials. As we increase production to support Phase 3 clinical trials and long-term commercial demand, we may experience significant scale-up issues, which may cause quality and cost problems. If we cannot produce the required number of the ELAD cartridges in a cost-effective manner, our business could be materially harmed.

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***Cellular therapy is complex and we do not have a complete understanding of the mechanism of action of the ELAD System.***

Cellular therapy is a complex treatment with multiple variables that are not fully understood. Our VTL C3A cells used in the ELAD cartridges produce hundreds of metabolites. Likewise, the plasma ultrafiltrate formed from blood, which has been treated by our VTL C3A cells in our ELAD cartridges, is a similarly complex material. The composition and stability of the treated blood can be affected by the conditions of its generation in the ELAD System bedside unit and could affect treatment outcomes. For instance, while subjects treated with the ELAD System typically only require a single set of cartridges, some subjects require more than one set during their three to ten day treatment period, which may have implications for not only efficacy, but also cost of goods. While we believe that we have identified the key parameters of the ELAD System VTL C3A cartridges and set them in an appropriate range, it is possible that there are other variables that are important to safety and efficacy that have not been anticipated. We believe that we have set these parameters at realistic levels that can be controlled by the specification set for a supplier and confirmed by us in our quality control procedures, but it is possible that unanticipated complications will emerge.

## **Risks Related to the ELAD System's Future Commercialization**

***It is difficult to forecast future performance; our financial results may fluctuate unpredictably.***

Our limited operating history makes it difficult for us to predict our future commercialization efforts. A number of factors, over which we have limited or no control, may contribute to fluctuations in our financial results, such as:

delays in receipt of anticipated purchase orders;

our ability to recruit, train and retain sales, marketing, training and support personnel;

our inability to educate physicians about the ELAD System and drive the adoption of the ELAD System therapy for any approved indications;

performance of our targeted sales force in the U.S. and Europe and future partners in other markets;

results of clinical trials evaluating the ELAD System therapy;

positive or negative media coverage of the ELAD System or products of our competitors or our industry;

our ability to obtain further regulatory clearances or approvals, including for other indications;

delays in, or failure of, product and component deliveries by our subcontractors and suppliers;

changes in the length of the sales process;

changes in healthcare coverage and reimbursement policies;

customer response to the introduction of new product offerings; and

fluctuations in foreign currencies.

***The human clinical trial results may not be representative of the results that are obtained after the ELAD System product launch.***

Human clinical trials are very complicated undertakings and working with subjects in acute liver failure is particularly difficult because of the serious nature of the disease and the co-morbidities experienced by the subjects. Not enough is known about the function of the liver to understand the progression of liver disease and any single subject can react differently to the ELAD System therapy. This means that clinical trials done at different times in different groups of subjects may obtain different results. Safety risks not identified in our clinical trials may first appear after we obtain approval and commercialize the ELAD System. Any new post-marketing adverse events may significantly impact our ability to market the ELAD System and may require that we recall and discontinue commercialization of the product. Any of these events will harm our business.

***The ELAD System is a very complicated therapy and will need to be delivered by well-trained staff. There is no guarantee that we will be able to implement such training and find sufficient numbers of people to enable us to grow at an acceptable rate.***

In the initial commercialization period, it will be essential for us to have our own trained staff present during the delivery of the ELAD System therapy. This may entail the construction and operation of training centers and will require the hiring of personnel of appropriate ability to be adequately trained. The differences in language and culture may make this a difficult undertaking. If we cannot recruit, train and retain significant numbers of physicians and nurses, our ability to grow will be restrained and we may find that the ELAD System therapy is being delivered by people with a substandard level of training, and with potentially material adverse results. If the ELAD System therapy is delivered improperly or the bedside device or the ELAD cartridges are not properly maintained by our customers, the ELAD System may not provide the intended benefit or could harm patients. This may in turn result in perceptions, even if unfounded, that the ELAD System is ineffective or that our bedside device or the ELAD cartridges are defective, which could materially harm our reputation and ability to market the ELAD System effectively.

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***We could lose our valuable employees and thereby lose our advantage in the marketplace.***

We are highly dependent on the efforts of our key employees, including senior management and senior scientific, clinical, regulatory, operational and other personnel. The development of new therapeutic products requires expertise from a number of different disciplines, some of which are not widely available.

Our key employees have a significant amount of know-how and experience in our company and the loss of one or more of them could have a material and adverse effect on our operations. While we have taken steps to incentivize and to retain our employees, including the granting of stock options, paying competitive salaries and implementing appropriate bonus programs, these factors may not be enough to retain the key employees that we need.

The loss of the services of existing personnel, the failure to recruit additional key scientific, managerial, clinical, regulatory, operational and other personnel in a timely manner, and the loss of our employees to our competitors would harm our research and development programs and our business. We may experience difficulty in hiring and retaining highly skilled employees with appropriate qualifications. If we fail to attract new personnel or fail to retain and motivate our current personnel, our business and future growth prospects would be harmed.

***Competitive products could be developed which make the ELAD System obsolete.***

The biotherapeutic and medical device industries are highly competitive and we face potential competition from pharmaceutical companies, specialty pharmaceutical, medical device and biotechnology companies worldwide. Given the significant unmet medical need for novel therapies to treat acute liver failure, many companies, universities and research organizations are actively engaged in the discovery, research and development of potential therapies in this field. Several of these entities are engaged in research on cell-based approaches to acute liver failure. Although we are not aware of any ongoing human clinical trials involving potentially competitive product candidates, such trials could be taking place or could begin in the near future. We are not aware of any company that is in human clinical trials with a human cell-based product for the treatment of acute liver failure. At least four companies have prior research work on various human hepatocyte cell lines including Exten Industries, Hepalife Technologies, Fresenius, and Hybrid Organ GmbH. In addition, the University College London, and the University of Amsterdam and its spinout Hep-Art Medical Devices are actively pursuing animal research in this area. Several companies have also attempted to develop extracorporeal therapy based upon primary porcine hepatocytes, although ongoing research in this area is difficult to ascertain. Two commercially available liver dialysis systems, from Baxter International and Fresenius, have undergone extensive clinical development, although both have failed to show an improvement in long-term survival among patients with acute liver failure. Both rely on not only traditional dialysis circuits to remove water-soluble toxins, but also albumin dialysis circuits to remove albumin-bound molecules. In addition, there are several drugs available to treat symptoms associated with acute liver failure, including steroids, pentoxifylline and N-acetylcysteine. These three drugs, alone or in combination, are used frequently in patients with acute liver failure. While we are not aware of any of these other entities being close to undergoing human clinical trials with a human cell-based product for the treatment of acute liver failure, it is possible that these trials are occurring without our knowledge and that such a product may get to market much faster than we expect, which could harm our business.

***The coverage and reimbursement status of new therapies is uncertain, and failure to obtain adequate coverage and reimbursement for the ELAD System therapy could limit our ability to generate revenue and become profitable.***

There is significant uncertainty surrounding the third-party coverage and reimbursement of novel and newly approved therapies, particularly for indications for which there is no current effective treatment or the current standard of care is relatively inexpensive. Due to the novel nature of the ELAD System and the potential for it to offer therapeutic benefit after a single administration of continuous therapy lasting three to ten days, we face additional uncertainty related to



coverage and reimbursement. We will depend in large part on the availability of coverage and the establishment of adequate reimbursement levels for the ELAD System from third-party payors, including government payors, such as the Medicare and Medicaid programs, and managed care organizations. Although we believe that the single largest category of ELAD-appropriate patients are covered by private insurance, followed by Medicaid and then Medicare, this analysis is based on small numbers, may not be accurate, and may change in the future.

Third-party payors are increasingly focused on containing healthcare costs by limiting both coverage and the level of reimbursement for new therapies and, as a result, they may not cover or provide adequate payment for the ELAD System. Obtaining adequate coverage and reimbursement approval for a product from a third-party payor is a time-consuming, costly and sometimes unpredictable process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of the ELAD System. However, we cannot guarantee that we will be able to provide data sufficient to gain acceptance with respect to adequate coverage and reimbursement. Payors may conclude that the ELAD System is less safe, less effective or less cost-effective than existing or later introduced therapies, and third-party payors may not approve the ELAD System for coverage and reimbursement or may cease providing or provide inadequate coverage and reimbursement. Coverage and reimbursement determinations are made on a payor-by-payor basis and it may take several years to obtain appropriate reimbursement codes, if ever. Obtaining acceptable coverage and reimbursement from one payor does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payor. As there is a large number of third-party payors, obtaining coverage and reimbursement in the U.S. and internationally will consume significant time and resources. A third-party payor's decision to provide coverage does not imply that an adequate reimbursement rate will be approved. There can be no assurance that our clinical data will allow for satisfactory pricing of the ELAD System and the failure to obtain coverage and adequate reimbursement for the ELAD System would materially and adversely affect our business. Moreover, healthcare cost containment initiatives that limit or deny reimbursement for the ELAD System would also materially and adversely affect our business.

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***Our relationships with investigators, healthcare professionals, institutional providers, consultants, third-party payors, and customers are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations.***

Healthcare providers, physicians and others play a primary role in the recommendation and prescribing of any product candidates for which we may obtain marketing approval. In the U.S., our current business operations and future arrangements with investigators, healthcare professionals, institutional providers, consultants, third-party payors and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our products that obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

the federal healthcare program anti-kickback statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return, for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, service or item for which payment is made, in whole or in part, under a federal healthcare programs;

the federal civil and criminal false claims laws and civil monetary penalties laws, including civil whistleblower or qui tam actions, prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly or willfully falsifying, concealing, or covering up by any trick, scheme or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, clearinghouses and healthcare providers;

the federal transparency law, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA), and its implementing regulations, require manufacturers of drugs, devices, biologicals and medical supplies to report to the U.S. Department of Health and Human Services information related to payments and other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

analogous state laws and regulations, including but not limited to: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state laws and regulations that require manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities.

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Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these or any other health regulatory laws or any other governmental regulations that may apply to us, we may be subject to penalties, including without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, enhanced government reporting and oversight under a corporate integrity agreement or other similar arrangement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare program, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses or divert our management's attention from the operation of our business. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable healthcare laws, they also may be subject to similar penalties.

***Healthcare policy changes, including recent laws to reform the U.S. healthcare system, may have a material adverse effect on us.***

In the U.S. and in other countries, there have been and we expect there will continue to be a number of legislative and regulatory proposals to change the healthcare system in ways that could significantly and adversely affect the business of developing and marketing new therapies by reducing the costs paid for medical products and services. For instance, the U.S. government and other governments have shown significant interest in pursuing healthcare reform, as evidenced by the passing of the ACA. Such government-adopted reform measures may adversely impact the pricing of healthcare products and services in the U.S. or internationally and the amount of reimbursement available from third-party payors. For instance, under the ACA, there is a new 2.3% U.S. federal excise tax on the sale of certain medical devices. While we do not believe the tax will be applicable to us, the U.S. may seek to enforce the tax on us. In addition, in some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell the ELAD System profitably, if it is ultimately approved. The continuing efforts of U.S. and other governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce healthcare costs may adversely affect the prices we are able to charge for the ELAD System, if approved, and our ability to generate revenues and achieve and maintain profitability.

## **Risks Related to Doing Business Internationally**

***We plan to do business internationally, which may prove to be difficult and fraught with economic, regulatory and political issues.***

We may commercialize the ELAD System in countries where the business, economic and political climates are very different from those of the U.S. We may not be aware of some of these issues and it may be difficult for a U.S. company to overcome these issues and ultimately become profitable. For instance, we completed our Chinese pivotal clinical trial in 2007 and submitted our data to the China FDA, or CFDA, showing a statistically significant improvement in transplant-free survival among the ELAD System-treated subjects compared with control subjects. However, in the past seven years this application has been neither approved nor rejected and the timing and nature of any potential decision is highly uncertain. Moreover, currency controls are in effect in many foreign countries and could become much tighter in the future, which will hinder our ability to repatriate any profits or capital. These foreign countries may also favor businesses that are owned by nationals of those countries as opposed to foreign-owned businesses operating locally. As a small company, we may not have the resources to engage in the negotiation and time-consuming work needed to overcome some of these potential issues.

In the event that we receive marketing approval in foreign countries outside of the U.S. and Europe, we currently anticipate, in most cases, creating wholly-owned subsidiaries in those countries. These subsidiaries will need to build an effective sales, marketing, distribution, training and support staff and system, find an effective marketing partner or both. Any internal sales, marketing, training and support capabilities of the subsidiaries will need to be developed by these subsidiaries and will need to be built from scratch. The culture and accepted practices related to selling medical products in many foreign countries are unique and it is possible that we will not be able to successfully penetrate these markets. A similar consideration applies to selling in the U.S. since each medical system is very different and requires a different strategic approach. We cannot guarantee that our approach to the U.S., European, Chinese or any other international market will be effective.

***The medical systems in many foreign countries are very different from that of the U.S. and could cause significant problems for the ELAD System.***

The medical systems in many countries around the world pose challenges to the commercialization of the ELAD System. For instance, most medical care in China is delivered on a private pay basis and it may be difficult to receive payment for the ELAD System therapy delivered or the price of our product, which we expect to be relatively high, may prove to be beyond the capability of the targeted Chinese patient to pay. Further, as we have encountered in our clinical trials, the standard and the operation of the delivery of care in China are different, causing problems with the operation of the ELAD System therapy. These issues include the withholding of necessary medicines, the inadequate staffing of Chinese hospitals, the shortage of blood products, the differing practice of delivery of extracorporeal therapies, and the attitude of physicians and nurses. These issues and others are likely to occur in other countries around the world and there is no assurance that we will overcome these challenges or succeed in commercializing the ELAD System in foreign countries.

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***We face increased risks of doing business due to the extent of our operations internationally.***

We currently anticipate our foreign commercialization efforts will be through wholly-owned, foreign domiciled subsidiaries. Our efforts to expand internationally pose risks that could adversely affect our business. These risks include, among others, the effects of:

fluctuations in foreign currency exchange rates and controls;

competitive disadvantages to established foreign businesses with significant current market share and business and customer relationships;

nationalization;

tax and regulatory policies of local governments and the possibility of trade embargoes;

political instability, war or other hostilities; and

laws and policies of the U.S. and foreign governments affecting foreign trade and investment.

Any of these risks could cause significant interruptions in our operations, which would adversely affect our ability to commercialize the ELAD System internationally and our financial condition, results of operations and business.

Revenues, profits and cash flows derived in foreign countries by foreign subsidiaries may be denominated in foreign currency. The value of this currency may be controlled or adjusted periodically by foreign governments, and may be subject to changes in the political and economic conditions.

***Foreign economic, political and social conditions and government policies could materially and adversely affect our business.***

A significant portion of our operations may be conducted in foreign countries and it is anticipated that a significant percentage of our revenues may be derived from these countries. Accordingly, our results of operations, financial condition and prospects are subject, to a significant degree, to economic, political, legal and social developments around the world. The economies of many of these countries differ from the economy of the U.S. in many respects, including:

level of government involvement;

economic structure;

allocation of resources;

level of development;

inflation rates;

growth rate; and

control of foreign exchange.

***The legal systems in many foreign countries have inherent uncertainties that could limit the legal protections available to us.***

We are subject to the laws and regulations of foreign governments, including those applicable to foreign investment and, in particular, laws applicable to wholly foreign-owned enterprises. Any litigation in these countries may be protracted and may result in substantial costs and diversion of resources and management attention. For example, in 2007, one of our clinical sites in China was sued in connection with the death of a subject of our clinical trial. An expert panel concluded that neither the ELAD System nor the clinical site was at fault and dismissed the lawsuit. Nevertheless, we were later informed that the subject's family had been awarded approximately \$100,000 in a subsequent civil proceeding brought against the clinical site. We ultimately decided to reimburse the clinical site for \$100,000, which was partially insured. In addition, these countries may enact new laws or amend current laws that may be detrimental to us, which may have a material adverse effect on our business operations.

***We have limited business insurance coverage internationally.***

The insurance industry in many parts of the world is still in an early stage of development. Insurance companies in many countries offer only limited business insurance options. As a result, we may not be able to maintain any liability, hazard or other insurance covering our services, business, operations, errors, acts or omissions, personnel or properties in all countries where we ultimately commercialize the ELAD System. To the extent that we are unable to recover from others for any uninsured losses, such losses could result in a loss of capital and significant harm to our business. If any action, suit, or proceeding is brought against us and we are unable to pay a judgment rendered against us or defend ourselves against such action, suit, or proceeding, our business, financial condition and operations could be negatively affected.

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***We must comply with the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws.***

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. Other countries, such as the U.K. and China, have similar laws with which we must comply. Although we attempt to rigidly adhere to the requirements of the U.S. Foreign Corrupt Practices Act and all similar laws to which we are subject, there remains the risk that an employee or agent of ours could be accused of violating one or more of these laws, particularly in geographies where significant overlap exists between local government and healthcare industries. Such an accusation, even if unwarranted, could prove disruptive to our developmental and commercialization efforts.

***We could be subject to additional income and other tax liabilities.***

We are subject to income and other taxes in the U.S. and may be subject to income and other taxes in various other foreign jurisdictions. Significant planning is required in evaluating a worldwide provision for income and other taxes. During the ordinary course of business, there may be transactions for which the ultimate tax determination is uncertain. We may be subject to audit in various jurisdictions and such jurisdictions may assess additional income or other tax against us. Although we believe our tax positions are reasonable, the final determination of tax audits and any related litigation could be materially different from our historical income tax provisions and accruals. The results of an audit or litigation could have a material and adverse effect on our operating results or cash flows in the period or periods for which that determination is made.

**Risks Related to Intellectual Property**

***Our patent rights may prove to be an inadequate barrier to competition.***

We hold a patent in the U.S. which claims a method of using C3A cells to treat a patient's blood, which we believe covers the ELAD System therapy. In addition, we have been granted a patent with claims covering an extracorporeal device configuration, which we believe includes our ELAD System, independent of cell-type used. Foreign counterparts of these patents have been issued in Australia, Canada, Indonesia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea and Taiwan and remain under review in certain other jurisdictions, including Europe, Brazil, China, India and the Philippines. In addition to these two U.S. patents, we hold three additional patents in the U.S., and additional patent applications related to developments in the ELAD System are pending. However, the lifespan of any one patent is limited, and each of these patents will ultimately expire and we cannot be sure that pending applications will be granted, or that we will discover new inventions which we can successfully patent. Moreover, any of our granted patents may be held invalid by a court of competent jurisdiction, and any of these patents may also be construed narrowly by a court of competent jurisdiction in such a way that it is held to not directly cover the ELAD System. Furthermore, even if our patents are held to be valid and broadly interpreted, third parties may find legitimate ways to compete with the ELAD System by inventing around our patent. Finally, the process of obtaining new patents is lengthy and expensive, as is the process for enforcing patent rights against an alleged infringer. Any such litigation could take years, cost large sums of money and pose a significant distraction to management. Indeed, certain jurisdictions outside of the U.S. and Europe where we hope to commercialize the ELAD System have a history of inconsistent, relatively lax or ineffective enforcement of patent rights. In such jurisdictions, even a valid patent may have limited value. Our failure to effectively prosecute our patents would have a harmful impact on our ability to commercialize the ELAD System in these jurisdictions.



***We do not hold any patents covering our VTL C3A cells or the production processes we use to grow the VTL C3A cells in the ELAD cartridges.***

C3A cells are publicly available and the proprietary methods and production process that we use to grow our VTL C3A cells in the ELAD cartridges are our trade secrets, but they are not currently covered by a patent and no patents are pending. Although we have sought patent protection for certain aspects of our technology, such as our method of using human liver-derived C3A cells to treat a patient's blood, and we have obtained orphan designation in the U.S. and Europe for the use of C3A cells to treat acute liver failure, we have not sought patent protection for the proprietary methods we use to grow VTL C3A cells in our facility. Although we believe that some of these methods may be patentable, we prefer to avoid the disclosure requirements inherent in the patenting process, as such disclosure could provide competitors with insights that allow them to invent around any granted patents. We believe that this concern is particularly appropriate since C3A cells are now publicly available, and have been available for research purposes for more than twenty years. Despite this availability, we are not aware of any third parties who have either demonstrated an ability to grow C3A cells in the quantities we do, or succeeded in treating a human subject with such cells. In addition, patent protection expires 20 years after the application's priority date which does not apply to trade secret protection. In light of the foregoing, we do not currently contemplate seeking patent protection for our production methods and instead intend to keep our production methods protected as trade secrets, which does not require us to publicly disclose these methods and which is not subject to a formal expiration date. However, trade secrets are vulnerable to inadvertent disclosure and misappropriation. In addition, independent discovery and publication of these methods by third parties, which is now more feasible given the public availability of C3A cells, would also destroy their trade secret protection. If any of these were to occur, our business may be harmed.

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***We protect much of our intellectual property as trade secrets. Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.***

Trade secrets offer a relatively limited form of protection as they do not create any barrier for third-parties who independently develop this information and who may even patent the information. In the course of our research and development activities and our business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements may be used, for example, when we talk to vendors of laboratory or clinical development services or potential strategic partners. In addition, each of our employees is required to sign a confidentiality agreement upon joining us. We take steps to protect our proprietary information, and our confidentiality agreements are carefully drafted to protect our proprietary interests. Nevertheless, there can be no assurance that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how, which would harm our business.

***If our ELAD cartridges or our VTL C3A cells are stolen, misappropriated or reverse engineered, others could produce competing products.***

Third parties, including those involved in shipping our ELAD System cartridges or in any manufacturing abroad that we may undertake, often have custody or control of our ELAD cartridges. If our ELAD cartridges, or VTL C3A cells from our proprietary VTL C3A cell bank that are stored to grow in these cartridges, were stolen, misappropriated or reverse engineered, they could be used by other parties who may be able to reproduce these cartridges for their own commercial gain. If this were to occur, it would be difficult for us to challenge this type of use, especially in countries with limited intellectual property protection or in countries in which we do not have patents covering the misappropriated ELAD cartridges. In such instance, our business would be harmed.

***Ownership of our intellectual property may be claimed by others.***

The ELAD System has been under development for over 20 years and certain of our predecessor companies have filed for reorganization and bankruptcy. We were founded in 2003 by acquisition of the assets of a prior company after a bankruptcy. While we believe we have performed extensive diligence on the ownership of the intellectual property rights and have developed our own innovative technology which is independent of prior intellectual property rights, there could be claims by parties associated with the prior entities that could lead to costly and time consuming legal actions. In addition, we have engaged in collaborations with third parties where intellectual property has been developed. In one instance, we were engaged in a dispute over the ownership of intellectual property when a collaborator of ours pursued patent rights over technology which we believe we may have held rights to under the collaboration agreement. Although a patent which claims a different configuration than our ELAD System was ultimately issued in the U.S. to our former collaborator, we do not hold any rights to this patent. We are unaware of any active development with respect to the claimed system. Other such disputes could arise in the future or emerge from past activities which could lead others to claim our intellectual property.

***We may be involved in future costly intellectual property litigation, which could impact our future business and financial performance.***

Our industry has been characterized by frequent intellectual property litigation. Our competitors or other patent holders may assert that our ELAD System and the methods we employ are covered by their patents. For instance, we are aware of other patents issued in the liver support field which we believe do not cover our ELAD System or its use. If our ELAD System or methods are found to infringe any valid patents, we could be prevented from marketing our ELAD System. In addition, we do not know whether our competitors or potential competitors have applied for, or will apply for or obtain, patents that will prevent, limit or interfere with our ability to make, use, sell, import or export our ELAD System.

Litigation related to infringement and other intellectual property claims, with or without merit, is unpredictable, can be expensive and time-consuming and could divert management's attention from our core business. If we lose this kind of litigation, a court could require us to pay substantial damages, and prohibit us from using technologies essential to our ELAD System, any of which would have a material adverse effect on our business, results of operations and financial condition. We do not know whether necessary licenses would be available to us on satisfactory terms, or whether we could redesign our ELAD System or processes to avoid infringement.

Competing products may also appear in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, we could be prevented from marketing our ELAD System in one or more countries.

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In addition, we may hereafter become involved in litigation to protect our trademark rights associated with our company name or the names used with our ELAD System. Names used with our ELAD System and procedures may be claimed to infringe names held by others or to be ineligible for proprietary protection. If we have to change the name of our company or our ELAD System, we may experience a loss in goodwill associated with our brand name, customer confusion and a loss of sales.

***We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets owned by third parties.***

Many of our employees were previously employed at universities or other life science companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other confidential or proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel could hamper our ability to develop and commercialize the ELAD System, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

## **Risks Related to Our Capital Requirements and Finances**

***Our future capital needs are uncertain and we will need to raise additional funds in the future.***

We will need to raise substantial additional capital to:

complete clinical trials and related regulatory applications;

fund our operations;

commence and expand the commercialization of our products; and

further our research and development.

Our future funding requirements will depend on many factors, including:

market acceptance of our products;

the cost of our research and development activities;

the cost and timing of our clinical development activities, in particular the rate of initiation of our clinical sites and the rate of enrollment of our clinical trials;

the cost of filing and prosecuting patent applications;

the cost of defending, in litigation or otherwise, any claims that we infringe third-party patents or violate other intellectual property rights;

the cost and timing of regulatory clearances or approvals, if any;

the cost and timing of establishing sales, marketing and distribution capabilities;

the cost and timing of establishing additional technical support capabilities;

the effect of competing technological and market developments; and

the extent to which we acquire or invest in businesses, products and technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

We cannot assure you that we will be able to obtain additional funds on acceptable terms, or at all. If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt. Any debt or additional equity financing that we raise may contain terms that are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, which we have no prior experience in, it may be necessary to relinquish some rights to our technologies or our products, or grant licenses on terms that are not favorable to us. If we are unable to raise adequate funds, we may have to liquidate some or all of our assets, or delay, reduce the scope of or eliminate some or all of our development programs.

If we do not have, or are not able to obtain, sufficient funds, we may have to delay development or commercialization of our products or license to third parties the rights to commercialize products or technologies that we would otherwise seek to commercialize. We also may have to reduce marketing, customer support or other resources devoted to our products or cease operations. Any of these factors could harm our operating results.

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### ***Any acquisitions that we make could disrupt our business and harm our financial condition.***

We expect to evaluate potential strategic acquisitions of complementary businesses, products or technologies. We may also consider joint ventures, licensing and other collaborative projects. We may not be able to identify appropriate acquisition candidates or strategic partners, or successfully negotiate, finance or integrate acquisitions of any businesses, products or technologies. Furthermore, the integration of any acquisition and management of any collaborative project may divert our management's time and resources from our core business and disrupt our operations. We do not have any experience with acquiring companies or products. Any cash acquisition we pursue would diminish the proceeds from our public offerings otherwise available to us for other uses, and any stock acquisition would dilute our stockholders' ownership. While we from time to time evaluate potential collaborative projects and acquisitions of businesses, products and technologies, and anticipate continuing to make these evaluations, we have no present understandings, commitments or agreements with respect to any acquisitions or collaborative projects.

### **Risks Related to Being a Public Company**

#### ***The requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain executive management and qualified board members.***

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Act, the listing requirements of the NASDAQ Stock Market LLC and other applicable securities rules and regulations. Compliance with these rules and regulations has and will continue to increase our legal and financial compliance costs, makes some activities more difficult, time-consuming or costly and increases demand on our systems and resources, particularly after we are no longer an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or the JOBS Act. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and operating results. Although we have already hired additional employees to assist us in complying with these requirements, we may need to hire more employees in the future or engage outside consultants, which will increase our costs and expenses.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies including, but

not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and financial statements in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote to approve executive compensation and shareholder approval of any golden parachute payments not previously approved. We will take advantage of these reporting exemptions until we are no longer an emerging growth company.

We will cease to be an emerging growth company upon the earliest of: (1) the beginning of the first fiscal year following the fifth anniversary of our initial public offering, or January 1, 2020, (2) the beginning of the first fiscal year after our annual gross revenue is \$1.0 billion or more, (3) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities and (4) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year.

As a public company it is more expensive for us to maintain and obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors may also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

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Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail our company of this exemption from new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***As a public company, we are obligated to develop and maintain proper and effective internal control over financial reporting. We may not complete our analysis of our system of internal control over financial reporting in a timely manner, or these internal controls may not be determined to be designed or operating effectively, which may adversely affect investor confidence in our company and, as a result, the value of our common stock.***

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting for the 2015 fiscal year. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting.

We are in the process of the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing or any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal controls are effective, which could result in a loss of investor confidence in the accuracy and completeness of our financial reports. This could cause the price of our common stock to decline, and we may be subject to investigation or sanctions by the Securities and Exchange Commission, or SEC.

We will be required to disclose changes made in our internal control and procedures on a quarterly basis. However, our independent registered public accounting firm will not be required to report on the effectiveness of our internal control over financial reporting pursuant to Section 404 until the later of our annual report for 2015, and the date we are no longer an emerging growth company pursuant to the exemptions contained in the JOBS Act. At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied that our internal controls over financial reporting are designed and operating effectively to prevent or detect a material misstatement to the financial statements. To comply with these requirements, we may need to undertake various additional actions, such as implementing new internal controls and procedures or hiring accounting or internal audit staff.

***If we do not remediate material weaknesses in our internal control over financial reporting, the accuracy and timeliness of our financial reporting may be adversely affected.***

We have not maintained an effective control environment to ensure that the design and execution of our controls has consistently resulted in effective review of our financial statements and supervision by appropriate individuals. As a result of these factors, certain misstatements in our annual financial statements were identified and brought to the attention of management by our independent registered public accounting firm for correction. We and our independent registered public accounting firm concluded that these control deficiencies constituted a material weakness in our internal control over financial reporting. A material weakness is a control deficiency, or a combination of control deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

We are in the process of implementing measures designed to improve our internal control over financial reporting to remediate the control deficiencies that led to our material weakness. We cannot assure you that the measures we have taken to date, or any measures we may take in the future, will be sufficient to remediate the control deficiencies that



led to our material weakness in our internal control over financial reporting or to avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has ever performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional significant deficiencies or material weaknesses may have been identified. If we are unable to successfully remediate any significant deficiency or material weakness in our internal control over financial reporting, or identify any additional significant deficiencies or material weaknesses that may exist, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our stock price may decline as a result.

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**Risks Related to our Common Stock**

***If securities or industry analysts do not continue to publish research or publish unfavorable research about our business, our stock price and trading volume could decline.***

The trading market for our common stock will rely in part on the research and reports that equity research analysts publish about us and our business. Although certain equity research analysts currently cover us, we do not have any control of the analysts or the content and opinions included in their reports or whether any such analysts will continue to, or whether new analysts will, cover us for any given period of time. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

***We expect that the price of our common stock will fluctuate substantially.***

The market price of our common stock has been and is likely to continue to be highly volatile and may fluctuate substantially due to many factors, including:

clinical data and government approvals relating to the ELAD System;

changes in governmental regulations or in the status of our regulatory approvals or applications;

disputes or other developments with respect to our intellectual property rights or the intellectual property rights of others;

product liability claims or other litigation;

sales of large blocks of our common stock, including sales by our executive officers and directors;

changes in earnings estimates or recommendations by securities analysts;

our ability to meet investors expectations regarding our future operating performance;

media exposure of the ELAD System or products of our competitors;

volume and timing of sales of the ELAD System;

the introduction of new products or product enhancements by us or our competitors;

our ability to develop, obtain regulatory clearance or approval for and market new and enhanced products on a timely basis;

quarterly variations in our or our competitors' results of operations;

developments in our industry; and

general market conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

In addition, an active and liquid market may not develop or persist and you may not be able to sell your shares quickly or at the recently reported price. These and other factors may make the price of our stock volatile and subject to unexpected fluctuations.

***Sale of a substantial number of shares of our common stock by existing stockholders or us may cause the price of our common stock to decline.***

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise adequate capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

As of December 31, 2014, we had 23,982,786 shares of common stock outstanding, 16,752,310 shares of which are freely tradable (subject in some cases to the provisions of Rules 144 or 701, and our insider trading policy), and 7,230,476 shares of which are subject to lock-up agreements entered into by our executive officers, directors and certain of our security holders in conjunction with our follow-on public offering.

The lock-up agreements entered into with us expire at the start of the third full trading day following the date of issuance of a press release that includes topline results from our VTI-208 Phase 3 clinical trial. Following the expiration of such lock-up agreements (or earlier if permitted by our board of directors), these shares will be eligible for sale in the public market, subject in some cases to compliance with Rule 144 and the manner of sale, volume limitation or notice provisions thereof, as well as our insider trading policy.

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Sales of our common stock by our current stockholders may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, and make it more difficult for you to sell shares of our common stock.

In addition, on June 6, 2014, we filed a registration statement on Form S-8 registering 3,732,152 shares of common stock subject to options or reserved for future issuance under our 2012 Stock Option Plan and 2014 Equity Incentive Plan. Shares registered under this registration statement on Form S-8 will be available for sale in the public market subject to vesting arrangements and the exercise of such options, the lock-up agreements described above and, in the case of our affiliates, the restrictions of Rule 144. As of December 31, 2014, options to purchase 2,981,319 shares of our common stock were exercisable.

Certain of our existing stockholders are also entitled, under contracts providing for registration rights, to require us to register shares of our common stock owned by them for public sale in the U.S. Any sales of securities by these stockholders, or the expectation that such sales may occur, could have a material adverse effect on the trading price of our common stock and make it more difficult for you to sell shares of our common stock.

To the extent we raise additional capital by selling and issuing common stock, convertible securities or other equity securities, it may result in material dilution to our existing stockholders and new investors could gain rights superior to our existing stockholders. Sales by us or by our current stockholders also could cause the price of our common stock to fall and make it more difficult for you to sell shares of our common stock.

***Our directors, officers and principal stockholders have significant voting power and may take actions that may not be in the best interests of our other stockholders.***

Our officers, directors and principal stockholders and their affiliates collectively control approximately 36.0% of our outstanding common stock, and in particular, one stockholder and his affiliates control approximately 28.5% of our outstanding common stock as of December 31, 2014. As a result, these stockholders, if they act together, will be able to exert substantial influence over the management and affairs of our company and most matters requiring stockholder approval, including the election of directors. This concentration of ownership may have the effect of delaying or preventing a change in control and might adversely affect the market price of our common stock. This concentration of ownership may not be in the best interests of our other stockholders.

***We have broad discretion in the use of proceeds from our public offerings for working capital and general corporate purposes.***

The net proceeds of our public offerings are being allocated to fund the continuing clinical development of the ELAD System and the remainder for working capital and other general corporate purposes. Our management has broad discretion over the use and investment of the net proceeds of our public offerings within those categories, and accordingly investors will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning management's specific intentions.

***Anti-takeover provisions in our amended and restated certificate of incorporation, amended and restated bylaws, and Fourth Amended and Restated Investors' Rights Agreement, as well as Delaware law, could discourage a takeover.***

Our amended and restated certificate of incorporation, bylaws, Fourth Amended and Restated Investors' Rights Agreement, and Delaware law, contain provisions that might enable our management to resist a takeover, and might make it more difficult for an investor to acquire a substantial block of our common stock. These provisions:

authorize our board of directors to issue, without further action by our stockholders, up to 20,000,000 shares of undesignated preferred stock;

require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;

specify that special meetings of our stockholders can be called only by a supermajority (75%) vote of our directors then in office;

specify that our board of directors may amend or repeal our bylaws only pursuant to a supermajority (75%) vote of our directors then in office;

specify that our stockholders may amend or repeal our bylaws only pursuant to a supermajority (75% and majority of the minority, if applicable) vote of the outstanding shares of our capital stock;

require in general the approval of a supermajority (75% and majority of the minority, if applicable) vote of our outstanding shares of capital stock to amend or repeal certain provisions of our certificate of incorporation;

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require the approval of a supermajority (75% and majority of the minority, if applicable) vote of our outstanding shares of capital stock to approve the sale or liquidation of the company;

establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;

provide that directors may be removed only for cause by a supermajority (75%) vote of our outstanding shares of capital stock;

provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;

provide that in general the number of directors on our board may only be fixed from time to time by a supermajority (75%) vote of our directors then in office;

establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms; and

provide that certain stockholders affiliated with Muneer A. Satter, referred to as the Satter Investors, have rights to nominate up to a specific percentage of our directors (currently 30%) based on the Satter Investors ownership percentage in our Company.

These provisions might discourage, delay or prevent a change in control of our company or a change in our management. The existence of these provisions could adversely affect the voting power of holders of common stock and limit the price that investors might be willing to pay in the future for shares of our common stock.

Our certificate of incorporation also contains a provision that provides us with protections similar to Section 203 of the Delaware General Corporation Law and will prevent us from engaging in a business combination with a person who acquires at least 15% of our common stock for a period of three years from the date such person acquired such common stock, except for certain of our current stockholders, including Mr. Satter and entities affiliated with him, and, in certain instances, persons who purchase common stock from certain of our current stockholders, and unless board or stockholder approval is obtained prior to the acquisitions. These anti-takeover provisions and other provisions under Delaware law could discourage, delay or prevent a transaction involving a change in control of our company, even if doing so would benefit our stockholders. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect or remove directors of your choosing and to cause us to take other corporate actions you desire.

***We have not paid dividends in the past and do not expect to pay dividends in the future, and any return on investment may be limited to the value of our stock.***

We have never paid cash dividends on our common stock and do not anticipate paying cash dividends on our common stock in the foreseeable future. The payment of dividends on our common stock will depend on our earnings, financial condition and other business and economic factors affecting us at such time as our board of directors may consider

relevant. If we do not pay dividends, our stock may be less valuable because a positive return on your investment will only occur if our stock price appreciates.

**Item 1B. Unresolved Staff Comments.**

Not applicable.

**Item 2. Properties.**

We lease approximately 39,100 square feet in San Diego in two different facilities under leases that expire in June 2017. Our corporate headquarters are in a 19,100 square foot facility, and we lease a 20,000 square foot facility for our manufacturing operations, which also includes laboratories for research and development. We believe that these facilities are adequate to meet our existing needs and that additional or substitute facilities will be available on commercially reasonable terms, if required. However, we expect to incur additional expenses in connection with any such new facilities.

**Item 3. Legal Proceedings.**

We are not currently a party to any litigation, and we are not aware of any pending or threatened litigation against us that we believe would adversely affect our business, operating results, financial condition or cash flows. Our industry is characterized by frequent claims and litigation, including claims regarding patent and other intellectual property rights as well as product liability. As a result, in the future, we may be involved in various legal proceedings from time to time.

**Item 4. Mine Safety Disclosures.**

Not applicable.

**Table of Contents****PART II****Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.****Market Information**

Our common stock began trading on The NASDAQ Global Market on April 17, 2014 under the symbol VTL. Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market for the periods indicated.

	<b>Price Range</b>	
	<b>High</b>	<b>Low</b>
<b>Year Ended December 31, 2014</b>		
Second Quarter (commencing April 17, 2014)	\$ 35.20	\$ 10.66
Third Quarter	\$ 28.36	\$ 16.80
Fourth Quarter	\$ 26.90	\$ 13.40

**Holders**

As of February 27, 2015, there were approximately 117 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Dividend Policy**

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

**Securities Authorized for Issuance under Equity Compensation Plans**

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

**Performance Graph**

The following graph shows a comparison from April 17, 2014 (the date our common stock commenced trading on The NASDAQ Global Market) through December 31, 2014 of the cumulative total return for our common stock, the NASDAQ Biotechnology Index and the NASDAQ Composite Index. The graph assumes an initial investment of \$100 on April 17, 2014. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.





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**Use of Proceeds**

Our initial public offering was effected through a registration statement on Form S-1 (File No. 333-191711), which was declared effective by the Securities and Exchange Commission, or SEC, on April 16, 2014. There has been no material change in our planned use of the net proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act and other periodic reports previously filed with the SEC. The amount and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from clinical trials, as well as any unforeseen cash needs.

**Issuer Purchases of Equity Securities**

None.

**Table of Contents****Item 6. Selected Financial Data.**

The following table summarizes our selected consolidated financial data for the periods and as of the dates indicated, which have been derived from our audited consolidated financial statements and related notes and should be read together with the section entitled Management's Discussion and Analysis of Financial Condition and Results of Operations and with our audited consolidated financial statements and their related notes, which are included elsewhere in this Annual Report.

	<b>Year Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Operating expenses:			
Research and development	\$ 39,479	\$ 21,787	\$ 5,097
General and administrative	10,863	9,615	4,483
Total operating expenses	50,342	31,402	9,580
Loss from operations	(50,342)	(31,402)	(9,580)
Revaluation of future purchase rights liabilities	2,600	(1,306)	3,101
Other income (expense), net	75	(10)	(222)
Net loss	(47,667)	(32,718)	(6,701)
Amortization of deemed dividend	(4,744)	(64)	
Accretion to redemption value of senior redeemable convertible preferred stock	(4,410)	(6,303)	(942)
Net loss attributable to common stockholders	\$ (56,821)	\$ (39,085)	\$ (7,643)
Net loss per share attributable to common stockholders, basic and diluted	\$ (3.54)	\$ (74.86)	\$ (17.89)
Weighted average common shares outstanding, basic and diluted <sup>(1)</sup>	16,054,452	522,102	427,117

- (1) Please refer to Note 2 of our consolidated financial statements appearing elsewhere in this Annual Report for an explanation of the method used to calculate basic and diluted net loss per share attributable to common stockholders and the number of shares used in the computation of the per share amounts.

	<b>As of December 31,</b>		
<b>Consolidated Balance Sheet Data:</b>	<b>2014</b>	<b>2013</b>	<b>2012</b>
Cash and cash equivalents	\$ 102,238	\$ 38,186	\$ 18,473
Working capital	94,538	36,409	17,403
Total assets	108,082	46,585	20,332
Preferred stock		83,475	26,176

Additional paid-in-capital	248,305	58,413	62,728
Accumulated deficit	(150,833)	(103,166)	(70,448)
Total stockholders' equity (deficit)	97,563	(44,657)	(7,632)

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

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this Annual Report. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in "Risk Factors" included elsewhere in this Annual Report.*

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**Table of Contents****Overview**

We are a biotherapeutic company focused on developing a cell-based therapy targeting treatment of all forms of acute liver failure. Our product candidate, the ELAD<sup>®</sup> System, is an extracorporeal bio-artificial liver therapy designed to allow the patient's own liver to regenerate to a healthy state, or to stabilize the patient until transplant. The ELAD System is the only bio-artificial liver support system containing immortal human liver-derived cells, or C3A cells, to enter Phase 3 clinical trials. We designed the ELAD System to supplement key aspects of normal liver function to improve patient survival. We estimate that at least 40,000 patients annually in the United States, or U.S., experience forms of acute liver failure, such as acute-on-chronic, surgery-induced and fulminant liver failures, for which the ELAD System may be a life-saving therapy. Outside of liver transplant, which is severely limited by the availability of organs and not available to many patients, the current standard of care for acute liver failure is primarily focused on the management of complications, which does not restore lost liver function and is associated with a high rate of mortality. The ELAD System has received orphan designation in the U.S. and Europe for the treatment of patients with acute liver failure. This designation provides tax credits for qualified clinical testing, seven years of market exclusivity in the U.S., and ten years of market exclusivity in Europe for the first orphan drug approved for a given indication. However, orphan designation does not alter the standard regulatory requirements or the process for obtaining marketing approval.

Vital Therapies, Inc. was formed in May 2003 to acquire the assets of VitaGen (formerly Hepatix) in a bankruptcy proceeding. Our predecessor companies developed the ELAD System, completing two pilot trials in acute liver failure and two randomized, controlled Phase 1 and Phase 2 trials in fulminant hepatic failure, or FHF, but failed to attract funds sufficient to continue development of the ELAD System. Beginning in June 2003, we refocused the company to pursue regulatory approval and commercialization of the ELAD System in China. In 2007, we completed a pivotal trial in acute liver failure in subjects principally with viral hepatitis in China, and we submitted an application for marketing in China. Our application is still under review in China; however, we do not expect approval in China until we have approval in the U.S.

We restarted our clinical program in the U.S. and Europe in 2008. Since then, we have run two Phase 2 trials and selected alcohol-induced liver decompensation, or AILD, and severe acute alcoholic hepatitis, or SAAH, as indications for our Phase 3 pivotal trial program in the U.S. and Europe. We have also made significant improvements in the ELAD System bedside unit and our proprietary cartridge cell growth production process, including (i) the incorporation of an updated version of the cardiovascular base unit that has improved features, functionalities and reliability; (ii) new and improved cartridges for ultrafiltrate, cell filters and the ELAD cartridges; (iii) tubing sets that have been optimized to recirculate smaller volumes of ultrafiltrate and blood through the system to reduce the risk of clotting and other potential adverse side effects; and (iv) improvements to our cell culture and growth processes to reduce cost and increase manufacturing efficiency and yield.

In January 2015, we completed enrollment in our leading Phase 3 clinical trial, VTI-208, of 203 subjects with AILD. During 2014, we initiated enrollment in a second Phase 3 trial, VTI-210, for subjects with SAAH and in a Phase 2 clinical trial, VTI-212, for subjects with FHF and surgery-induced acute liver failure, referred to as SILF.

VTI-210 is Phase 3 randomized, controlled, open-label clinical trial in subjects with SAAH, who we believe are at a substantially increased risk of mortality. VTI-210 has regulatory allowance in the U.S., United Kingdom, or U.K., Germany and Spain. The statistical plan for VTI-210 provides for an event-driven clinical design (a statistical plan that allows the study sample size to be adjusted according to aggregate mortality) with a minimum of 150 subjects. The primary endpoint of VTI-210 is overall survival up to at least study day ninety-one. As of March 18, 2015, we had enrolled six subjects in VTI-210 and had 18 clinical sites open for enrollment.

We have also enrolled four subjects in VTI-212, an open-label Phase 2 study that is part of a Phase 2/3 clinical program in subjects with either fulminant hepatic failure or surgery-induced acute liver failure. We are beginning this program with a Phase 2 single-arm component enrolling 40 subjects, which may later be followed by a randomized, controlled Phase 3 component. Results from the single-arm component will be compared with historical or case-matched controls, and we currently anticipate Phase 2 data in 2016. In the event that randomized or other Phase 3 data are necessary for approval in FHF and SILF, we expect to perform the randomized Phase 3 portion of the program or evaluate other Phase 3 trials, the design of which would be finalized upon analysis of the Phase 2 component.

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We have incurred net losses since inception of \$150.8 million through December 31, 2014. We anticipate that we will continue to incur increasing losses for at least the next several years. Due to the uncertainties involved with biological product development and the clinical trial process, we cannot predict the timing or accuracy of future expenses, when product approval for the ELAD System might occur, or when profitability may be achieved or sustained.

In January and February 2014, we raised an aggregate of \$18.2 million in private placements through the issuance and sale of 2,296,016 shares of senior redeemable convertible preferred stock, or senior preferred stock, at a price of \$8.00 per share.

Then, in April 2014, we completed our initial public offering, or IPO, of 4,500,000 shares of common stock at an offering price of \$12.00 per share. We received net proceeds of approximately \$44.4 million, after deducting underwriting discounts, commissions and offering-related transaction costs. In May 2014, the underwriters exercised their option to purchase an additional 675,000 shares of our common stock at \$12.00 per share in full. As a result, we received an additional \$7.5 million in net proceeds after underwriters' discounts and commissions, for total net proceeds of \$51.9 million from the offering.

In October 2014, we completed a follow-on public offering selling 2,000,000 shares of our common stock at \$17.50 per share and received net proceeds of \$32.0 million after deducting underwriting discounts, commissions and offering related transaction costs. In November 2014, the underwriters exercised a portion of their option and purchased an additional 50,000 shares of our common stock at \$17.50 per share. As a result, we received an additional \$814,000 in net proceeds after underwriters' discounts and commissions, for total net proceeds from the follow-on public offering of \$32.9 million, net of discounts, commissions and costs.

## **Financial Operations Overview**

### ***Research and development expenses***

Research and development expenses relate to the development of the ELAD System and are expensed as incurred. Our research and development expenses consist primarily of:

expenses incurred under agreements with clinical sites, clinical research organizations, or CROs, and statistical and regulatory consultants that assist us with our clinical trials;

employee-related expenses, which include salaries, benefits, travel and stock-based compensation;

the cost of acquiring and manufacturing clinical trial materials;

costs associated with other research and regulatory activities; and

facilities, depreciation, and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets.

We anticipate that our research and development expenses will increase substantially as we continue to conduct our Phase 3 and Phase 2 clinical trials of the ELAD System, expand our research and development activities and begin the regulatory approval process for commercialization over the next year.

We do not track our employee and facility related research and development costs by clinical trial, as we typically use our employee and infrastructure resources across multiple clinical trials and the allocation of such costs would be arbitrary and would not provide a meaningful assessment. During the second half of 2012, we began tracking direct costs related to VTI-208 and, for VTI-210 and VTI-212, we began tracking costs in 2014.

The costs of clinical trials may vary significantly over the life of a project owing to, but not limited to, the following:

per subject trial costs;

the number of sites included in the trials;

the countries in which the trial is conducted;

the number of subjects that participate in the trials;

continuing quality assurance activities and standards consistent with the U.S. Food and Drug Administration, or FDA, and other regulatory requirements;

potential additional safety monitoring or other studies requested by regulatory agencies; and

the frequency and duration of subject follow-up visits.



## **Table of Contents**

A change in the outcome of any of these variables could result in a significant change in the costs and timing associated with the development of the ELAD System. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of the ELAD System or if we experience significant delays in enrollment in any clinical trial, we could be required to expend significant additional financial resources and time on the completion of the clinical development of the ELAD System.

### ***General and administrative expenses***

General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, information technology, marketing, and legal functions. Other general and administrative expenses include facility costs, stock-based compensation, and professional fees for legal, consulting, accounting and tax services.

We anticipate that our general and administrative expenses will increase for primarily the following reasons:

increased payroll, expanded infrastructure and higher consulting, legal, accounting and investor relations costs, and director and officer insurance premiums associated with being a public company;

expansion of our facilities to support our growth;

to support our business activities, which we expect to expand as we continue the development of the ELAD System; and

to build a marketing, reimbursement, training and support team before we receive regulatory approval of the ELAD System in anticipation of commercial launch.

### ***Other Income (Expense)***

#### ***Interest Income***

Our cash and cash equivalents are or have been invested primarily in money market funds and U.S. treasury bills, which generate a small amount of interest income, but in our opinion provide liquidity and protection from loss of principal. We expect to continue to make similar investments with any additional financing proceeds.

#### ***Interest Expense***

Interest expense has consisted primarily of interest paid on debt and an equipment lease line, and non-cash interest associated with amortization of debt discount and financing costs. As of December 31, 2012, we no longer have any debt outstanding.

#### ***Revaluation of Future Purchase Rights Liabilities***

Future rights to purchase shares of our senior preferred stock granted in connection with our senior preferred stock financing were accounted for as liabilities and their value was re-measured at the end of each financial reporting

period. The value of these future purchase rights liabilities fluctuated in conjunction with increases or decreases in the fair value of our common stock and the number of preferred and common shares and future purchase rights outstanding relative to our enterprise value at each reporting date. We recognized a gain or loss based on fluctuations in the fair value of these future purchase rights liabilities. In conjunction with our IPO in April 2014, the remaining purchase rights liabilities at that date were terminated and the balance of the future purchase rights liabilities was recognized as income.

### **Critical Accounting Policies and Estimates**

The preparation of financial statements in conformity with generally accepted accounting principles in the U.S., or GAAP, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. On an on-going basis, management makes its best estimate of the ultimate outcome for these items based on historical trends and other information available when the financial statements are prepared. Changes in estimates are typically recognized in the period when new information regarding estimates becomes available to management. Actual results could differ from those estimates.

Our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Annual Report. However, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

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**Table of Contents*****Clinical Trial Accruals***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. Our clinical trial accrual process seeks to account for expenses resulting from our obligations under agreements with clinical sites, CROs, vendors, and consultants in connection with conducting our clinical trials. We account for these expenses according to the progress of each trial as measured by subject enrollment, the timing of various aspects of the trial and if available, information from our service providers. During the course of a clinical trial, we adjust our rate of clinical expense recognition if actual results differ from our estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are over or understated for a particular period and adjustments to our research and development expenses may be necessary in future periods. Through December 31, 2014, there have been no material adjustments to our prior period estimates of accrued expenses for clinical trials.

***Future Purchase Rights Liabilities***

In September 2012, we entered into a senior preferred stock purchase agreement (as amended in December 2013, the Senior Preferred Purchase Agreement). Pursuant to the Senior Preferred Purchase Agreement, we granted to the investors in the senior preferred stock financing future purchase rights, subject to the satisfaction of certain conditions, to purchase additional shares of senior preferred stock for a purchase price of \$8.00 per share at multiple subsequent closings in accordance with a schedule provided in the Senior Preferred Purchase Agreement. These future purchase rights for additional shares of our senior preferred stock were legally detachable from the shares of the underlying senior preferred stock and, as a result, were considered freestanding instruments accounted for separately from the shares of senior preferred stock. As the future purchase rights were exercisable for shares of our senior preferred stock, the future purchase rights were instruments that embodied obligations to transfer assets and were classified as liabilities under the accounting guidance that distinguishes liabilities from equity.

These future purchase rights liabilities were recorded at their estimated fair value on the date of issuance as a discount on the underlying preferred stock and were re-measured to reflect changes in the estimated fair value at each reporting date, with any decrease or increase in the estimated fair value being recorded as other income or expense, respectively. The fair value of these liabilities was estimated using a binomial lattice model based on the characteristics of the common and preferred stock on the valuation date, probabilities related to our operations and clinical development, as well as assumptions for volatility, remaining expected life, risk-free interest rate and, in some cases, credit spread. Changes in the fair value of the future purchase rights fluctuated in conjunction with increases or decreases in the fair value of our common stock, and the number of preferred and common shares and future purchase rights outstanding relative to our enterprise value at each reporting date. In April 2014, the remaining future purchase rights terminated upon the conversion of all senior preferred stock to common stock in conjunction with our IPO and the remaining balance of the future purchase rights liabilities was recorded as other income in our statement of operations for the period.

***Stock-based Compensation***

We measure and recognize compensation expense for all stock-based payments made to employees, directors, and consultants based on estimated fair value, net of an estimated forfeiture rate. Currently, our stock-based awards consist only of stock options; however, future grants under our equity compensation plans may consist of shares of restricted stock and restricted stock units. We estimate the fair value of stock options granted using the Black-Scholes-Merton, or BSM, option pricing model, which requires the use of estimates to value employee and director stock-based compensation at the date of grant.

We recognize stock-based compensation cost for employees and directors on a straight-line basis over the requisite service period of the award. Stock-based compensation expense is recognized only for those awards that are ultimately expected to vest. We estimate forfeitures based on an analysis of our historical employee turnover and will continue to evaluate the appropriateness of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover and other factors. We will revise the forfeiture estimate, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Changes in forfeiture estimates, which have not been material to date, impact compensation cost in the period in which the change in estimate occurs.

The fair value of options granted to non-employees is estimated using the BSM option pricing model and is re-measured at each reporting date until vested with changes in fair value recognized as expense in the consolidated statements of operations.

### ***Income Taxes***

Income taxes are provided for tax effects of transactions reported in the financial statements and consist of income taxes currently due plus deferred income taxes related to temporary differences between the basis of certain assets and liabilities for financial statement purposes and for income tax reporting purposes. Deferred taxes are determined based on the difference between the financial statement value and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance is provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Based on our analysis of both positive and negative factors, we have determined that it is more likely than not that we will not be able to realize our deferred tax assets, and therefore we have recorded a full valuation allowance against our deferred tax assets. Our analysis included an assessment of our lack of profitability and our future projections of forecasted revenue and expense levels.

**Table of Contents****Results of Operations*****Comparison of Fiscal Years Ended December 31, 2014 and 2013***

The following table summarizes our operating expenses for the years ended December 31, 2014 and 2013 (dollars in thousands):

	<b>Year Ended December 31,</b>		<b>Change</b>	
	<b>2014</b>	<b>2013</b>	<b>\$</b>	<b>%</b>
Operating expenses:				
Research and development	\$ 39,479	\$ 21,787	\$ 17,692	81%
General and administrative	10,863	9,615	1,248	13%
Total operating expenses	\$ 50,342	\$ 31,402	\$ 18,940	60%

The \$17.7 million increase in research and development expense during the year ended December 31, 2014, as compared to the year ended December 31, 2013 was primarily associated with an increase in our Phase 3 clinical trial activities for VTI-208 reflecting increases in the number of participating clinical sites and in the number of subjects enrolled. The higher costs were principally attributable to increases of \$4.4 million in fees paid to clinical sites and related costs; \$5.1 million in salaries and wages and other compensation related costs due to increased headcount, including a \$1.1 million increase in stock-based compensation; \$4.6 million in consulting and professional service fees; \$1.6 million in manufacturing supplies and related costs; \$714,000 in travel and conference expenses; and \$1.3 million in facilities related costs, which includes depreciation, computer and equipment costs, utilities and lease expenses.

The \$1.2 million increase in general and administrative expense during the year ended December 31, 2014, as compared to the year ended December 31, 2013 was principally attributable to a \$1.3 million increase in salaries and wages and other compensation related expenses due to increased headcount to support our operations, including a \$453,000 increase in stock-based compensation, and higher insurance costs of \$547,000 related to corporate insurance coverage increases. Such increases are due in part to support becoming a publicly-traded company in the second quarter of 2014. These increases were partially offset by a \$640,000 reduction in recruiting costs in 2014 as compared to 2013.

Other income (expense) primarily reflects the \$2.6 million recognized as other income for the re-measurement of future purchase rights liabilities for the year ended December 31, 2014, as all remaining purchase rights liabilities outstanding at December 31, 2013 were exercised or terminated in conjunction with the completion of our IPO in April 2014. Other expense of \$1.3 million for the year ended December 31, 2013 reflects the re-measurement of future purchase rights liabilities during the period.

***Comparison of Fiscal Years Ended December 31, 2013 and 2012***

The following table summarizes our operating expenses for the years ended December 31, 2013 and 2012 (dollars in thousands):

	<b>Year Ended December 31,</b>		<b>Change</b>	
	<b>2013</b>	<b>2012</b>	<b>\$</b>	<b>%</b>
Operating expenses:				
Research and development	\$ 21,787	\$ 5,097	\$ 16,690	327%
General and administrative	9,615	4,483	5,132	114%
Total operating expenses	\$ 31,402	\$ 9,580	\$ 21,822	228%

The \$16.7 million increase in research and development expense during the year ended December 31, 2013, as compared to the year ended December 31, 2012, was principally associated with an increase in our Phase 3 clinical trial activities for VTI-208. The higher costs were primarily attributable to increases of \$6.7 million in fees paid to CROs, clinical sites, and other related costs, primarily due to subject enrollment that commenced in March 2013; \$4.5 million in salaries and wages, stock-based compensation, and other compensation related costs due to increased headcount; \$2.5 million in manufacturing supplies and related costs; \$1.7 million in consulting fees related to professional services; \$0.7 million in travel costs to support our clinical trial activities; and \$0.4 million of allocated facilities costs attributable to additional clinical office space in 2013.

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The \$5.1 million increase in general and administrative expense during the year ended December 31, 2013, as compared to the year ended December 31, 2012, was primarily attributable to increases of \$2.1 million in salaries and wages, stock-based compensation, and other compensation related expenses due to increased headcount to support our operations; \$1.0 million in consulting fees primarily related to professional services for accounting, marketing and information technology consultants; \$0.7 million in expenses related to executive and board member recruitment; and \$0.5 million in facilities related to additional office space in 2013.

The \$413,000 decrease in interest expense for 2013, as compared to 2012, was attributable to no outstanding convertible notes or loans during 2013. Our convertible notes were converted into shares of our senior preferred stock in September 2012 and our term loan was repaid in October 2012.

The \$180,000 decrease in revaluation of preferred stock warrant liabilities was attributable to the final valuation adjustment of our preferred stock warrant liabilities in 2012, as these warrants were converted to common stock warrants in connection with the junior preferred stock offering in February 2012.

The \$1.3 million recognized for the re-measurement of future purchase rights liabilities for the year ended December 31, 2013 was the result of an increase in the estimated fair value of future purchase rights liabilities associated with our senior preferred stock financings and an increase during 2013 in the number of shares available under such rights from December 31, 2012 to December 31, 2013. The increase in the estimated fair value of the future purchase rights was primarily the result of an increase to our enterprise value offset in part by an increase in the number of shares of senior preferred stock outstanding as of December 31, 2013 as compared to the prior year.

## **Liquidity and Capital Resources**

### ***Overview***

We have incurred losses since inception and negative cash flows from operating activities for the years ended December 31, 2014, 2013 and 2012. As of December 31, 2014, we had an accumulated deficit of \$150.8 million. We anticipate that we will continue to incur net losses for the foreseeable future as we continue the development and potential commercialization of our ELAD System and incur additional costs associated with being a public company. In particular, we expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may seek to obtain through a combination of equity offerings, debt financings, government or other third-party financing, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

To date, we have financed our operations through preferred equity financings, our initial public offering completed in April 2014 and our follow-on public offering completed in October 2014. In January and February 2014, we raised an aggregate of \$18.2 million in private placements through the issuance and sale of 2,296,016 shares of senior preferred stock at a price of \$8.00 per share. In April 2014, we completed our initial public offering selling 4,500,000 shares of our common stock and, in May 2014, the underwriters exercised their option to purchase an additional 675,000 shares of our common stock, at \$12.00 per share. In total, we received net proceeds of \$57.8 million after underwriters discounts and commissions and before transaction-related costs of \$5.8 million. In October 2014, we completed a follow-on public offering selling 2,000,000 shares of our common stock and, in November 2014, the underwriters exercised a portion of their option and purchased an additional 50,000 shares of our common stock, at \$17.50 per share. In total, we received net proceeds of \$33.4 million after underwriters discounts and commissions and before transaction-related costs of \$511,000.

As of December 31, 2014, we had cash and cash equivalents of approximately \$102.2 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with an intent to maximize liquidity and preserve capital. As of December 31, 2014, such balances were held in cash and money market funds.



**Table of Contents*****Cash Flows***

The following table shows a summary of our cash flows for each of the three years ended December 31, 2014, 2013, and 2012 (in thousands):

	<b>2014</b>	<b>2013</b>	<b>2012</b>
Cash (used in) provided by:			
Operating activities	\$ (40,825)	\$ (28,648)	\$ (9,244)
Investing activities	(2,040)	11,909	(14,588)
Financing activities	106,918	50,445	27,501

***Net cash used in operating activities***

During the year ended December 31, 2014, operating activities used \$40.8 million of cash. The use of cash was primarily related to our net loss of \$47.7 million adjusted for non-cash income of \$2.6 million related to the re-measurement of future purchase rights liabilities, non-cash charges of \$1.1 million and \$2.5 million for depreciation and stock-based compensation, respectively, and \$5.8 million of net changes in our operating assets and liabilities. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2014 consisted primarily of an increase of \$5.5 million in accounts payable and accrued liabilities, reflecting an increase in clinical activities, related research and development expenditures and the timing of payments made by us to vendors since the beginning of the year. The decrease of \$279,000 in other current assets and prepaid expenses was attributable to a reduction in prepaid clinical costs of \$737,000 related to the utilization of prepayments to our CROs, offset by an increase of \$329,000 in prepaid expenses primarily attributable to payments on corporate insurance policies.

During the year ended December 31, 2013, operating activities used \$28.6 million of cash. The use of cash primarily related to our net loss of \$32.7 million, partially offset by \$3.0 million of non-cash charges related to the re-measurement of future purchase rights, depreciation, deferred rent, and stock-based compensation and \$1.0 million of net changes in our operating assets and liabilities. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2013 consisted primarily of an increase of \$2.2 million in accounts payable and accrued liabilities, reflecting an increase in clinical activities and the timing of payments made by us to vendors, partially offset by an increase in prepaid clinical costs of \$841,000, an increase in lease deposits of \$198,000, and an increase of \$102,000 related to other assets.

During the year ended December 31, 2012, operating activities used \$9.2 million of cash. The use of cash during 2012 primarily related to our net loss of \$6.7 million, adjusted for \$3.1 million in non-cash income related to the re-measurement of future purchase rights, \$473,000 of net changes in our operating assets and liabilities, and adjustments to our net loss of \$180,000 due to the non-cash revaluation of the preferred stock warrant liabilities, partially offset by \$1.2 million of non-cash charges related to depreciation, interest, and stock-based compensation. Changes in our operating assets and liabilities consisted primarily of a decrease of \$231,000 in accounts payable and accrued liabilities, due primarily to the timing of payments made by us to vendors, and an increase in prepaid expenses of \$242,000 due primarily to increases in prepaid clinical costs of \$54,000.

***Net cash (used in) provided by investing activities***

During the year ended December 31, 2014, investing activities used \$2.0 million of cash, primarily related to \$1.4 million in purchases of capital equipment for manufacturing and clinical operations and a net increase of \$631,000 in

restricted cash requirements. The net increase in our restricted cash is primarily related to an increase in our clinical trial obligations of \$917,000, which was offset by \$288,000 related to the elimination of certain restrictions associated with an agreement we entered into with certain investors in February 2012 related to the sale of junior preferred stock.

During the year ended December 31, 2013, investing activities provided \$11.9 million of cash, primarily related to sales of short-term investments of \$17.0 million, partially offset by \$3.0 million of purchases of short-term investments, as well as \$1.5 million in purchases of capital equipment and a \$608,000 increase in restricted cash requirements primarily related to our clinical trial obligations and lease arrangements.

During the year ended December 31, 2012, investing activities used \$14.6 million of cash due to the purchase of \$14.0 million in short-term investments, capital equipment purchases of \$261,000, and an increase in restricted cash requirements of \$355,000 associated with clinical trial obligations and potential corporate wind-down and employee related expenses.

*Net cash provided by financing activities*

During the year ended December 31, 2014, financing activities provided \$106.9 million of cash, which included net proceeds after underwriters' discounts and commissions, as applicable, and offering costs paid in 2014 of \$55.0 million from our IPO, \$32.9 million from our follow-on offering and \$18.2 million from the sale of senior redeemable convertible preferred stock. In addition to these equity offerings, we received proceeds of \$852,000 related to the exercise of options during 2014.

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During the year ended December 31, 2013, financing activities provided \$50.4 million of cash, compared to \$27.5 million during the year ended December 31, 2012. The increase in cash provided by financing activities during 2013 primarily related to the sale of additional senior preferred stock for \$53.2 million, net of offering costs. These increases were partially offset by deferred financing costs of \$3.1 million related to our IPO, which was not completed until April 2014.

Our 2012 financing activities included the sale of senior preferred stock for \$21.1 million, net of offering costs, and proceeds of \$6.9 million from a loan that was converted to senior preferred stock during 2012. These financings were partially offset by principal payments of \$533,000 on our term loan, which was repaid in October 2012.

To date, we have not generated any revenues from product sales, and we do not have any approved products. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize the ELAD System. Even assuming no commercialization costs, we anticipate that we will continue to incur losses for the foreseeable future, and we expect the losses to increase over the next year as we continue the development of, and seek regulatory approvals for, our ELAD System. We are subject to all of the risks incident in the development of new therapeutic products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Based on our current business plan, we believe that our existing cash and cash equivalents as of December 31, 2014 will be sufficient to fund our operations into the third quarter of 2016, assuming we do not begin building any significant commercial infrastructure during the period. Under this plan, our existing cash and cash equivalents will be sufficient to fund development through the completion of enrollment and receipt of topline results from our VTI-208 Phase 3 clinical trial; however, we believe we will need additional funds to complete enrollment in both our VTI-210 Phase 3 clinical trial and our VTI-212 Phase 2 clinical trial. This is a change from our prior projections of the fourth quarter of 2016 reflecting higher expected costs, principally related to preparations for a potential filing of a biologics license application, or BLA. However, if the VTI-208 clinical trial has good results and we proceed to file the BLA and to prepare for market launch, we anticipate increasing our cash burn and raising additional funds. A decision to build commercial infrastructure will be based on a variety of factors, most importantly the outcome of our clinical trials. If the VTI-208 clinical trial results do not support the filing of a BLA, we expect to focus on conserving cash in order to enable completion of the VTI-210 clinical trial. The amount and timing of our actual expenditures also depend on numerous factors, including the rate of subject enrollment in our clinical trials, filing requirements with various regulatory agencies, and any unforeseen cash needs.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. Our future capital requirements are difficult to forecast and will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of research and development and clinical trials related to the ELAD System or any future product candidates;

- the cost and timing of scaling up and validating the manufacturing process for the ELAD System or any other product candidates for commercialization;

- the cost and timing of commercialization activities, including reimbursement, marketing, sales and distribution costs, both before and after product approval (if any);

our ability to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;

the number and characteristics of any future product candidates we pursue;

the costs involved with being a public company;

the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and

the timing, receipt and amount of sales of, or royalties on the ELAD System and any future product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of stock offerings, debt financings, collaborations and licensing arrangements. In any event, we do not expect to achieve revenue from product sales prior to the use of the net proceeds from our recently completed initial public offering and follow-on public offering. We do not have any committed external source of funds. Additional funds may not be available on acceptable terms, if at all. To the extent that we raise additional capital through the sale of equity securities, the ownership interest of our stockholders will be diluted and may be on terms that are not favorable to us or our stockholders. Debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt or other terms that are not favorable to us or our stockholders. If we raise additional funds through collaborations and licensing arrangements with third parties, which we have no prior experience in, we may have to relinquish some rights to our technologies or our products, or grant licenses on terms that are not favorable to us. If we are unable to raise adequate funds, we may have to liquidate some or all of our assets, or delay, reduce the scope or eliminate some or all of our development programs. We may have also have to delay development or commercialization of our products or license to third parties the rights to commercialize products or technology that we would otherwise seek to commercialize. Any of these factors could harm our operating results.

**Table of Contents****Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in Item 303(a)(4) of Regulation S-K.

**Contractual Obligations**

Some of our most significant clinical trial expenditures are to investigative sites and to CROs. The agreements are cancellable by either party at any time upon written notice and do not have any cancellation penalties, but do obligate us to reimburse the providers for any time or costs incurred through the date of termination. These items are not included in the table below. We lease office and manufacturing space in San Diego, California. The following table summarizes our contractual obligations at December 31, 2014 and the effect such obligations are expected to have on our cash flow in future periods:

	Total	Payments Due by Period			
		Less Than 1 Year	2-3 Years	3-5 Years	More Than 5 Years
(In thousands)					
Operating lease obligations	\$ 2,200	\$ 856	\$ 1,344	\$	\$
Purchase obligations	758	758			
Total contractual obligations	\$ 2,958	\$ 1,614	\$ 1,344	\$	\$

As of December 31, 2014, our purchase obligations include existing purchase commitments for future minimum payments of \$391,000 with a vendor for raw materials that will be manufactured and utilized on an as needed basis. During the years ended December 31, 2014, 2013 and 2012, we purchased \$1.2 million, \$724,000 and \$462,000, respectively, of materials from this vendor. Our purchase obligations also include a purchase order with a vendor for cartridges that will be manufactured and delivered on an agreed upon schedule during 2015 for a future payment of \$367,000. During the years ended December 31, 2014 and 2013, we purchased \$1.2 million and \$439,000 of materials from this vendor. During the year ended 2012, we purchased no material from this vendor. If we cancel any future shipment, we would be required to pay 50% of the scheduled invoice amount for that shipment.

**Recent Accounting Pronouncements**

In August 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 will require management to assess, at each annual and interim reporting period, the entity’s ability to continue as a going concern. The amendments in ASU 2014-15 do not have any application to an entity’s financial statements, but only to disclosure in the related notes. ASU 2014-15 is effective for annual periods ending after December 15, 2016 and early application is permitted. We intend to apply ASU 2014-15 beginning with the first quarter of fiscal year 2016.

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities (Topic 915) – Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*, or ASU 2014-10, which eliminates the concept of a development stage entity in its entirety from current accounting guidance and provides for certain amendments to the consolidation guidance in Topic 810 in the

Accounting Standards Codification, or ASC. Prior to the issuance of this guidance, we were considered a development stage entity and as a result we included certain inception-to-date disclosures in our financial statements. The guidance related to the elimination of the concept of a development stage entity is effective for public companies for annual reporting periods beginning after December 15, 2014, and interim periods therein. The amendment of the consolidation guidance in Topic 810 is effective for public companies for annual reporting periods beginning after December 15, 2015. Early adoption of the new standard is permitted. We adopted ASU No. 2014-10 during the quarter ended June 30, 2014. As such, all inception-to-date disclosures have not been included in our consolidated financial statements.

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**JOBS Act**

In April 2012, the Jumpstart Our Business Startups Act, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other companies.

**Item 7A. Quantitative and Qualitative Disclosures about Market Risk.**

***Interest Rate Sensitivity***

We had cash and cash equivalents of \$102.2 million at December 31, 2014, which was held for working capital purposes. We do not enter into investments for trading or speculative purposes. We do not believe that we have any material exposure to changes in the fair value of these investments as a result of changes in interest rates due to their short-term nature. Declines in interest rates, however, will reduce future investment income.

***Foreign Currency Exchange Risk***

We have been and are continuing to enter into international agreements, primarily for clinical studies. Accordingly, we have an increasing exposure to foreign currency exchange rates. To date, we have not entered into, and do not have any current plans to enter into, any foreign currency hedging transactions or derivative financial transactions. We expect our transactions outside of the U.S. in the near-term will primarily entail payments for clinical trials, and for vendors and consultants supporting those trials within Europe and Australia, which may increase our exposure to foreign currency risk in future periods. We do not expect to maintain any significant amount of assets outside of the U.S.

The functional currency of our foreign subsidiaries are the local currencies. Accordingly, the effects of exchange rate fluctuations on the net assets of these operations are accounted for as translation gains or losses in accumulated other comprehensive income within stockholders' equity. We do not believe that a change of 10% in such foreign currency exchange rates would have a material impact on our financial position or results of operations.

Our balance sheet as of December 31, 2014 includes cash and cash equivalent balances of \$190,000 denominated in Renminbi at our Chinese subsidiary, VTI China. The majority of VTI China's operational activities are denominated and transacted in Renminbi with the exception of intercompany investments and loans that are transacted in U.S. dollars. Exchange rate losses recognized for all periods presented were insignificant. We plan to contract directly or through wholly-owned foreign subsidiaries with clinical investor sites, CROs and consultants outside the U.S. based primarily on tax and liability considerations. Accordingly, we may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of December 31, 2014, substantially all of our total liabilities were denominated in the functional currency.

***Effects of Inflation***

We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

**Item 8. Financial Statements and Supplementary Data.**

The consolidated financial statements required pursuant to this item are included in Part IV, Item 15 of this Annual Report, and are presented beginning on page F-1.

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

None.

**Item 9A. Controls and Procedures.**

*Disclosure Controls and Procedures*

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the Securities and Exchange Commission, or SEC, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.



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In connection with past audits of our financial statements, our independent registered public accounting firm identified and reported adjustments to management. Certain of these adjustments were deemed to be the result of internal control deficiencies that constitute material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. If one or more material weaknesses persist or if we fail to establish and maintain effective internal control over financial reporting, our ability to accurately report our financial results could be adversely affected.

We have not maintained an effective control environment in that the design and execution of our controls was limited due to the lack of a proper segregation of duties resulting from inadequate staffing levels, the ineffective review over financial transactions and the inadequate maintenance of our books and records. The lack of adequate staffing levels resulted in insufficient time spent on review and approval of certain information used to prepare our financial statements and the maintenance of effective controls to adequately monitor and review significant transactions for financial statement completeness and accuracy. Such examples include the correct financial statement classification, the valuation of financing transactions entered into during the period, and maintenance of documentation in support of such transactions. These control deficiencies, although varying in severity, contributed to the material weaknesses in the control environment noted by our independent registered public accounting firm.

Although remediation efforts are still in progress, management is taking steps to address the causes of our audit adjustments and to improve our internal control over financial reporting, including the implementation of new accounting processes and control procedures and the identification of gaps in our skills base and the expertise of our staff as required to meet the financial reporting requirements of a public company. We have hired additional accounting personnel who are degreed accountants, which has enabled us to expedite our month-end close process, thereby facilitating the timely preparation of financial reports and to strengthen our segregation of duties. We intend to hire incremental qualified staff as part of a comprehensive review of our internal controls and formalization of our review and approval processes. As a part of these efforts, we may identify additional control deficiencies, which could give rise to significant deficiencies and other material weaknesses in addition to the material weaknesses previously identified.

We have made substantial progress in the costly and challenging process of compiling the systems and processing documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing or any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal controls are designed and operating effectively, which could result in a loss of investor confidence in the accuracy and completeness of our financial reports. This could cause the price of our common stock to decline and we may be subject to investigation or sanctions by the SEC.

Our independent registered public accounting firm will not be required to report on the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act until the date we are no longer an emerging growth company based on the exemptions contained in the Jumpstart Our Business Startups Act, or JOBS Act. At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied that our internal controls over financial reporting are designed and operating effectively to prevent or detect a material misstatement to the financial statements. To comply with the requirements of being a public company, we may need to undertake various actions, such as implementing new internal controls and procedures or hiring accounting or internal audit staff.

### *Evaluation of Disclosure Controls and Procedures*

Our management has evaluated, with the participation of our Chief Executive Officer and Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of December 31, 2014 pursuant to Rule 13a-15(b) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2014, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were not effective at the reasonable assurance level because of the material weaknesses in our internal controls over financial reporting as described above. Notwithstanding the existence of the material weaknesses described above, management believes that the consolidated financial statements in this Annual Report Form 10-K fairly present, in all material respects, our financial position, results of operations and cash flows for the periods presented in accordance with generally accepted accounting principles.

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*Management's Annual Report on Internal Control over Financial Reporting and Attestation Report of the Registered Public Accounting Firm*

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies. Further, our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting as long as we are an emerging growth company pursuant to the provisions of the JOBS Act.

*Changes in Internal Control over Financial Reporting*

No change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act occurred during the three months ended December 31, 2014 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information.**

None.

**Table of Contents****PART III****Item 10. Directors, Executive Officers and Corporate Governance.****Executive Officers and Directors**

The following table sets forth the names, ages and positions of our executive officers and directors as of February 28, 2015:

<b>Name</b>	<b>Age</b>	<b>Position</b>
<b>Executive Officers:</b>		
Terence E. Winters, Ph.D.	72	Co-Chairman and Chief Executive Officer
Robert A. Ashley, M.A.	57	Executive Vice President, Chief Technical Officer
Duane Nash, M.D., J.D.	44	Executive Vice President, Chief Business Officer
Michael V. Swanson, M.B.A.	60	Chief Financial Officer
Aron P. Stern, M.B.A.	61	Chief Administrative Officer
John M. Dunn	63	General Counsel and Secretary
Andrew Henry	50	Vice President, Clinical Operations
Andrea Loewen	47	Vice President, Regulatory Affairs and Quality Assurance
Richard Murawski	66	Vice President, Manufacturing
<b>Non-Employee Directors:</b>		
Muneer A. Satter, J.D., M.B.A. <sup>(2)(3)</sup>	54	Co-Chairman and Lead Director
Jean-Jacques Bienaimé <sup>(2)</sup>	61	Director
Philip M. Croxford, M.B.A. <sup>(4)</sup>	54	Director
Douglas E. Godshall, M.B.A. <sup>(1)</sup>	50	Director
Errol R. Halperin, J.D., L.L.M. <sup>(1)(3)</sup>	74	Director
J. Michael Millis, M.D. <sup>(3)(4)</sup>	56	Director
Lowell E. Sears, M.B.A. <sup>(1)(2)</sup>	64	Director
Randolph C. Steer, M.D., Ph.D. <sup>(2)(4)</sup>	65	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of Nominating and Governance Committee.

(4) Member of Quality and Technology Committee.

**Executive Officers**

**Terence E. Winters, Ph.D.** has served as the Chairman of our board of directors from June 2003 to March 2013. Dr. Winters became Co-Chairman of our board of directors in March 2013 and currently serves as such. Dr. Winters has served as our Chief Executive Officer since June 2003. Dr. Winters is also a Special Limited Partner of Valley Ventures, an investor in Vital Therapies since May 2003. He was formerly a General Partner of Columbine Venture Funds and Vice President of DS Ventures, a venture capital subsidiary of Diamond Shamrock Corp., a chemical, life science and petroleum company. Dr. Winters was previously a director of three public companies: CollaGenex Pharmaceuticals, Inc., a developer and marketer of proprietary medical therapies to the dermatology market, Orthologic Corp., a biotechnology company focused on development and commercialization of novel synthetic

peptides for tissue repair and healing, and Clinuvel Pharmaceuticals, a global biopharmaceutical company committed to developing drugs for the treatment of a range of severe skin disorders. Dr. Winters has also served as a director of over 20 private companies. He earned a B.Sc. as well as a Ph.D. in chemistry from the University of Wales, U.K. He also completed a post-doctoral fellowship at the University of California, Los Angeles.

We believe Dr. Winters is qualified to serve on our board of directors based on his experience with corporate governance as a director of many private and public life science companies and over 30 years of experience as a general partner of venture capital funds with investments in life sciences and medical technology companies.

**Robert A. Ashley, M.A.** has served as our Executive Vice President and Chief Technical Officer since September 2013. Between May 2008 and September 2013 he served as our Vice President and Chief Operating Officer. Mr. Ashley's career in the pharmaceutical industry extends for 34 years. He was formerly Chairman, President and Chief Executive Officer of AmpliMed Corporation, a privately-held cancer drug development company, from January 2004 to March 2007, and Senior Vice President of Commercial Development at CollaGenex Pharmaceuticals, Inc., a publicly-held pharmaceutical company, from September 1994 to December 2003. Prior to that he held positions of increasing responsibility at Bristol-Myers Squibb from January 1989 to September 1994, and with Amersham International from 1979 to 1989. He earned a Master's Degree in Biochemistry from Oxford University. Mr. Ashley is the inventor of several issued and pending patents, as well as the author of several scientific papers. He serves on the Board of Directors of Rowpar Pharmaceuticals, a privately-held manufacturer of proprietary dental pharmaceuticals.

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**Duane Nash, M.D., J.D.** has served as our Executive Vice President since May 2013 and as our Chief Business Officer since March 2012. Between March 2012 and May 2013, he also served as our Medical Director. Dr. Nash completed his internship in general surgery at the University of California at San Francisco during which he served as a member of the liver transplant team. Dr. Nash also practiced as an attorney from November 2002 to February 2008, most recently at the law firm of Davis Polk, where he focused on intellectual property litigation and corporate matters. Dr. Nash joined Vital Therapies from Wedbush PacGrow Life Sciences where he was employed from March 2009 to March 2012 serving most recently as Vice President in Equity Research. Before that he was a research analyst at Pacific Growth Equities from April 2008 through March 2009, which was subsequently acquired by Wedbush Securities, Inc. Dr. Nash has served on the board of directors of Akebia Therapeutics, Inc., a publicly-traded biotech company focused on the treatment of anemia and vascular disease, since May 2013, and on the board of directors of Aerpio Therapeutics Inc., a clinical-stage biopharmaceutical company focused on advancing innovative therapies for vascular diseases, since September 2012. Dr. Nash earned a B.A. in biology from Williams College, an M.D. from Dartmouth Medical School, a J.D. from the University of California, Berkeley, and an M.B.A. from the University of Oxford.

**Michael V. Swanson, M.B.A.** joined us in August 2013 as our Chief Financial Officer. Mr. Swanson has over 20 years of experience in senior financial positions in both public and private life sciences companies. Mr. Swanson was Chief Financial Officer of Amira Pharmaceuticals, Inc., a pharmaceutical company focused on the discovery and early development of drugs to treat inflammatory and fibrotic diseases, from May 2008 until the company was acquired in September 2011, and of Panmira Pharmaceuticals, LLC, a spin out from Amira from September to December 2011. Since January 2012, Mr. Swanson has been providing financial consulting services to development stage companies. From July 2000 to April 2008, Mr. Swanson served in senior finance positions including Senior Vice President, Finance and Chief Financial Officer at Prometheus Laboratories Inc., a specialty pharmaceutical company marketing and selling pharmaceutical products and diagnostic testing services for gastrointestinal diseases and disorders. Previously, Mr. Swanson was Senior Vice President and Chief Financial Officer of Advanced Tissue Sciences, Inc., a publicly-traded biomedical company, where he served in senior financial positions for over ten years. Mr. Swanson also served as Director of Finance of the Fisher Scientific Group, Inc., a health and scientific technology company, and its parent, The Henley Group, Inc., a widely diversified holding company. Mr. Swanson began his career working approximately nine years with the public accounting firm of Deloitte Haskins & Sells, now Deloitte & Touche LLP. Mr. Swanson earned a B.S. in business administration from the California Polytechnic State University at San Luis Obispo and an M.B.A. from the University of Southern California. He is also a Certified Public Accountant (inactive).

**Aron P. Stern, M.B.A.** has served as our Chief Administrative Officer since August 2013 and as our Secretary from October 2005 to February 2015. Between June 2003 and August 2013, Mr. Stern served as our Treasurer, Vice President and Chief Financial Officer. Mr. Stern has over 20 years of experience in capital formation, acquisitions, financial strategy and financial and operational management in growth-stage high technology and biotechnology companies. He previously was Chief Financial Officer at each of Protein Polymer Technologies, Inc., a developer of a protein-based technology, 4-D Neuroimaging, a medical equipment manufacturing company, and VitaGen, Inc., our predecessor company. Mr. Stern also held positions at Apple Computer and Isis Pharmaceuticals, a developer of antisense drugs. Mr. Stern earned a B.S. in economics and business administration and an M.B.A. in finance and marketing from the University of California, Berkeley.

**John M. Dunn** has served as our General Counsel since November 2014 and as our Secretary since February 2015. Mr. Dunn has over 25 years of national law firm and in-house general counsel experience. Mr. Dunn was Senior Vice President Legal and Compliance, General Counsel and Secretary of IDEC Pharmaceuticals from 2002 until its merger with Biogen in late 2003. From 2004 to 2012, Mr. Dunn served as an Executive Vice President at Biogen Idec where he was in charge of Biogen Idec's internal corporate venture fund and Innovation Incubator. Most recently, Mr. Dunn has been providing legal and corporate development advisory services to emerging life science companies. Previously,

Mr. Dunn was a partner for 16 years in the Corporate, Securities and Technology Group at the Pillsbury Winthrop law firm where his practice focused on the healthcare industry. Mr. Dunn earned a B.S. in finance and his J.D. from the University of Wyoming. He serves as an advisor to TVM Capital, a life science venture capital firm and is a member of the Board of Directors of Agility-Clinical, a privately held consulting and contract research organization.

**Andrew Henry** has served as our Vice President of Clinical Operations since April 2013. Mr. Henry is responsible for the global implementation of our clinical program. Mr. Henry has 25 years of experience managing clinical trials in life science companies with roles at Schering-Plough Oncology, Novartis Oncology and MedImmune. Between January 2009 and February 2013, Mr. Henry served as Senior Director of Clinical Trial Management and Senior Director of Global Clinical Operational Strategy of MedImmune, a biopharmaceutical company that is under AstraZeneca's biologics division. At MedImmune Mr. Henry oversaw operations of all clinical studies being performed by the company across all therapeutic areas. From November 1997 to August 2008, Mr. Henry held roles as Senior Clinical Research Scientist and Head Clinical Resources and Development Director at Novartis Oncology, an ethical pharmaceutical company, where he oversaw clinical studies and the Department of Clinical Research Scientists/Clinical Trial Heads. Mr. Henry earned a B.S. in biology and biopsychology from William Paterson University.

**Andrea Loewen** has served as our Vice President of Regulatory Affairs and Quality since July 2013 and oversees our quality and regulatory systems and develops regulatory strategies. Ms. Loewen has 24 years of experience in regulatory and quality management roles, including positions at Baxter Healthcare, Biogen Idec, and Shire Pharmaceuticals. From June 2009 to July 2013, she served as the Head of Regulatory Affairs for Shire Pharmaceuticals Regenerative Medicine business unit, where she was responsible for global regulatory strategy and filings for development stage and commercial combination products. Between March 2008 and June 2009, Ms. Loewen served as Senior Director of Regulatory Affairs for Ceregene, Inc., a development stage biotech company, and was responsible for global regulatory strategy and filings for combination products. Ms. Loewen earned her B.A. in biology from Gustavus Adolphus College.

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**Richard Murawski** has served as our Vice President of Manufacturing since July 2013. Mr. Murawski has more than 40 years of experience in manufacturing facility design, construction, start-up, validation, and supply chain management, both domestically and internationally, including 17 major plant start-ups. From February 2013 to July 2013, Mr. Murawski was self-employed as a consultant. From June 2010 to February 2013, Mr. Murawski served as the Vice President/General Manager for Dendreon Corporation, a biotech manufacturing company, with responsibility for, among others, manufacturing, engineering, materials management, and facilities. Between June 2008 and July 2010, Mr. Murawski served as Chief Executive Officer of Murawski and Associates, a biotech consulting company, where he consulted companies on managing operations and biopharmaceutical facilities. From June 2002 to July 2008, Mr. Murawski served as Senior Vice President of Operations and Corporate Officer of Favril, Inc., a biotech manufacturing company, and was responsible for manufacturing, engineering, materials management, facilities, technical services, and environmental, health and safety functions. Mr. Murawski earned his B.S. in chemical engineering from the Newark College of Engineering at the New Jersey Institute of Technology.

**Board of Directors    Non-employee Directors**

**Muneer A. Satter, J.D., M.B.A.** has served on our board of directors since March 2013 and is our Co-Chairman and Lead Director. Mr. Satter manages Satter Investment Management, or SIM, a private investment firm and family office with significant investments in several life sciences and medical technology companies. He has also managed the Satter Foundation, a private family foundation since 1997. Mr. Satter has served as Chairman or Co-Chairman of Akebia Therapeutics, a publicly-traded biotech company focused on the treatment of anemia and vascular disease, since May 2013. Since October 2013, he has served as Co-Chairman of Aerpio Therapeutics, a biotech company focused on diabetic macular edema and vascular leaks. He is a director of Annexon which is a complement cascade pathway company focused on autoimmune and neurologic diseases. Mr. Satter is Co-Founder and has served as Chairman of Restorsea, a company which holds exclusive rights to a unique enzyme for an anti-aging cream since May 2013. He has served as Chairman of Linq3, a unique secure payment platform for lottery transactions since May 2013. He is Vice Chairman of the Board of the Goldman Sachs Foundation and GS Gives, where he is also Chairman of the Investment Committee overseeing \$1.2 billion of assets. He is on the Board of the Nature Conservancy where he is Chairman of the Finance Committee overseeing a \$1.6 billion endowment. He is also on the Board of Trustees of Northwestern University. He is on the Board of Advisors of the American Enterprise Institute. He is a member of the Council on Foreign Relations and is on the board of World Business Chicago, which is chaired by Chicago's Mayor Rahm Emanuel. He is also a member of the Board of the Navy SEAL Foundation. Mr. Satter is a retired partner at Goldman Sachs, where he was at the firm for twenty-four years and a partner of the firm for sixteen years in the Merchant Banking Division. He was the Global Head of the Mezzanine Group, where he raised and managed over \$30 billion of assets. He was also a senior member of the Investment Committee and Chairman of the Risk Committee for the Merchant Banking Division, which at the time had over \$80 billion of assets under management. Additionally, he was former Co-Chairman of Room to Read, which builds 2,000 libraries and schools per year in developing countries. Mr. Satter earned a B.A. from Northwestern University and a J.D. and M.B.A. from Harvard Law School and Harvard Business School.

We believe Mr. Satter is qualified to serve on our board of directors because of his extensive experience in merchant banking and venture capital investments and his experience as an investor and director of other companies in the life sciences and medical technology industries.

**Jean-Jacques Bienaimé** has served on our board of directors since September 2013. Since May 2005, Mr. Bienaimé has served as the chief executive officer and as a director of BioMarin Pharmaceutical Inc., a publicly-traded company that develops and commercializes innovative pharmaceuticals for serious diseases and medical conditions. From November 2002 to April 2005, Mr. Bienaimé served as chairman, chief executive officer and president of Genencor, a biotechnology company focused on industrial bioproducts and targeted cancer biotherapeutics. Prior to joining



Genencor, Mr. Bienaimé was chairman, president and chief executive officer of SangStat Medical Corporation, another biotechnology company. He became president of SangStat Medical Corporation, a global pharmaceutical company, in 1998 and chief executive officer in 1999. Prior to joining SangStat Medical Corporation, Mr. Bienaimé held various management positions from 1992 to 1998 with Rhône-Poulenc Rorer Pharmaceuticals (now known as Sanofi-Aventis), including Senior Vice President of Corporate Marketing and Business Development, and Vice President and General Manager of the Advanced Therapeutic and Oncology division. Mr. Bienaimé has served on the board of BioMarin Pharmaceuticals Inc. since May 2005, and the board of Incyte Corporation, a publicly-traded biopharmaceutical company, since January 2015. In addition, he serves on the board of The Biotech Industry Organization. Mr. Bienaimé served on the boards of Intermune, Inc., a publicly-traded biotechnology company, from March 2012 until its acquisition by Roche Holdings, Inc. in September 2014, and Portola Pharmaceuticals, Inc., a publicly-traded biopharmaceutical company, from September 2010 through June 2014. Mr. Bienaimé earned an M.B.A. from the Wharton School at the University of Pennsylvania and a B.S. in economics from the Ecole Supérieure de Commerce de Paris.

We believe that Mr. Bienaimé is qualified to serve on our board of directors based on his extensive experience in the management of biotechnology organizations, business development, and sales and marketing of both biotechnology and pharmaceutical products.

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***Philip M. Croxford, M.B.A.*** has served on our board of directors since 2008 and as a healthcare president and chief executive officer executive for over 15 years. Mr. Croxford most recently held the position of Global President of LifeCell Corporation, a tissue biotechnology engineering company, from September 2013 until September 2014, and was a member of its parent, Acelity (formerly KCI), Executive Leadership Team. From December 2012 to August 2013, Mr. Croxford was Senior Vice President of Global Commercial Operations for LifeCell. From June 2008 to December 2012 he was President and Chief Executive Officer of ArjoHuntleigh, North America, a member of The Getinge AB Group, a global medical and safety technology company listed on the OMX Nordic Exchange. He served on their Executive Leadership Team during his term in office. From February 2006 to October 2007, Mr. Croxford was President and Chief Executive Officer and member of the board of directors of Draeger Medical, Inc., a private medical device company. Mr. Croxford also served as Group Vice President and Worldwide General Manager of Arrow International, Inc. and as an Operating Company Board Member and Vice President for the Worldwide Wound Management Business of Ethicon, a Johnson & Johnson Company. Mr. Croxford also held other executive management positions with Johnson & Johnson Company and Smith & Nephew. He earned a B.Sc. (Honors) degree in pharmacy from the University of Manchester, School of Pharmacy, in England. Mr. Croxford is also a licensed member of the Royal Pharmaceutical Society of Great Britain. He earned a Post Graduate Diploma in marketing from the Royal Chartered Institute of Marketing, and is a Chartered Member of the Institute. He earned his M.B.A. from Heriot Watt University, Edinburgh Business School, U.K.

We believe Mr. Croxford is qualified to serve on our board of directors based on his significant operational and leadership experience, including, without limitation, senior management experience of public international companies, extensive experience in the life sciences and medical technology industries, and a strong academic background, including degrees in pharmacy, marketing and business.

***Douglas E. Godshall, M.B.A.*** has served on our board of directors since May 2013. Mr. Godshall has been the Chief Executive Officer of HeartWare International, Inc., a developer of a range of implantable mechanical circulatory assist devices, since September 2006 and a director since October 2006. Prior to joining HeartWare, Mr. Godshall served in various executive and managerial positions at Boston Scientific Corporation, a manufacturer and a developer of medical supplies and medical devices in a variety of fields, including as a member of Boston Scientific's Operating Committee and President, Vascular Surgery. Previously, Mr. Godshall spent five years as Vice President, Business Development, at Boston Scientific, where he was focused on acquisition strategies for the cardiology, electrophysiology, neuroradiology and vascular surgery divisions. In March 2012, Mr. Godshall was appointed a director of pSivida Corp., a developer of drug delivery products for treatment of back-of-the-eye diseases. Mr. Godshall earned a B.A. in business from Lafayette College and an M.B.A from Northeastern University.

We believe that Mr. Godshall is qualified to serve on our board of directors based on his experience as an executive officer and director of several life sciences and medical technology companies.

***Errol R. Halperin, J.D., L.L.M.*** has served on our board of directors since December 2012. Mr. Halperin has been a senior partner of DLA Piper since January 1979 until December 2013. At the present time, Mr. Halperin is a senior strategic advisor to DLA Piper (U.S.). In his practice, Mr. Halperin has provided general business advice to clients in a broad range of sectors, including the manufacturing, real estate industry and real estate investment trust industry. Mr. Halperin's practice was concentrated in the areas of mergers and acquisitions, corporate law, international transactions, real estate law and federal income tax law. Mr. Halperin has also served on the board of Equity Residential, a public REIT, and private company boards. Currently, he is a director of Elkay Manufacturing Company, a privately held corporation, and Pangea Properties, a real estate investment and management company. He also currently serves as a director of other late stage private venture companies, including LINQ3, LLC and Restorsea, LLC. Before joining DLA Piper, from June 1972 to January 1979 he was legislation counsel of the Joint Committee on Taxation of the U.S. Congress; and was an assistant branch chief of the Legislation and Regulations Division of the

Chief Counsel for the Internal Revenue Service from June 1968 to June 1972. Mr. Halperin earned a B.S. and a J.D. from DePaul University and an L.L.M. in taxation from New York University.

We believe that Mr. Halperin is qualified to serve on our board of directors based on his experience as an attorney practicing for a nationally known firm in the areas of mergers and acquisitions and corporate transactions and his involvement in advising venture capital backed companies.

**J. Michael Millis, M.D.** has served on our board of directors since 2006. Dr. Millis is a Professor of Surgery and Chief of the Section of Transplantation at the University of Chicago. Dr. Millis currently serves on the medical staff at the University of Chicago Hospital. His current research explores the application of cellular technology on patient care, including how hepatocyte transplantation, extracorporeal assist technology and stem cells can assist in the care of patients with liver disease or liver tumors. Dr. Millis has been associated with the ELAD System since 1994, and was an investigator on the Phase 1 clinical trial. He has been the chairman of the Vital Therapies Clinical Advisory Board since 2003. Dr. Millis currently serves or has served in the past on a variety of committees, such as the American Association for the Study of Liver Diseases Ethics Committee, the American Society of Transplant Surgeons, Studies of Pediatric Liver Transplantation Scientific Advisory Board and Publication and Research Committee, and the ROBI Liver Intestinal Subcommittee, for which he is the former chairman. Dr. Millis is also a member of the Medical Advisory Committee of the American Liver Foundation Illinois Chapter. He also serves on the board of directors of Gift of Hope (the organ procurement organization for Illinois) and the Editorial Board of the American Journal of Transplantation, Transplantation, and Liver Transplantation. He earned a B.A. in chemistry and political science from Emory University and an M.D. with high honors from the University of Tennessee. He completed his surgical residency, clinical and research fellowship in liver transplantation at the University of California, Los Angeles.

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We believe that Dr. Millis is qualified to serve on our board of directors based on his participation on multiple advisory committees and boards and his research in the treatment of liver disease.

**Lowell E. Sears, M.B.A.** has served on our board of directors since May 2013. Mr. Sears is the Chairman and CEO of Sears Capital Management, a venture investment and portfolio management firm specializing in life sciences. He has served on the board of directors of Cellerant Therapeutics, Inc., a clinical stage biotechnology company focused on the regulation of the hematopoietic, or blood-forming, system, since February 2012 and has been Chairman of the Board since June 2012. Mr. Sears has also served on the board of directors of SymBio Pharmaceuticals, KK, Ltd., a biotechnology company that is engaged in identifying and developing therapeutics for the treatment of leukemia, multiple myeloma and lymphoma, since September 2005. From 1986 until 1994, Mr. Sears was a part of the senior management team of Amgen, Inc., a developer and manufacturer of therapeutics targeting cancers, kidney ailments, inflammatory disorders, and metabolic diseases, where he was Chief Financial Officer as well as the Senior Vice President responsible for the Asia Pacific Region. Prior to joining Amgen, Mr. Sears held senior planning and financial positions with Atlantic Richfield Company, an oil company from 1976 until 1986, including Chief Financial Officer for its Ventures Division. He earned a B.A. in economics from Claremont McKenna College and an M.B.A. from the Stanford University Graduate School of Business.

We believe that Mr. Sears is qualified to serve on our board of directors based on his experience as a senior manager and director of private and publicly-traded companies, including several in the life sciences industry.

**Randolph C. Steer, M.D., Ph.D.** has served on our board of directors since May 2005. Dr. Steer has been an independent pharmaceutical, biotechnology and medical devices consultant since 1989. Dr. Steer has served as Associate Director of Medical Affairs at Marion Laboratories, a then-public pharmaceutical company; Medical Director at Ciba Consumer Pharmaceuticals (a division of Ciba-Geigy Corporation, a then-public pharmaceutical company); Vice President, Senior Vice President and Member of the Executive Committee at Physicians World Communications Group; Chairman, President and Chief Executive Officer of Advanced Therapeutics Communications International, a drug regulatory group serving the U.S., Mexico, Latin America, the Pacific Rim, Europe and Japan; Chairman and Chief Executive Officer of Vicus.com, Inc.; and President and Chief Operating Officer of Capstone Therapeutics Corp., a public biotechnology company. Dr. Steer is a member of the board of directors of Techne Corporation, a public biotechnology company, and the Board of Trustees of the Mayo Clinic. He earned his B.A. in Physiology from University of Minnesota. He earned an M.D. from the Mayo Medical School and a Ph.D. from the University of Minnesota where he also completed a residency and subspecialty training in clinical and chemical pathology. He is a Fellow of the American College of Clinical Pharmacology.

We believe that Dr. Steer is qualified to serve on our board of directors based on his experience as a senior manager in multiple biotechnology and medical device companies.

## **Family Relationships**

There are no family relationships among any of our directors and executive officers.

## **Board Composition**

Our board of directors is currently composed of nine members. Eight of the nine directors that comprise our board of directors are independent within the meaning of the independent director guidelines of the NASDAQ Stock Market. Please see the section entitled *Director Independence* in Item 13 below for further information. Our certificate of incorporation and bylaws currently in effect provide that the number of directors shall be at least one and will be fixed from time to time by resolution of our board of directors.

Our board of directors is divided into three classes of directors. At each annual meeting of stockholders, a class of directors will be elected for a three-year term to succeed the class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2015 for the Class I directors, 2016 for the Class II directors and 2017 for the Class III directors.

The Class I directors are Mr. Croxford and Drs. Steer and Winters.

The Class II directors are Messrs. Bienaimé, Godshall and Satter.

The Class III directors are Messrs. Halperin and Sears and Dr. Millis.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our board of directors or a change in control.

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Certain of our stockholders affiliated with Mr. Satter, referred to as the Satter Investors, retain, contractual rights to nominate up to 30% of our directors, as provided in our Fourth Amended and Restated Investors Rights Agreement, dated as of August 28, 2013, as amended, or the Senior Preferred IRA. To date, the Satter Investors have not exercised their rights to designate any candidates for nomination but have reserved the right to do so in the future.

### **Lead Director**

Our board of directors determined as part of our bylaws that one of our directors should serve as a lead director. Mr. Satter has been appointed to serve as our Lead Director and Co-Chairman. As Lead Director, Mr. Satter, among other responsibilities, coordinates the scheduling of, and preparing the agenda for, meetings of our board of directors, stockholders and independent directors, presides (or designates another director to preside) over such meetings, and defines the scope, quality, quantity and timeliness of the flow of information between management and our board of directors that is necessary for our board of directors to effectively and responsibly perform its duties. While we have offered Mr. Satter the same compensation for his service as a member of our board of directors and as Lead Director as we pay to each other non-employee member of our board of directors, Mr. Satter has declined to receive (and has not received) any compensation for his service on our board of directors or as Lead Director.

The Senior Preferred IRA provides that for so long as Mr. Satter and Dr. Winters both serve as members of our board of directors, each shall serve as Co-Chairman of our board of directors and Mr. Satter shall serve as our Lead Director. In the event that Mr. Satter serves as a member of our board of directors at a time when Dr. Winters does not, Mr. Satter will serve as our Chairman of the board and Lead Director. Dr. Winters will serve as Co-Chairman only so long as he is both a director and our Chief Executive Officer. As the Satter Investors ownership percentage decreases, their right to nominate directors similarly decreases.

### **Audit Committee**

Our board of directors has a separately-designated audit committee. Our audit committee members currently consist of Messrs. Godshall, Halperin and Sears. Mr. Sears serves as the chairman. Our board of directors has determined that Mr. Sears qualifies as an audit committee financial expert within the meaning of the rules and regulations of the Securities and Exchange Commission, or SEC, and is independent under Rule 10A-3 of the Exchange Act and the current rules of the NASDAQ Stock Market and financially literate under the rules of the SEC and NASDAQ Stock Market.

### **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Exchange Act requires our executive officers and directors, and persons who own more than 10% of a registered class of our equity securities, to file reports of ownership and changes of ownership on Forms 3, 4 and 5 with the SEC. Such directors, executive officers and 10% stockholders are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file.

Based solely on our review of the copies of such forms we have received and written representations from certain reporting persons that they filed all required reports, we believe that all of our officers, directors and greater than 10% stockholders complied with all Section 16(a) filing requirements applicable to them with respect to transactions during 2014.

### **Code of Business Conduct and Ethics**

Our board of directors has adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code of business conduct is available on the corporate governance section of our website, which is located at <http://www.vitaltherapies.com>. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website.

### **Considerations in Evaluating Director Nominees**

In its evaluation of director candidates, including the members of the board of directors eligible for reelection, our nominating and governance committee will consider the following:

The current size and composition of our board of directors and the needs of the board and its respective committees;

Factors such as character, integrity, judgment, diversity of experience, independence, area of expertise, corporate experience, length of service, potential conflicts of interest, other commitments, and the like. Our nominating and governance committee evaluates these factors, among others, and does not assign any particular weighting or priority to any of these factors; and

Other factors that our nominating and governance committee may consider appropriate.

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The nominating and governance committee also focuses on issues of diversity, such as diversity in experience, international perspective, background, expertise, skills, age, gender, and ethnicity. The nominating and governance committee does not have a formal policy with respect to diversity; however, our board of directors and the nominating and governance committee believe that it is essential that members of our board of directors represent diverse viewpoints.

Any nominee for a position on the board must satisfy the following minimum qualifications:

The highest personal and professional ethics and integrity;

Proven achievement and competence in the nominee's field and the ability to exercise sound business judgment;

Skills that are complementary to those of the existing board;

The ability to assist and support management and make significant contributions to the company's success; and

An understanding of the fiduciary responsibilities required of a member of the board and the commitment of time and energy necessary to diligently carry out those responsibilities.

If our nominating and governance committee determines that an additional or replacement director is required, the committee may take such measures as it considers appropriate in connection with its evaluation of a director candidate, including candidate interviews, inquiry of the person or persons making the recommendation or nomination, engagement of an outside search firm to gather additional information, or reliance on the knowledge of the members of the committee, board, or management.

After completing its review and evaluation of director candidates, our nominating and governance committee recommends to our full board of directors the director nominees for selection. Our nominating and governance committee has discretion to decide which individuals to recommend for nomination as directors and our board of directors has the final authority in determining the selection of director candidates for nomination to our board.

### ***Requirements for Stockholder Recommendations of a Candidate to our Board***

Our nominating and governance committee will consider recommendations for candidates to our board of directors from our stockholders. A stockholder that wishes to recommend a candidate for consideration by the committee as a potential candidate for director must direct the recommendation in writing to Vital Therapies, Inc., 15010 Avenue of Science, Suite 200, San Diego, California 92128, Attention: Secretary, and must include the candidate's name, home and business contact information, detailed biographical data, relevant qualifications, a signed letter from the candidate confirming willingness to serve, information regarding any relationships between us and the candidate and evidence of the recommending stockholder's ownership of our stock. Such recommendation must also include a statement from the recommending stockholder in support of the candidate, particularly within the context of the criteria for board



membership, including issues of character, integrity, judgment, diversity of experience, independence, area of expertise, corporate experience, length of service, potential conflicts of interest, other commitments and the like and personal references. Our nominating and governance committee will consider the recommendation but will not be obligated to take any further action with respect to the recommendation.

***Requirements for Stockholder Nominations to be brought before an Annual Meeting***

Separately, our bylaws contain specific requirements governing the processes and procedures for stockholders who wish to formally nominate a candidate and ensure that he or she is nominated and eligible for election at an annual meeting of stockholders. Generally, nominations for the election of directors may be made by stockholders of record (both on the date of the applicable written notice and at the time of annual meeting) who have timely delivered written notice to us at Vital Therapies, Inc., 15010 Avenue of Science, Suite 200, San Diego, California 92128, Attention: Secretary in compliance with the advance notice provisions included in our bylaws. Such notice must contain specified information concerning the nominees such as the nominees' name, age, home and business contact information, principal occupation or employment, the class and number of shares beneficially owned directly or indirectly by the nominee, the date such shares were acquired and the investment intent of such acquisition, a written questionnaire completed by the nominee, a written representation from the nominee that he/she will not become a party to any agreement, arrangement or understanding with any person or entity as to how such person will act or vote and would be in compliance with all applicable publicly disclosed policies and guidelines, and any other information required to be disclosed about the nominee if proxies were to be solicited to elect the nominee as a director pursuant to Regulation 14A of the Exchange Act. In addition, such notice must contain specified information concerning the nominating stockholder such as the stockholder's name, address, the class and number of shares beneficially owned directly or indirectly by the stockholder, a description of any derivative positions held or beneficially held by the stockholder, whether and the extent to which a hedging transaction has been entered into by or on behalf of the stockholder, a description of all arrangements or understandings between the stockholder and the proposed nominee, a representation that the stockholder is a holder of record entitled to vote at the annual meeting and that the stockholder intends to appear in person or by proxy at the meeting to nominate the person named in its notice, a representation as to whether such stockholder intends to deliver a proxy statement and/or form of proxy to the holders of a sufficient number of our outstanding shares reasonably believed by the stockholder to elect the proposed nominee or otherwise to solicit proxies or votes from stockholders in support of the nomination, and any other information required to be disclosed about the stockholder if proxies were to be solicited to elect the nominee as a director pursuant to Regulation 14A of the Exchange Act. For a stockholder recommendation to be considered by our nominating and governance committee as a potential candidate at an annual meeting, written notice of nominations must be received on or before the deadline for receipt of stockholder proposals for such meeting. In the event a stockholder decides to nominate a candidate for director and solicits proxies for such candidate, the stockholder will need to follow the rules set forth by the SEC and in our bylaws.

**Table of Contents****Item 11. Executive Compensation.**

Our named executive officers for the year ended December 31, 2014, which consist of our principal executive officer and our two other most highly compensated executive officers, are Terence E. Winters, Ph.D., our Co-Chairman and Chief Executive Officer, John M. Dunn, J.D., our General Counsel, Secretary and Duane Nash, M.D., J.D., our Executive Vice President and Chief Business Officer.

Name and Principal Position	Year	Salary (\$)	Option Awards \$(1)	Non-Equity Incentive Plan Compensation	All Other Compensation	Total (\$)
				\$(2)	\$(3)	
Terence E. Winters, Ph.D. <i>Co-Chairman and Chief Executive Officer</i>	2014	450,000		171,900	16,010	637,910
	2013	418,125		110,719	16,104	544,948
John M. Dunn, J.D. (4) <i>General Counsel and Secretary</i>	2014	35,625	665,120			700,745
Duane D. Nash, M.D., J.D. (5) <i>Executive Vice President, Chief Business Officer</i>	2014	350,000		100,030		450,030

- (1) The amounts in the Option Awards column reflect the aggregate grant date fair value of stock options granted during the calendar year computed in accordance with the provisions of Accounting Standards Codification (ASC) 718, *Compensation Stock Compensation*. The assumptions that we used to calculate these amounts are discussed in Note 9 to our financial statements appearing at the end of this Annual Report. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.
- (2) Amounts approved by our board of directors on February 2, 2015 under our Executive Incentive Compensation Plan (as described below).
- (3) Includes company-paid reimbursement for Medicare and prescription drug coverage.
- (4) Mr. Dunn became a full-time employee in November 2014. In connection with his appointment as an executive officer, our board of directors granted to Mr. Dunn an option to purchase 50,000 shares of our common stock on November 17, 2014 at an exercise price of \$19.03 per share.
- (5) Dr. Nash was not a named executive officer in 2013.

**Option Awards**

In connection with the commencement of Mr. Dunn's employment with us and his appointment as one of our executive officers in November 2014, on November 17, 2014, our board of directors granted to Mr. Dunn an option to purchase 50,000 shares of our common stock at an exercise price of \$19.03 per share. The shares subject to the option vest monthly over four years, subject to Mr. Dunn's continued service on each such date, and is otherwise subject to the terms of our 2014 Equity Incentive Plan, or 2014 Plan, and form of option agreement for our 2014 Plan. In connection with the option grant, Mr. Dunn entered into a standard form of option agreement under our 2014 Plan.

**Non-Equity Incentive Plan Compensation and Bonus**

***Executive Incentive Compensation Plan***

Our Executive Incentive Compensation Plan, or Incentive Plan, was adopted by our board of directors on July 8, 2013. Our Incentive Plan is administered by our compensation committee; provided, however, that our board of directors must approve any award or any amendment to any award made thereunder. Our compensation committee determines the performance goals applicable to any award, which goals may include, without limitation, the attainment of research and development milestones, sales bookings, business divestitures and acquisitions, cash flow, cash position, earnings (which may include earnings before interest and taxes, earnings before taxes and net earnings) per share, net income, net profit, net sales, operating cash flow, operating expenses, operating income, operating margin, overhead or other expense reduction, product defect measures, product release timelines, productivity, profit, return on assets, return on capital, return on equity, return on investment, return on sales, revenue, revenue growth, sales results, sales growth, stock price, time to market, total shareholder return, working capital, and individual objectives such as peer reviews or other subjective or objective criteria. Performance goals that include the Company's financial results may be determined in accordance with United States generally accepted accounting principles, or GAAP, or such financial results may consist of non-GAAP financial measures. The performance goals may be on an individual, divisional, business unit, functional or company-wide basis. The performance goals may differ from participant to participant and from award to award.

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Pursuant to the employment letter agreements entered into between us and our named executive officers, our named executive officers are each eligible to receive annual bonuses as a percentage of their annual base salary based upon achievement of the performance goals determined by our compensation committee. For additional information regarding the terms of these employment letter agreements, see below under **Agreements With Our Named Executive Officers**.

Notwithstanding the eligibility for bonus awards, our board of directors may, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, or increase, reduce or eliminate the amount allocated to the bonus pool for a particular performance period. The actual award may be below, at or above a participant's target award, in the discretion of our board. Our board may determine the amount of any reduction on the basis of such factors as it deems relevant, and it is not required to establish any allocation or weighting with respect to the factors it considers.

Actual awards are paid in cash only after they are earned, which usually requires continued employment through the date of payment of the award. Payment of bonuses occurs as soon as administratively practicable after they are earned, but no later than the dates set forth in the Incentive Plan.

Our board of directors has the authority to amend, alter, suspend or terminate the Incentive Plan provided such action does not impair the existing rights of any participant with respect to any earned bonus.

For the fiscal year ended December 31, 2014, bonus awards for our named executive officers (other than Mr. Dunn) were based on the achievement of corporate performance goals, which carried a 50% weighting, and individual performance, which carried a 50% weighting, except with respect to Dr. Winters for whom a bonus award was based solely on the achievement of corporate performance goals. Our compensation committee established the categories of corporate performance goals as relating to the attainment of research and development milestones and financings. Our compensation committee determined that the performance goals of our named executive officers were met at approximately 95% of target and payments were approved at that payout percentage by our board on February 2, 2015. Mr. Dunn became a full-time employee in November 2014 and was not eligible for a bonus under the Executive Incentive Compensation Plan for fiscal 2014.

## **Agreements With Our Named Executive Officers**

### ***Terence E. Winters***

We entered into an employment letter agreement, dated October 31, 2013, with Dr. Winters, which sets forth the terms and conditions of his employment with us. The employment letter agreement has no specific term and provides for at-will employment. This agreement supersedes all existing agreements he may have with us concerning his employment relationship. The agreement provides that Dr. Winters' current annual base salary is \$450,000 and he is eligible for an annual bonus equal to 40% of his base salary.

### ***Duane Nash***

We entered into an employment letter agreement, dated October 30, 2013, with Dr. Nash, our current Executive Vice President, Chief Business Officer, which sets forth the terms and conditions of his employment with us. The employment letter agreement has no specific term and provides for at-will employment. This agreement supersedes all existing agreements he may have with us concerning his employment relationship. The agreement provides that Dr. Nash's current annual base salary is \$350,000 and he is eligible for an annual bonus equal to 30% of his annual base salary.

***John M. Dunn***

We entered into an employment letter agreement, dated March 5, 2015, with Mr. Dunn, our current General Counsel and Secretary, which sets forth the terms and conditions of his employment with us. The employment letter agreement has no specific term and provides for at-will employment. Mr. Dunn's current annual base salary is \$285,000 and he is eligible for an annual bonus equal to 25% of his annual base salary. In addition, Mr. Dunn received an option grant to purchase 50,000 shares of our common stock on November 17, 2014 at an exercise price per share of \$19.03 that vests over a period of four years from his employment start date in equal monthly installments, subject to Mr. Dunn continuing to provide services to us.

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**Executive Change of Control and Severance Agreements**

We have entered into a change of control and severance agreement, with each of our executive officers, which require us to make payments if the executive officer's employment with us is terminated in certain circumstances.

If prior to the two-month period before or after the twelve-month period following a change of control (such period, the Change of Control Period), an executive officer's employment is terminated without cause or an executive officer resigns for good reason (as such terms are defined in the change of control and severance agreement), such officer will be eligible to receive the following benefits if such officer timely signs and does not revoke a release of claims:

continued payment of base salary for a period of six months (12 months in the case of Dr. Winters); and

reimbursement by us for up to six months (12 months in the case of Dr. Winters) of COBRA premiums to continue health insurance coverage for such officer and such officer's eligible dependents, or taxable monthly payments for the equivalent period in the event payment for COBRA premiums would violate applicable law.

If, within the Change of Control Period, such officer's employment is terminated without cause or such officer resigns for good reason, such officer will be entitled to the following benefits if such officer timely signs a release of claims:

a lump sum payment equal to (x) 12 months (18 months in the case of Dr. Winters) his annual base salary (for the year of the change of control or such officer's termination, whichever is greater), plus (y) 1x (1.5x in the case of Dr. Winters) the greater of: (A) such officer's target annual bonus (for the year of the change of control or such officer's termination, whichever is greater) or (B) such officer's actual bonus for performance relating to the calendar year immediately prior to the calendar year of such officer's termination;

reimbursement by us for up to 12 months (18 months in the case of Dr. Winters) of COBRA premiums to continue health insurance coverage for such officer and such officer's eligible dependents, or taxable monthly payments for the equivalent period in the event payment for COBRA premiums would violate applicable law; and

100% accelerated vesting of all outstanding equity awards.

In addition, in the event any of the amounts provided for under these agreements or otherwise payable to our executive officers would constitute parachute payments within the meaning of Section 280G of the Internal Revenue Code and could be subject to the related excise tax, the executive officer would be entitled to receive either full payment of benefits under this agreement or such lesser amount which would result in no portion of the benefits being subject to the excise tax, whichever results in the greater amount of after-tax benefits to the executive officer. The agreements do not require us to provide any tax gross-up payments.

Drs. Winters and Nash may become eligible for accelerated vesting of their option awards in connection with a change in control under our 2012 Stock Option Plan, or 2012 Plan, and option agreements under the 2012 Plan, as described below. The option grant to Mr. Dunn was made pursuant to our 2014 Plan, which provides for accelerated vesting in

connection with a change in control in limited circumstances, as described below.

***2014 Equity Incentive Plan***

Our 2014 Plan provides that in the event of a merger or change in control, as defined in the 2014 Plan, each outstanding award will be treated as the administrator determines, including, without limitation, that awards may be assumed or substituted for by the acquiring or succeeding corporation, awards may be terminated immediately prior to the consummation of the merger or change in control, awards may vest in whole or in part prior to or upon consummation of the merger or change in control and, to the extent the administrator determines, terminate on or immediately prior to the effectiveness of the merger or change in control, or awards may be terminated in exchange for cash or property or replaced with other rights or property. If a successor corporation does not assume or substitute an equivalent award for any outstanding award, then such award will fully vest, all restrictions on such award will lapse and all performance goals or other vesting criteria applicable to such award will be deemed achieved at one hundred percent (100%) of target levels. Additionally, if a successor corporation does not assume or substitute an option or stock appreciation right, the administrator will notify the participant in writing or electronically that such award will be exercisable for a specified period of time determined by the administrator prior to the transaction, and such award will then terminate upon the expiration of such period.

In addition, pursuant to their stock option agreements, certain optionees, including one of our named executive officers, are eligible for full vesting acceleration of their outstanding options in the event their service is terminated other than for cause within twelve months following a change in control.

***2012 Stock Option Plan and Option Agreements***

Our 2012 Plan provides that in the event of a change in control, as defined in the 2012 Plan, the surviving, continuing, successor, or purchasing corporation or other business entity or parent thereof may assume or substitute an equivalent award for each outstanding option under the 2012 Plan. If there is no assumption or substitution of outstanding options, such options will terminate upon the expiration of a stated notice period.

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In addition, pursuant to their stock option agreements, certain optionees, including our named executive officers, are eligible for full vesting acceleration of their outstanding options in the event their service is terminated other than for cause or they resign from their service for good reason, in either case, within twelve months following a change in control.

**Outstanding Equity Awards at Fiscal Year-End for Fiscal 2014**

The following table sets forth certain information concerning outstanding equity for our named executive officers awards at fiscal year-end December 31, 2014:

<b>Name</b>	<b>Vesting Commencement Date<sup>(2)</sup></b>	<b>Number of Securities Underlying Unexercised Options Exercisable<sup>(1)</sup></b>	<b>Number of Securities Underlying Unexercised Options Unexercisable</b>	<b>Option Exercise Price</b>	<b>Option Expiration Date</b>
Terence E. Winters, Ph.D. <i>Co-Chairman and Chief Executive Officer</i>	2/8/2012 <sup>(3)</sup>	128,394		\$ 0.43	3/31/2022
	9/13/2012 <sup>(4)</sup>	386,672		\$ 8.00	9/25/2022
John M. Dunn, J.D. <i>General Counsel and Secretary</i>	11/17/2014 <sup>(5)</sup>	1,041	48,959	\$ 19.03	11/16/2024
Duane D. Nash, M.D., J.D. <i>Executive Vice President, Chief Business Officer</i>	2/8/2012 <sup>(6)</sup>	93,377		\$ 0.43	3/31/2022
	4/25/2012 <sup>(7)</sup>	23,344		\$ 0.43	4/24/2022
	9/13/2012 <sup>(8)</sup>	241,670		\$ 8.00	9/25/2022

- (1) The options listed above to Dr. Winters and Dr. Nash are subject to an early exercise right and may be exercised in full prior to the vesting of the shares underlying such options. Any shares purchased by early exercising unvested options are subject to repurchase by the company in the event the optionee ceases providing services to the company and are released from this repurchase right in accordance with the options original vesting schedule. Vesting of all options or early exercised shares is subject to continued service on the applicable vesting date. The option listed above for Mr. Dunn was granted under the 2014 Plan and, therefore, have no early exercise rights.
- (2) All options listed above vest in equal monthly installments over the four year period following the vesting commencement date.
- (3) 73,923, or 58%, of the shares subject to Dr. Winters' outstanding options were vested as of December 31, 2014.
- (4) 217,502, or 56%, of the shares subject to these options were vested as of December 31, 2014.
- (5) 1,041 or 2% of the shares subject to these options were vested as of December 31, 2014.
- (6) 66,142, or 71%, of the shares subject to these options were vested as of December 31, 2014.
- (7) 15,562, or 67%, of the shares subject to these options were vested as of December 31, 2014.
- (8) 135,939 or 56% of the shares subject to these options were vested as of December 31, 2014.

**Perquisites, Health, Welfare and Retirement Benefits**

Our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, vision, group life, disability and accidental death and dismemberment insurance plans, in each case on the same basis



as all of our other employees. We provide a 401(k) plan to our employees, including our current named executive officers, as discussed in the section below entitled *401(k) Plan*.

We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances and as noted in the Summary Compensation Table above. Our board of directors may elect to adopt qualified or non-qualified benefit plans in the future if it determines that doing so is in our best interests.

#### **401(k) Plan**

We maintain a tax-qualified retirement plan that provides eligible employees, including named executive officers, with an opportunity to save for retirement on a tax advantaged basis. All participants' interests in their deferrals are 100% vested when contributed. Pre-tax and after-tax contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participant's directions. Currently, we do not make matching contributions into the plan. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Internal Revenue Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan, and all contributions, if any, are deductible by us when made.

**Table of Contents****Director Compensation**

The following table summarizes compensation paid to our non-employee directors during or with respect to the fiscal year ended December 31, 2014.

<b>Name</b>	<b>Fees Earned or Paid in Cash (\$)</b>	<b>Option Awards (\$)<sup>(1)</sup></b>	<b>All Other Compensation <sup>(2)</sup></b>	<b>Total (\$)</b>
Jean-Jacques Bienaimé	38,000	25,500 <sup>(3)</sup>		63,500
Philip M. Croxford	37,375	8,308 <sup>(4)</sup>		45,683
Douglas E. Godshall	39,250	69,242 <sup>(5)</sup>		108,492
Errol R. Halperin	46,125	45,791 <sup>(6)</sup>		91,916
J. Michael Millis, M.D.	45,500	<sup>(7)</sup>	33,500	79,000
Lowell E. Sears	50,500	69,242 <sup>(8)</sup>		119,742
Randolph C. Steer, M.D., Ph.D.	50,500	<sup>(9)</sup>		50,500

- (1) The amounts in the Option Awards column reflect the aggregate grant date fair value of stock options granted during the calendar year computed in accordance with the provisions of ASC 718. The assumptions that we used to calculate these amounts are discussed in Note 9 to our financial statements appearing at the end of this Annual Report. These amounts do not reflect the actual economic value that will be realized by the director upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options. Mr. Satter, Co-Chairman and a director of the company, has no stock options. As of December 31, 2014, Dr. Winters, our Co-Chairman and Chief Executive Officer had outstanding and unexercised option awards for 515,066 shares.
- (2) Dr. Millis was paid an aggregate of \$33,500 in consideration for services as a consultant and for services rendered as chair of our Clinical Advisory Board in fiscal 2014.
- (3) Mr. Bienaimé had a total of 75,000 stock options outstanding as of December 31, 2014. In February 2014, this option grant was re-priced, lowering the exercise price from \$10.50 to \$8.00 per share. The amount in this column reflects the incremental fair value of the option awards as of the modification date, computed in accordance with the provisions of ASC 718.
- (4) Mr. Croxford had a total of 39,191 stock options outstanding as of December 31, 2014.
- (5) Mr. Godshall had a total of 94,818 stock options outstanding as of December 31, 2014.
- (6) Mr. Halperin has a total of 39,699 stock options outstanding as of December 31, 2014.
- (7) Dr. Millis had a total of 33,834 stock options outstanding as of December 31, 2014.
- (8) Mr. Sears has a total of 94,818 stock options outstanding as of December 31, 2014.
- (9) Dr. Steer had a total of 50,175 stock options outstanding as of December 31, 2014.

Dr. Winters is not eligible to receive any board compensation because he is an employee. Mr. Satter has declined board compensation. We reimburse our directors for their reasonable expenses incurred in connection with attending board and committee meetings (other than Mr. Satter, who is not seeking reimbursement for such expenses).

**Director Compensation Policy**

In May 2013, our board of directors approved a compensation policy for our non-employee directors (other than Mr. Satter, who has elected not to receive any compensation for his service as Co-Chairman or a director) which provides for the following compensation to our non-employee directors:

each non-employee director receives an annual base retainer of \$30,000;

in addition to the \$30,000 annual base retainer, the chairman of our audit committee receives an annual fee of \$15,000 and other members of our audit committee receives an annual fee of \$7,500;

in addition to the \$30,000 annual base fee, the chairman of our other committees receives an annual fee of \$10,000 and other members of our other committees receives an annual fee of \$5,000;

in addition to the fees listed above, each director shall receive \$2,500 for each board of directors meeting in excess of four meetings per year or \$500 for each telephonic meeting.

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Pursuant to this policy, except as approved by our board of directors, each new director will receive an initial grant of 50,175 non-qualified common stock options at a strike price not less than fair market value of a share of our common stock on the date of grant with vesting monthly over forty-eight months, subject to the director's continued service with us.

**Compensation Committee Interlocks and Insider Participation**

During 2014, the members of our compensation committee were, and currently are, Messrs. Satter, Sears and Bienaimé, and Dr. Steer. None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past year has served, as a member of the compensation committee (or other board committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) or director of any entity that has one or more executive officers serving on our compensation committee or our board of directors.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.****Securities Authorized for Issuance Under Equity Compensation Plans**

The following table summarizes information about our equity compensation plans as of December 31, 2014. All outstanding option awards relate to our common stock.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Option Warrants and Rights		Weighted-average Price of Outstanding Options and Warrants and Rights		Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a))
	(a)	(b)	(c)	(d)	
Equity compensation plans approved by security holders:					
2012 Stock Option Plan	2,954,921	\$ 6.54			
2014 Equity Incentive Plan (1)	255,772	\$ 19.09			373,803
Warrants				N/A	
Equity compensation plans not approved by security holders:				N/A	
Total	3,210,693	\$ 7.54			373,803

- (1) Our 2014 Equity Incentive Plan provided for an annual increase in the number of shares available for issuance thereunder beginning upon the effectiveness of our initial public offering, and on each anniversary date thereafter,

equal to the lower of: (i) 1,200,000 shares of our common stock; (ii) 3% of the outstanding shares of our common stock on the second-to-last day prior to each anniversary date; (iii) an amount as our board of directors may determine.

**Security Ownership of Certain Beneficial Owners and Management**

The following table sets forth the beneficial ownership of our common stock as of February 2, 2015 by:

each person, or group of affiliated persons, who we know to beneficially own more than 5% of our common stock;

each of our named executive officers;

each of our directors; and

all of our executive officers and directors as a group.

The percentage ownership information shown in the table is based on an aggregate of 23,985,268 shares of our common stock outstanding as of February 2, 2015.

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We have determined beneficial ownership in accordance with the rules of the Securities and Exchange Commission. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options and warrants that are either immediately exercisable or exercisable on or before April 3, 2015, which is 60 days after February 2, 2015. These shares are deemed to be outstanding and beneficially owned by the person holding those options and warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Unless otherwise noted below, the address of each of the individuals and entities named in the table below is c/o Vital Therapies, Inc., 15010 Avenue of Science, Suite 200, San Diego, California 92128. Beneficial ownership representing less than 1% is denoted with an asterisk (\*).

	<b>Number of Shares of Common Stock Beneficially Owned</b>	<b>Percentage of Common Stock Beneficially Owned</b>
<i>5% Stockholders:</i>		
Trusts and Other Entities Affiliated with Muneer		
A. Satter <sup>(1)</sup>	6,858,926	28.60%
FMR LLC and Other Entities <sup>(2)</sup>	1,750,000	7.30%
<i>Named Executive Officers and Directors:</i>		
Terence E. Winters, Ph.D. <sup>(3)</sup>	697,629	2.85%
Duane Nash, M.D., J.D. <sup>(4)</sup>	367,715	1.51%
John M. Dunn, J.D. <sup>(5)</sup>	6,246	*
Muneer A. Satter <sup>(1)</sup>	6,858,926	28.60%
Jean-Jacques Bienaimé <sup>(6)</sup>	100,119	*
Douglas E. Godshall <sup>(7)</sup>	164,193	*
Philip M. Croxford <sup>(8)</sup>	64,282	*
J. Michael Millis, M.D. <sup>(9)</sup>	51,514	*
Randolph C. Steer, M.D., Ph.D. <sup>(10)</sup>	51,862	*
Errol R. Halperin <sup>(11)</sup>	139,116	*
Lowell E. Sears <sup>(12)</sup>	153,390	*
All directors and executive officers as a group		
(17 people) <sup>(13)</sup>	9,409,868	36.13%

- (1) Consists of 6,732,277 shares and warrants to acquire 126,649 shares that are held by the Muneer A. Satter Revocable Trust and various other trusts and other entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over all such shares.

(2)

The address of FMR LLC, or FMR, is 245 Summer Street, Boston, Massachusetts 02210. FMR, along with certain of its subsidiaries and affiliates, and other companies, has the sole power to dispose or direct the disposition of 1,750,000 shares of common stock. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR, representing 49% of the voting power of FMR. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR. Neither FMR nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ( Fidelity Funds ) advised by Fidelity Management & Research Company ( Fidelity Co ), a wholly-owned subsidiary of FMR, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. This information is based solely upon a Schedule 13G filed by FMR on February 13, 2015 for beneficial ownership as of December 31, 2014.

- (3) Consists of 59,878 shares held by Terence E. Winters, 122,258 shares held by Terence E. Winters and Eileen Y. Winters, 427 shares that may be acquired pursuant to the exercise of warrants held of record by Terence E. Winters, and options to purchase 515,066 shares of common stock.
- (4) Consists of 9,324 shares held and options to purchase 358,391 shares of common stock.
- (5) Consists of options to purchase shares of common stock.

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- (6) Consists of 25,119 shares held and options to purchase 75,000 shares of common stock.
- (7) Consists of 69,375 shares held and options to purchase 94,818 shares of common stock.
- (8) Consists of 25,091 shares held and options to purchase 39,191 shares of common stock.
- (9) Consists of 17,680 shares held and options to purchase 33,834 shares of common stock.
- (10) Consists of 1,550 shares held, 137 shares that may be acquired pursuant to the exercise of warrants, and options to purchase 50,175 shares of common stock.
- (11) Consists of 40,000 shares held by Errol R. Halperin, 49,417 shares held by Errol R. Halperin and Libby G. Halperin, 10,000 shares held by Errol Halperin IRA FBO Errol Halperin, and options to purchase 39,699 shares of common stock.
- (12) Consists of 58,572 shares held and options to purchase 94,818 shares of common stock.
- (13) Consists of 7,226,921 shares held or beneficially owned, 127,268 shares that may be acquired pursuant to the exercise of warrants, and options to purchase 2,055,679 shares of common stock that are or will be vested and fully exercisable within 60 days of February 2, 2015.

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

The following is a summary of transactions since January 1, 2014 to which we have been a party in which the amount involved exceeded \$120,000 and in which any of our executive officers, directors, promoters or beneficial holders of more than 5% of our capital stock had or will have a direct or indirect material interest, other than compensation arrangements which are described under the section of this Annual Report titled Executive Compensation.

**Follow-On Public Offering**

In connection with our follow-on public offering, which was completed in October 2014, we entered into a directed share letter with the underwriters pursuant to which, at the public offering price, our directors and executive officers, and their affiliated entities, could indicate an interest in purchasing shares of our common stock offered thereby. The sale of these shares was made on the same terms and conditions as the sale of shares to the public. The following table presents the number of shares of common stock issued to our directors and officers, and their affiliated entities, at the follow-on offering:

<b>Purchaser</b>	<b>Shares of Common Stock</b>
Trusts and Other Entities Affiliated with Muneer A. Satter <sup>(1)</sup>	74,286
Errol R. Halperin <sup>(2)</sup>	5,476
Douglas E. Godshall	2,857
Lowell E. Sears	1,429
Jean-Jacques Bienaimé	4,286
Duane Nash	100

- (1) Includes shares held by the Muneer A. Satter Revocable Trust and various other trusts and entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over such shares.
- (2) Consists of (i) 1,667 shares held by Errol Halperin IRA FBO Errol Halperin and (ii) 3,809 shares held by Errol R. Halperin and Libby G. Halperin.

**Directed Share Program**



In connection with our IPO, which was completed in April 2014, the underwriters of our IPO reserved for sale, at the initial public offering price, up to \$20.0 million in shares of our common stock offered thereby for our directors, employees, existing investors and their affiliated entities, business associates and related persons who expressed an interest in purchasing shares of common stock in our IPO. The sale of these shares was made through a directed share program, or DSP. The participants in the DSP included certain of our directors and officers, and their affiliated entities. The following table presents the number of shares of common stock issued to our directors and officers, and their affiliated entities, through the DSP:

<b>Purchaser</b>	<b>Shares of Common Stock</b>
Trusts and Other Entities Affiliated with Muneer A. Satter <sup>(1)</sup>	360,966
Errol R. Halperin <sup>(2)</sup>	14,524
Douglas E. Godshall	12,500
Lowell E. Sears	12,500
Jean-Jacques Bienaimé	8,333
Philip M. Croxford	1,500
Aron Stern	83

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- (1) Includes shares held by the Muneer A. Satter Revocable Trust and various other trusts and entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over such shares.
- (2) Consists of (i) 8,333 shares held by Errol Halperin IRA FBO Errol Halperin and (ii) 6,191 shares held by Errol R. Halperin and Libby G. Halperin.

**Senior Preferred Stock Financing**

The participants in our senior preferred financing included the Muneer A. Satter Revocable Trust and certain affiliated trusts and other entities, or the Satter Investors, certain of our directors and officers and certain unaffiliated third-party investors, all of which are collectively referred to herein as the Investors. Muneer A. Satter is a member of our board of directors and is the trustee of the Muneer A. Satter Revocable Trust and the trustee, investment advisor or manager of each other Satter Investor. In his capacity as trustee, investment advisor or manager as applicable, Mr. Satter has sole voting and dispositive power over all shares held by the Satter Investors. Between January 2014 and February 2014, we raised an aggregate of \$18.2 million in private placements through the issuance and sale of 2,296,016 shares of senior redeemable convertible preferred stock, or senior preferred stock, at a price of \$8.00 per share to investors including under a Senior Preferred Stock Purchase Agreement, as amended, or the Senior Preferred Purchase Agreement. Upon the closing of our initial public offering, all rights and obligations under the Senior Preferred Purchase Agreement with respect to the issuance and sale of additional shares of our senior preferred stock terminated automatically and were of no further force or effect.

The following table presents the number of shares of senior preferred stock issued to our directors, officers and holders of more than 5% of our capital stock or entities affiliated with them pursuant to the Senior Preferred Purchase Agreement in 2014. Such shares of senior preferred stock converted to common stock in conjunction with our initial public offering in April 2014.

<b>Purchaser</b>	<b>Shares of Senior Preferred Stock</b>	<b>Aggregate Purchase Price</b>
Trusts and Other Entities Affiliated with Muneer A. Satter <sup>(1)</sup>	555,000	\$ 4,440,000
Douglas E. Godshall <sup>(2)</sup>	9,375	75,000

- (1) Includes shares held by the Muneer A. Satter Revocable Trust and various other trusts and other entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive control over such shares.
- (2) Shares acquired by Douglas E. Godshall in connection with his exercise of preemptive rights under the terms of the Fourth Amended and Restated Investor Rights Agreement, dated August 28, 2013.

The Senior Preferred Purchase Agreement provided to certain of the Investors (including the Satter Investors) certain rights relating to the delivery of certain financial statements and other information. In addition, the Senior Preferred Purchase Agreement restricted the issuance of stock options or any comparable equity or equity-based incentives to any person who was a director, officer or other member of senior management as of September 25, 2012 unless such person shall have received a material promotion and commensurate increase in duties and responsibilities. While the information rights described above are suspended for so long as we are subject to and remain in compliance with the

periodic reporting requirements of the Securities and Exchange Commission, or SEC, the restrictions on future equity awards described in this paragraph, as well as certain other covenants and agreements contained in the Senior Preferred Purchase Agreement, survived completion of our initial public offering and remain in full force and effect in accordance with their terms.

### **Senior Preferred Investors Rights Agreement**

We and certain of our directors, executive officers and stockholders, including the Satter Investors, are parties to the Senior Preferred IRA. The Senior Preferred IRA contains customary preemptive rights in favor of our stockholders party thereto, as well as customary registration rights and related provisions, including customary market standoff provisions. All preemptive rights in favor of our stockholders under the Senior Preferred IRA terminated upon the closing of our initial public offering.

The Senior Preferred IRA also provides that, for so long as the Satter Investors hold at least 30% of our outstanding common stock, the Satter Investors have the right to nominate 40% of our directors (rounded up to the nearest whole number). If the Satter Investors hold less than 30% (but at least 20%) of our outstanding common stock, they have the right to nominate 30% of our directors (rounded up to the nearest whole number). If the Satter Investors hold less than 20% (but at least 10%) of our outstanding common stock, they have the right to nominate 20% of our directors (rounded up to the nearest whole number). If the Satter Investors hold less than 10% (but at least 2%) of our outstanding common stock, they have the right to nominate 10% of our directors (rounded up to the nearest whole number). For so long as the Satter Investors hold less than 2% of our outstanding common stock, they do not have the contractual right to nominate any representatives to our board of directors. To date the Satter Investors have not exercised their rights to nominate any directors, but they have reserved the right to do so in the future.

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The Senior Preferred IRA provides that for so long as Mr. Satter and Dr. Winters both serve as members of our board of directors, each shall serve as co-chairman of our board of directors and Mr. Satter shall serve as our Lead Director. In the event that Mr. Satter serves as a member of our board of directors at a time when Dr. Winters does not, Mr. Satter will serve as our chairman of the board and Lead Director. Dr. Winters will serve as Co-Chairman only so long as he is both a director and our Chief Executive Officer.

## **Series D Investors Rights Agreement**

We and certain of our directors, executive officers and stockholders, including the Satter Investors, are or were parties to an investors rights agreement, dated June 7, 2011, or the Series D IRA. The Series D IRA contains restrictions on transfer (for compliance with applicable securities laws) and customary registration rights. Upon the closing of our initial public offering in April 2014, all covenants in this agreement, except for the rights relating to the registration of shares under the Securities Act, terminated. The rights of any of our directors, officers or stockholders under the Series D IRA, who became parties to the Senior Preferred IRA, were superseded by the Senior Preferred IRA.

## **Indemnification of Officers and Directors**

We have also entered into indemnification agreements with each of our directors, executive officers and certain controlling persons. The indemnification agreements and our amended and restated certificate of incorporation and amended and restated bylaws require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law.

## **Related-Person Transactions Policy**

We adopted a written Related Person Transactions Policy that sets forth our policies and procedures regarding the identification, review, consideration, approval and oversight of related person transactions. For purposes of our policy only, a related-person transaction is a past, present or future transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any related person are participants, the amount involved exceeds \$120,000 and a related person has a direct or indirect material interest. Various transactions are not covered by this policy, including transactions involving compensation for services provided to us as an employee, director, consultant or similar capacity by a related person, equity and debt financing transactions with a related person that are approved by the Board, and other transactions not otherwise required to be disclosed under Item 404 of Regulation S-K. A related person, as determined since the beginning of our last fiscal year, is any executive officer, director or nominee to become director, a holder of more than 5% of our common stock, including any immediate family members of such persons. Any related-person transaction may only be consummated if approved or ratified by the affirmative vote of seventy-five percent (75%) of our dis-interested directors then in office in accordance with the policy guidelines set forth below.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee for review and recommendation for approval to our board of directors. In considering related-person transactions, our audit committee and board of directors take into account the relevant available facts and circumstances including, but not limited to whether the terms of such transaction are no less favorable than terms generally available to an unaffiliated third-party under the same or similar circumstances and the extent of the related persons interest in the transaction. In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval process.

## **Director Independence**

As a company listed on The NASDAQ Global Market we are required under the listing rules of the NASDAQ Stock Market, LLC, or NASDAQ, to maintain a board comprised of a majority of independent directors as determined affirmatively by our board. In addition, the rules of NASDAQ require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees must be independent. Audit committee members and compensation members must also satisfy separate independence criteria set forth in the NASDAQ rules and in Rule 10A-3 and Rule 10C-1, respectively, under the Securities Exchange Act of 1934, as amended. Under the rules of NASDAQ, a director will only qualify as an independent director if, among other things, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered independent for purposes of Rule 10A-3 and under the rules of NASDAQ, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, our board of directors, or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

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To be considered independent for purposes of Rule 10C-1 and under the rules of NASDAQ, the board of directors must affirmatively determine that the member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director; and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors determined that a majority of our directors during 2014 were independent directors as defined under applicable NASDAQ rules, including Drs. Millis and Steer and Messrs. Croxford, Godshall, Halperin, Satter, Bienaimé and Sears. In March 2014, our board of directors undertook another review of the independence of our directors and considered whether any director has a material relationship with us that could compromise his ability to exercise independent judgment in carrying out his responsibilities. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that none of Drs. Millis and Steer and Messrs. Croxford, Godshall, Halperin, Satter, Bienaimé and Sears, representing eight of our nine directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is an independent director as that term is defined under the rules of NASDAQ. Dr. Winters is not considered an independent director because of his position as our chief executive officer.

In making these determinations, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances our board of directors deemed relevant in determining their independence, including consulting relationships, family relationships and the beneficial ownership of our capital stock by each non-employee director.

*Audit Committee.* The members of our audit committee are Messrs. Godshall, Halperin and Sears. Mr. Sears serves as the chairman. Our board of directors has determined that each of the members of our audit committee is independent under Rule 10A-3 of the Exchange Act and the current rules of NASDAQ and financially literate under the rules of the SEC and NASDAQ, and that Mr. Sears qualifies as an audit committee financial expert within the meaning of the rules and regulations of the SEC.

*Compensation Committee.* The members of our compensation committee are Messrs. Bienaimé, Satter and Sears and Dr. Steer. Dr. Steer is the chairman of our compensation committee. Our board of directors has determined that each member of our compensation committee is independent under Rule 10C-1 of the Exchange Act and the current rules of NASDAQ.

*Nominating and Governance Committee.* The members of our nominating and governance committee are Messrs. Halperin and Satter and Dr. Millis. Mr. Halperin serves as the chairman. Our board of directors has determined that each member of our nominating and governance committee is independent under the current rules of NASDAQ.

**Item 14. Principal Accounting Fees and Services.**

The audit committee of our board of directors selected PricewaterhouseCoopers LLP to be our independent registered public accounting firm for the year ended December 31, 2014.

The following table represents aggregate fees billed to us for the fiscal years ended December 31, 2014 and 2013 by PricewaterhouseCoopers LLP, our principal accountant. All fees below were pre-approved by the Audit Committee:

	<b>Fiscal Year Ended</b>	
	<b>2014</b>	<b>2013</b>
Audit Fees <sup>(1)</sup>	\$ 853,113	\$ 1,436,640
Audit-related Fees <sup>(2)</sup>		
Tax Fees <sup>(3)</sup>		
All Other Fees <sup>(4)</sup>	1,800	1,800
<b>Total Fees</b>	<b>\$ 856,927</b>	<b>\$ 1,438,440</b>

- (1) Audit fees consist of fees billed for professional services by PricewaterhouseCoopers LLP for audit and quarterly reviews of our financial statements, reviews of our registration statements on Form S-1 and related services that are normally provided in connection with statutory and regulatory filings or engagements.
- (2) We did not engage PricewaterhouseCoopers LLP to perform audit-related services.
- (3) Represents fees for tax advisory services.
- (4) Represents annual licensing fees for an accounting database subscription.

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In connection with the audit of the 2014 financial statements, we entered into an engagement agreement with PricewaterhouseCoopers LLP that sets forth the terms by which PricewaterhouseCoopers LLP will perform audit services for us. Such engagement was approved in advance by our audit committee.

### **Pre-Approval Policy**

Our audit committee's policy is to pre-approve all audit and permissible non-audit services provided by the independent accountants. These services may include audit services, audit-related services, tax services and other services. Our audit committee generally pre-approves particular services or categories of services on a case-by-case basis. The independent registered public accounting firm and management are required to periodically report to our audit committee regarding the extent of services provided by the independent registered public accounting firm in accordance with these pre-approvals, and the fees for the services performed to date.

All of the services of PricewaterhouseCoopers LLP for 2014 and 2013 described above were pre-approved by our audit committee.



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**PART IV**

**Item 15. Exhibits, Financial Statement Schedules.**

1. *Financial Statements.* We have filed the following documents as part of this Annual Report:

	<b>Page</b>
Report of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations	F-4
Consolidated Statements of Comprehensive Loss	F-5
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)	F-6
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2. *Financial Statement Schedules.* None.

3. *Exhibits.* The following exhibits are filed herewith or are incorporated by reference to exhibits previously filed with the U.S. Securities and Exchange Commission.

**Table of Contents****EXHIBITS**

<b>Exhibit Number</b>	<b>Exhibit Title</b>	<b>Incorporated by Reference</b>			
		<b>Form</b>	<b>File No.</b>	<b>Exhibit</b>	<b>Filing Date</b>
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	S-1/A	333-191711	3.2	November 6, 2013
3.2	Second Amended and Restated Bylaws of the Registrant.	S-1/A	333-191711	3.4	November 6, 2013
4.1	Specimen Common Stock Certificate of the Registrant.	S-1/A	333-191711	4.1	November 6, 2013
4.2	Fourth Amended and Restated Investors Rights Agreement, dated August 28, 2013.	S-1	333-191711	4.2	October 11, 2013
4.3	Investors Rights Agreement, dated February 23, 2012.	S-1	333-191711	4.3	October 11, 2013
4.4	Amended and Restated Investors Rights Agreement, dated June 7, 2011.	S-1	333-191711	4.4	October 11, 2013
10.1+	Form of Indemnification Agreement between the Registrant and its directors and officers.	S-1/A	333-191711	10.1	November 6, 2013
10.2+	Employment Letter Agreement between the Registrant and Duane Nash, dated October 30, 2013.	S-1/A	333-191711	10.2	November 6, 2013
10.3+	Employment Letter Agreement between the Registrant and Robert A. Ashley, dated October 30, 2013.	S-1/A	333-191711	10.3	November 6, 2013
10.4+	Employment Letter Agreement between the Registrant and Terence E. Winters, dated October 31, 2013.	S-1/A	333-191711	10.4	November 6, 2013
10.5+	Employment Letter Agreement between the Registrant and Michael V. Swanson, dated August 30, 2013.	S-1/A	333-191711	10.5	November 6, 2013
10.6+	Employment Letter Agreement between the Registrant and Andrew Henry, dated October 30, 2013.	S-1/A	333-191711	10.6	April 3, 2014
10.7+	Employment Letter Agreement between the Registrant and Aron P. Stern, dated October 30, 2013.	S-1/A	333-191711	10.7	March 11, 2014
10.8+	Employment Letter Agreement between the Registrant and Andrea Loewen, dated October 30, 2013.	S-1/A	333-191711	10.8	April 3, 2014

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10.9+	Employment Letter Agreement between the Registrant and Richard Murawski, dated October 30, 2013.	S-1/A	333-191711	10.9	March 11, 2014
10.10+*	Employment Letter Agreement between the Registrant and John Dunn, dated March 5, 2015.				
10.11+	2012 Stock Option Plan and form of agreements.	S-1	333-191711	10.6	October 11, 2013
10.12+	2014 Equity Incentive Plan and form of agreements.	S-1/A	333-191711	10.11	March 11, 2014
10.13+*	Global Stock Option Agreement under 2014 Equity Incentive Plan.				
10.14+	Executive Incentive Compensation Plan.	S-1	333-191711	10.8	October 11, 2013
10.15+	Form Change of Control and Severance Agreement.	S-1	333-191711	10.9	October 11, 2013
10.16+	Non-Employee Director Compensation Policy.	S-1/A	333-191711	10.10	November 15, 2013
10.17	Standard Industrial/Commercial Multi-Tenant Lease and Addendum between DermTech International and R.E. Hazard Contracting Company, dated April 5, 2001, as amended.	S-1	333-191711	10.11	October 11, 2013
10.18	Standard Office Lease between Arden Realty Limited Partnership and the Registrant, dated May 7, 2013.	S-1	333-191711	10.12	October 11, 2013
21.1*	List of subsidiaries of the Registrant.				
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.				

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24.1*	Power of Attorney (included on the signature page).
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	XBRL Instance Document.
101.SCH*	XBRL Taxonomy Extension Schema Document.
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Database.
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.

+ Indicates a management contract or compensatory plan or arrangement.

\* Filed herewith.

\*\* In accordance with Item 601(b)(32)(ii) of Regulation S-K and SEC Release No. 33-8238 and 34-47986, Final Rule: Management's Reports on Internal Control Over Financial Reporting and Certification of Disclosure in Exchange Act Periodic Reports, the certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-K and will not be deemed filed for purposes of Section 18 of the Exchange Act. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act or the Exchange Act, except to the extent that the registrant specifically incorporates it by reference.

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**VITAL THERAPIES, INC.**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of

Vital Therapies, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Vital Therapies, Inc. and its subsidiaries at December 31, 2014 and 2013, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Diego, California

March 19, 2015

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**Table of Contents****VITAL THERAPIES, INC.****Consolidated Balance Sheets****(In thousands, except share and per share amounts)**

	<b>December 31,</b>	
	<b>2014</b>	<b>2013</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 102,238	\$ 38,186
Restricted cash	1,592	963
Deferred financing costs		3,506
Other current assets and prepaid expenses	986	1,200
Total current assets	104,816	43,855
Property and equipment, net	3,068	2,467
Other assets	198	263
Total assets	\$ 108,082	\$ 46,585
<b>Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)</b>		
Current liabilities:		
Accounts payable	\$ 1,153	\$ 1,224
Accrued expenses	8,875	3,253
Future purchase rights liabilities		2,600
Other current liabilities	250	369
Total current liabilities	10,278	7,446
Other long-term liabilities	241	321
<b>Commitments and contingencies</b>		
Convertible preferred stock (Junior); \$0.0001 par value, no and 3,501,401 shares designated at December 31, 2014 and 2013, respectively; 3,501,400 shares issued and outstanding at December 31, 2013		1,359
Redeemable convertible preferred stock (Senior); \$0.0001 par value, no and 17,000,000 shares designated at December 31, 2014 and 2013, respectively; 10,212,007 shares issued and outstanding at December 31, 2013		82,116
<b>Stockholders' equity (deficit):</b>		
Preferred stock, \$0.0001 par value; 20,000,000 and 25,000,000 (4,498,599 undesignated) authorized at December 31, 2014 and 2013, respectively; no shares issued and outstanding at December 31, 2014 and 2013		
Common stock, \$0.0001 par value; 130,000,000 and 29,250,000 shares authorized at December 31, 2014 and 2013, respectively; 23,982,786 and 606,238 shares issued and	2	

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outstanding at December 31, 2014 and 2013, respectively

Additional paid-in capital	248,305	58,413
Accumulated other comprehensive income	89	96
Accumulated deficit	(150,833)	(103,166)
Total stockholders' equity (deficit)	97,563	(44,657)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	\$ 108,082	\$ 46,585

The accompanying notes are an integral part of these financial statements.

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**Table of Contents****VITAL THERAPIES, INC.****Consolidated Statements of Operations****(In thousands, except share and per share amounts)**

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Operating expenses:			
Research and development	\$ 39,479	\$ 21,787	\$ 5,097
General and administrative	10,863	9,615	4,483
Total operating expenses	50,342	31,402	9,580
Loss from operations	(50,342)	(31,402)	(9,580)
Other income (expense):			
Interest income	19	5	4
Interest expense			(413)
Other income (expense), net	56	(15)	7
Revaluation of preferred stock warrant liabilities			180
Revaluation of future purchase rights liabilities	2,600	(1,306)	3,101
Total other income (expense)	2,675	(1,316)	2,879
Net loss	(47,667)	(32,718)	(6,701)
Amortization of deemed dividend	(4,744)	(64)	
Accretion to redemption value of redeemable convertible preferred stock	(4,410)	(6,303)	(942)
Net loss attributable to common stockholders	\$ (56,821)	\$ (39,085)	\$ (7,643)
Net loss per share attributable to common stockholders, basic and diluted	\$ (3.54)	\$ (74.86)	\$ (17.89)
Weighted-average common shares outstanding, basic and diluted	16,054,452	522,102	427,117

The accompanying notes are an integral part of these financial statements.

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**VITAL THERAPIES, INC.**

**Consolidated Statements of Comprehensive Loss**

**(In thousands)**

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Net loss	\$ (47,667)	\$ (32,718)	\$ (6,701)
Other comprehensive (loss) income:			
Foreign currency translation	(7)	8	5
Total comprehensive loss	\$ (47,674)	\$ (32,710)	\$ (6,696)

The accompanying notes are an integral part of these financial statements.

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Table of Contents**VITAL THERAPIES, INC.****Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)**

(In thousands, except shares)

	Series A-D, Junior Convertible, and Senior Redeemable Convertible Preferred Stock		Common Stock		Accumulated Additional Other Paid- <del>in</del> Comprehensive Income		Total Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Capital			
<b>Balance at January 1, 2012</b>	90,267	\$ 54,658	9,097	\$	\$ 8,811	\$ 83	\$ (63,747)	\$ (54,853)
Net loss							(6,701)	(6,701)
Other comprehensive income						5		5
Stock-based compensation					144			144
Conversion of Series A-D preferred stock to common stock	(90,267)	(54,715)	458,070		54,715			54,715
Private placement of junior convertible preferred stock from February to March 2012	3,501,400	1,326						
Private placement senior redeemable convertible preferred stock from September to October 2012 and conversion of loans	3,518,199	23,965						
Accretion to redemption value of redeemable convertible preferred stock		942			(942)			(942)
<b>Balance at December 31, 2012</b>	7,019,599	26,176	467,167		62,728	88	(70,448)	(7,632)
Net loss							(32,718)	(32,718)
Other comprehensive income						8		8
Exercise of stock options, net of repurchase liability			139,071		135			135
Stock-based compensation					948			948
Private placement senior redeemable convertible preferred stock from February to December 2013	6,693,808	50,996			905			905
Accretion to redemption value of redeemable convertible preferred stock		6,303			(6,303)			(6,303)

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<b>Balance at December 31, 2013</b>	13,713,407	83,475	606,238		58,413	96	(103,166)	(44,657)
Net loss							(47,667)	(47,667)
Other comprehensive loss						(7)		(7)
Exercise of stock options and release of stock option early exercise repurchase liability			142,041		956			956
Stock-based compensation					2,510			2,510
Private placement senior redeemable convertible preferred stock from January to March 2014	2,296,016	18,167						
Amortization of deemed dividend		4,744			(4,744)			(4,744)
Accretion to redemption value of redeemable convertible preferred stock		4,410			(4,410)			(4,410)
Initial public offering, net of issuance costs			5,175,000	1	51,932			51,933
Conversion of redeemable convertible preferred stock to common stock	(16,009,423)	(110,796)	16,009,423	1	110,795			110,796
Adjustment for fractional shares			84					
Issuance of common stock, net of issuance costs			2,050,000		32,853			32,853
<b>Balance at December 31, 2014</b>	\$		23,982,786	\$ 2	\$ 248,305	\$ 89	\$ (150,833)	\$ 97,563

The accompanying notes are an integral part of these financial statements.

**Table of Contents****VITAL THERAPIES, INC.****Consolidated Statement of Cash Flows****(In thousands)**

	<b>Year Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
<b>Cash flows from operating activities:</b>			
Net loss	\$ (47,667)	\$ (32,718)	\$ (6,701)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,087	799	651
Stock-based compensation	2,510	948	144
Non-cash interest expense			382
Revaluation of preferred stock warrant liabilities			(180)
Revaluation of future purchase rights liabilities	(2,600)	1,306	(3,101)
Gain on sale of equipment			(7)
Other	21	(17)	41
Changes in operating assets and liabilities:			
Other assets and prepaid expenses	279	(1,141)	(242)
Accounts payable	46	(91)	(219)
Accrued expenses	5,499	2,266	(12)
Net cash used in operating activities	(40,825)	(28,648)	(9,244)
<b>Cash flows from investing activities:</b>			
Purchases of short-term investments		(2,999)	(13,992)
Sales of short-term investments		17,000	
Proceeds from sale of equipment			20
Increase in restricted cash	(631)	(608)	(355)
Purchases of property and equipment	(1,409)	(1,484)	(261)
Net cash (used in) provided by investing activities	(2,040)	11,909	(14,588)
<b>Cash flows from financing activities:</b>			
Proceeds from debt, net of issuance costs			6,934
Deferred financing costs		(3,112)	
Principal payments on term loan			(533)
Proceeds from issuance of common stock, net of issuance costs	87,899		
Proceeds from issuance of preferred stock, net of issuance costs	18,167	53,195	21,100
Proceeds from exercise of stock options	852	135	
Proceeds from early exercise of stock options		227	
Net cash provided by financing activities	106,918	50,445	27,501
Effect of exchange rate changes on cash and cash equivalents	(1)	3	5

Net change in cash and cash equivalents	64,052	33,709	3,674
Cash and cash equivalents, beginning of period	38,186	4,477	803
Cash and cash equivalents, end of period	\$ 102,238	\$ 38,186	\$ 4,477

**Supplemental cash flow information:**

Cash paid for interest	\$	\$	\$ 32
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**Supplemental disclosure of non-cash investing and financing activities:**

Deferred offering costs included in liabilities	\$	\$ 394	\$
Purchase of property and equipment included in liabilities	\$ 277	\$ 170	\$ 502
Leasehold improvements paid for by landlord	\$	\$ 478	\$
Release of stock option early exercise repurchase liability	\$ 104	\$	\$
Conversion of debt for redeemable convertible preferred stock	\$	\$	\$ 7,296
Conversion of redeemable convertible preferred stock to common stock	\$ 110,796	\$	\$ 54,715
Valuation of future purchase rights upon issuance	\$	\$ 1,294	\$ 3,101
Beneficial conversion underlying the senior preferred stock	\$	\$ 969	\$
Accretion to redemption value of redeemable convertible preferred stock	\$ 4,410	\$ 6,303	\$ 942
Amortization of deemed dividend	\$ 4,744	\$	\$

The accompanying notes are an integral part of these financial statements.

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**VITAL THERAPIES, INC.**

**Notes to Consolidated Financial Statements**

**1. Description of Business and Basis of Financial Statements**

***Description of Business***

We are a biotherapeutic company focused on developing a cell-based therapy targeting the treatment of all forms of acute liver failure. Our product candidate, currently in Phase 3 clinical trials, the ELAD<sup>®</sup> System or ELAD, is an extracorporeal human cell-based bio-artificial liver therapy designed to allow the patient's own liver to regenerate to a healthy state, or to stabilize the patient until transplant. Since inception, we have devoted essentially all of our efforts to product development, clinical testing and pilot manufacturing and have not realized revenues from our planned principal operations. Our business, operating results, financial condition, and growth prospects are subject to significant risks and uncertainties, including failing to obtain regulatory approval to commercialize and failing to secure additional funding to complete development of and to commercialize our product candidate.

We began operations as a California corporation on May 23, 2003 through the acquisition of the assets and business of VitaGen, Inc. and in June 2003 changed our name to Vital Therapies, Inc. In January 2004, we were re-incorporated in Delaware. Our headquarters are located in San Diego, California.

***Basis of Presentation and Consolidation***

The accompanying consolidated financial statements have been prepared in conformity with United States generally accepted accounting principles, or GAAP, and include the accounts of Vital Therapies, Inc. and its wholly-owned subsidiaries located in the United Kingdom (currently inactive) and China. All intercompany accounts and transactions have been eliminated in consolidation. We manage our operations as a single segment for the purposes of assessing performance and making operating decisions.

We previously were classified as a development stage entity under GAAP and, as such, were required to present inception-to-date information in our statements of operations, comprehensive loss, stockholders' equity, and cash flows. In June 2014, the Financial Accounting Standards Board, or FASB, issued an accounting standards update that eliminates the concept of a development stage entity from GAAP and removes the related incremental reporting requirements, which we elected to early adopt. See Note 2 for additional information on this standard.

**2. Summary of Significant Accounting Policies**

***Use of Estimates***

The preparation of financial statements in conformity with GAAP requires us to make certain estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ materially from those estimates and assumptions.

***Cash and Cash Equivalents***

Cash and cash equivalents consist of cash and highly-liquid investments with original maturities of three months or less when acquired and are stated at cost, which approximates market value.

***Restricted Cash***

Restricted cash relates to amounts reserved for various clinical trial obligations and lease arrangements at December 31, 2014 and 2013, respectively, as well as for certain provisions of the junior preferred stock agreement at December 31, 2013.

***Fair Value of Financial Instruments***

Fair value is defined as the price that would be received to sell an asset or be paid to transfer a liability in an orderly transaction between market participants on the measurement date. Accounting guidance establishes a fair value hierarchy that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1 Quoted prices in active markets for identical assets or liabilities. Our Level 1 assets consisted of U.S. treasuries and money market funds for the periods presented. We had no Level 1 liabilities for any period presented.



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Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets with insufficient volume or infrequent transactions (less active markets), or model-derived valuations in which all significant inputs are observable or can be derived principally from or corroborated with observable market data for substantially the full term of the assets or liabilities. We had no Level 2 assets or liabilities for any period presented.

Level 3 Unobservable inputs to the valuation methodology that are significant to the measurement of the fair value of assets or liabilities. Our Level 3 liabilities included preferred stock warrants and future purchase rights liabilities during the periods presented. We had no Level 3 assets in any period presented. We estimated the fair value of the preferred stock warrants and the future purchase rights using a binomial lattice model depending on the underlying attributes of the preferred stock warrants or future purchase rights, as applicable. Upon the completion of our initial public offering, or IPO, in April 2014, the future purchase rights liabilities terminated. See Future Purchase Rights Liabilities below.

The carrying value of cash and cash equivalents, restricted cash, other current assets and prepaid expenses, accounts payable, and accrued expenses approximate fair value due to the short period of time to maturity.

The future purchase rights were recorded at their estimated fair value at the date of issuance. The binomial lattice model used in the determination of the estimated fair value of the future purchase rights was based on various assumptions, including the estimated fair value of our senior preferred and common stock. We recorded subsequent adjustments to reflect the increase or decrease in estimated fair value at each reporting date as a gain or loss.

***Deferred Financing Costs***

Deferred financing costs represent direct costs associated with the issuance of our corporate securities. Direct costs include, but are not limited to, the legal, accounting and printing costs. Indirect costs associated with the issuance of corporate securities are expensed as incurred. Deferred financing costs as of December 31, 2013 were offset against the proceeds from our IPO in April 2014.

***Property and Equipment, Depreciation and Amortization***

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally three to five years). Leasehold improvements are stated at cost and amortized on a straight-line basis over the lesser of the remaining term of the related lease or the estimated useful lives of the assets. Construction in progress is not depreciated until the underlying asset is placed in service. Repairs and maintenance costs are charged to expense as incurred.

***Impairment of Long-lived Assets***

Long-lived assets consist primarily of property and equipment. We review long-lived assets when events and circumstances indicate that the carrying amount of an asset may not be recoverable. If an asset is considered to be impaired, the impairment recognized is the amount by which the carrying value of the asset exceeds its fair value.

***Redeemable Convertible Preferred Stock***

Our junior convertible and senior redeemable convertible preferred stock were classified as mezzanine in accordance with authoritative guidance for the classification and measurement of potentially redeemable securities, as the preferred stock was conditionally redeemable at the holder's option or upon certain change in control events that are

outside our control, including liquidation, sale, or transfer of control of the company. In conjunction with our IPO in April 2014, all shares of our junior convertible and senior redeemable convertible preferred stock were converted to common stock.

***Warrants to Purchase Redeemable Convertible Preferred Stock***

We classify our preferred stock warrants that are either puttable or that are redeemable as liabilities on the consolidated balance sheets at fair value. At the end of each reporting period, changes in fair value during the period are recorded as a component of other income (expense), net. In February 2012, a final valuation adjustment was recognized for these preferred stock warrants prior to their conversion to common stock warrants in conjunction with a junior preferred stock offering.

***Future Purchase Rights Liabilities***

The future purchase rights liabilities were recorded at their estimated fair value on the date of issuance as a discount on the underlying preferred stock and are re-measured to reflect changes in the estimated fair value at each reporting date, with any decrease or increase in the estimated fair value being recorded as other income or expense, respectively. The fair value of these liabilities was estimated using a binomial lattice model based on the characteristics of the common and preferred stock on the valuation date, probabilities related to our operations and clinical development, as well as assumptions for volatility, remaining expected life, risk-free interest rate and, in some cases, credit spread. Changes in the fair value of the future purchase rights fluctuated in conjunction with increases or decreases in the implied fair value of our common stock, and the number of preferred and common shares and future purchase rights outstanding relative to our enterprise value at each reporting date. In April 2014, the remaining future purchase rights terminated upon the conversion of all senior preferred stock to common stock in conjunction with our IPO and the remaining balance of the future purchase rights liabilities was recorded as other income in our consolidated statement of operations for the period.

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***Research and Development***

Research and development costs consist primarily of employee-related expenses, costs incurred for clinical trial sites, contractors and contract research organizations engaged in the development of the ELAD System, expenses associated with obtaining regulatory approvals, and the cost of acquiring and manufacturing clinical trial materials. All research and development costs are expensed as incurred.

***Stock-based Compensation***

We measure and recognize compensation expense for all stock-based payments made to employees and directors based on estimated fair value, net of an estimated forfeiture rate, and to consultants based on estimated fair value. Currently, our stock-based awards consist only of stock options; however, future grants under our equity compensation plans may consist of shares of restricted stock and restricted stock units. We estimate the fair value of stock options granted using the Black-Scholes-Merton, or BSM, option pricing model, which requires the use of estimates to value employee stock-based compensation at the date of grant.

We recognize stock-based compensation cost for employees and directors on a straight-line basis over the requisite service period of the award. Stock-based compensation expense is recognized only for those awards that are ultimately expected to vest. We estimate forfeitures based on an analysis of our historical employee turnover and will continue to evaluate the appropriateness of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover and other factors. We will revise the forfeiture estimate, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Changes in forfeiture estimates, which have not been material to date, impact compensation cost in the period in which the change in estimate occurs.

The fair value of options granted to consultants is estimated using the BSM option pricing model and is re-measured at each reporting date with changes in fair value recognized as expense in the consolidated statements of operations.

The BSM option pricing model requires the input of highly subjective assumptions, including the risk-free interest rate, the expected dividend yield of our common stock, the expected volatility of the price of our common stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future. These assumptions are estimated as follows:

***Risk-free Interest Rate***

We base the risk-free interest rate assumption on zero-coupon U.S. treasury instruments appropriate for the expected term of the stock option grants.

***Expected Dividend Yield***

We base the expected dividend yield assumption on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. Consequently, we used an expected dividend yield of zero.

***Expected Volatility***

The expected stock price volatility for our common stock is estimated based on volatilities of a peer group of similar publicly-traded, biotechnology companies by taking the average historic price volatility for the peers for a period equivalent to the expected term of the stock option grants. We do not use our average historic price volatility as we

have only been a publicly-traded company since April 2014.

*Expected Term*

The expected term represents the period of time that options are expected to be outstanding. As we do not have sufficient historical experience for determining the expected term of the stock option awards granted we have determined the expected life assumption using either the simplified method, which is an average of the contractual term of the option and its ordinary vesting period, or the comparable average expected term utilizing those companies in the peer group as noted above.

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***Common Stock Valuation***

Due to the absence of a public market trading our common stock prior to the completion of our IPO in April 2014, it is necessary to estimate the fair value of the common stock underlying our stock-based awards when performing fair value calculations using the BSM option pricing model. The fair value of the common stock underlying our stock-based awards was assessed for each grant date by our board of directors. All options to purchase shares of our common stock have been granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant.

In the absence of a public trading market for our common stock prior to our IPO, we determined the estimated fair value of our common stock using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants, or AICPA, Audit and Accounting Practice Aid Series: *Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Aid.

***Leases***

We lease all of our office space and enter into various other lease agreements in conducting our business. At the inception of each lease, we evaluate the lease agreement to determine whether the lease is an operating or capital lease. Some of our lease agreements may contain renewal options, tenant improvement allowances, rent holidays or rent escalation clauses. When such items are included in a lease agreement, we record a deferred rent asset or liability equal to the difference between the rent expense and future minimum lease payments due. The rent expense related to operating leases is recognized on a straight-line basis in the statements of operations over the terms of the leases. In cases where the lessor grants leasehold improvement allowances that reduce our rent expense, we capitalize the improvements as incurred and recognize deferred rent, which is amortized over the shorter of the lease term or the expected useful life of the improvements.

***Comprehensive Loss***

Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss has been reflected in the consolidated statements of comprehensive loss and as a separate component of the consolidated statements of redeemable convertible preferred stock and stockholders' equity (deficit) for all periods presented.

***Foreign Currency Translation and Transactions***

The functional currencies of each of our subsidiaries in the United Kingdom (currently inactive) and China is the local currency. Assets and liabilities of the subsidiaries are translated at the rate of exchange at the balance sheet date. Expenses are translated at the average rate of exchange rates in effect during the reporting period. Gains and losses resulting from foreign currency translation are included in accumulated other comprehensive income in the accompanying consolidated balance sheets. Gains and losses resulting from foreign currency transactions are included in the results of operations, which to date, have not been significant.

***Income Taxes***

We account for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for

the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

We recognize net deferred tax assets to the extent we believe these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that we would be able to realize our deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes. As of December 31, 2014 and 2013, respectively, we maintained a full valuation allowance against our entire balance of deferred tax assets.

We record uncertain tax positions in accordance with ASC 740 on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority. We recognize interest and penalties related to unrecognized tax benefits, if any, within income tax expense and any accrued interest and penalties are included within the related tax liability line.

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**Table of Contents*****Net Loss Per Share***

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for common stock equivalents. Excluded from the weighted-average number of shares outstanding are shares that have been issued upon the early exercise of stock options and are subject to future vesting, which was a total of 24,444 shares as of December 31, 2014. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock and common stock equivalents outstanding for the period determined using the treasury-stock method. Common stock equivalents are comprised of redeemable convertible preferred stock, warrants for the purchase of common stock, and options outstanding under our stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding as the common stock equivalents are anti-dilutive due to our net loss position.

Potentially dilutive securities not included in the calculation of diluted net loss per share attributable to common stockholders because to do so would be anti-dilutive are as follows (in common stock equivalent shares):

	<b>As of December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Redeemable convertible preferred stock		13,713,407	7,019,599
Options to purchase common stock	3,210,693	3,098,573	2,336,314
Warrants to purchase common stock	250,646	250,646	250,646

***Recently Issued and Adopted Accounting Pronouncements***

In August 2014, the FASB issued Accounting Standards Update, or ASU, No. 2014-15, *Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 will require management to assess, at each annual and interim reporting period, the entity’s ability to continue as a going concern. The amendments in ASU 2014-15 do not have any application to an entity’s financial statements, but only to disclosure in the related notes. ASU 2014-15 is effective for annual periods ending after December 15, 2016 and early application is permitted. We intend to apply ASU 2014-15 beginning with the first quarter of fiscal year 2016.

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities (Topic 915) – Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*, or ASU 2014-10, which eliminates the concept of a development stage entity in its entirety from current accounting guidance and provides for certain amendments to the consolidation guidance in Topic 810 in the Accounting Standards Codification, or ASC. Prior to the issuance of this guidance, we were considered a development stage entity and as a result we included certain inception-to-date disclosures in our financial statements. The guidance related to the elimination of the concept of a development stage entity is effective for public companies for annual reporting periods beginning after December 15, 2014, and interim periods therein. The amendment of the consolidation guidance in Topic 810 is effective for public companies for annual reporting periods beginning after December 15, 2015. Early adoption of the new standard is permitted. We adopted ASU No. 2014-10 during the quarter ended June 30, 2014. As such, all inception-to-date disclosures have not been included in these consolidated financial statements.





**Table of Contents****3. Other Financial Information*****Property and Equipment***

Property and equipment, leasehold improvements, and related accumulated depreciation and amortization were as follows (in thousands):

	<b>December 31,</b>	
	<b>2014</b>	<b>2013</b>
Manufacturing and laboratory equipment	\$ 3,177	\$ 3,229
Office furniture and equipment	113	112
Clinical equipment	2,115	1,606
Computer equipment and software	152	122
Leasehold improvements	3,367	2,830
Construction in progress	922	323
	9,846	8,222
Less: accumulated depreciation and amortization	(6,778)	(5,755)
<b>Total</b>	<b>\$ 3,068</b>	<b>\$ 2,467</b>

Depreciation and amortization expense was \$1.1 million, \$851,000 and \$651,000 for the years ended December 31, 2014, 2013 and 2012, respectively.

In cases where our lessor grants to us leasehold improvement allowances that reduce our rent expense, we capitalize the improvements as incurred and recognize deferred rent, which is amortized over the shorter of the lease term or the expected useful life of the improvements. During the year ended December 31, 2013, we capitalized \$478,000 in such leasehold improvements.

***Accrued Expenses***

Accrued expenses consist of (in thousands):

	<b>December 31,</b>	
	<b>2014</b>	<b>2013</b>
Accrued clinical and related costs	\$ 6,072	\$ 2,067
Accrued compensation and related taxes	2,554	512
Accrued offering costs		496
Accrued other	249	178
<b>Total</b>	<b>\$ 8,875</b>	<b>\$ 3,253</b>

**4. Debt**

***Term Loan and Troubled Debt Restructuring***

In September 2008, we entered into a term loan with CIT Healthcare LLC (the Term Loan) at a fixed interest rate of approximately 10.6% that provided a maximum of \$4.0 million to be used for capital expenditures.

In May 2012, CIT Healthcare LLC agreed to modify the scheduled payment terms of the Term Loan and deferred 50% of the remaining monthly payments to a final balloon payment due at the end of the original loan term. These modifications were determined to meet the definition of a troubled debt restructuring. The outstanding debt and accrued interest were paid in full in accordance with the amended provisions in October 2012.

**5. Commitments and Contingencies**

***Operating Leases***

We lease office, manufacturing and research and development facilities, and equipment under various non-cancellable operating lease agreements. Facility leases generally provide for periodic rent increases and many contain escalation clauses and renewal options. Certain leases require us to pay property taxes and routine maintenance.

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Future minimum annual obligations under all non-cancellable operating lease commitments at December 31, 2014 are as follows (in thousands):

	<b>Year Ending December 31, 2014</b>					
	<b>Total</b>	<b>2015</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>
Operating lease obligations	\$ 2,200	\$ 856	\$ 853	\$ 491	\$	\$

Total rent expense under our operating leases was \$835,000, \$659,000 and \$459,000 during the years ended December 31, 2014, 2013 and 2012, respectively.

We recognize rent expense for our facility operating leases on a straight-line basis. We account for the difference between the minimum lease payments and the straight-line rent expense as deferred rent. Current and long-term deferred rent totaled \$126,000 and \$241,000 at December 31, 2014 and \$142,000 and \$321,000 at December 31, 2013, respectively.

**Purchase Commitments**

The following table summarizes our purchase obligations at December 31, 2014 (in thousands):

	<b>Payments Due by Period</b>				
	<b>Total</b>	<b>Less Than 1 Year</b>	<b>2-3 Years</b>	<b>3-5 Years</b>	<b>More Than 5 Years</b>
Purchase obligations	\$ 758	\$ 758	\$	\$	\$

As of December 31, 2014, our purchase obligations include existing purchase commitments for future minimum payments of \$391,000 with a vendor for raw materials that will be manufactured and utilized on an as needed basis. During the years ended December 31, 2014, 2013 and 2012, we purchased \$1.2 million, \$724,000 and \$462,000, respectively, of materials from this vendor. Our purchase obligations also include a purchase order with a vendor for cartridges that will be manufactured and delivered on an agreed upon schedule during 2015 for a future payment of \$367,000. During the years ended December 31, 2014 and 2013, we purchased \$1.2 million and \$439,000 of materials from this vendor. During the year ended 2012, we purchased no material from this vendor. If we cancel any future cartridge shipment, we would be required to pay 50% of the scheduled invoice amount for that shipment.

**Legal Proceedings**

We are not currently a party to any litigation, nor are we aware of any pending or threatened litigation against us that we believe would materially affect our business, operating results, financial condition or cash flows. Our industry is characterized by frequent claims and litigation, including claims regarding patent and other intellectual property rights, as well as for product liability. As a result, in the future, we may be involved in various legal proceedings from time to time.

**6. Fair Value**

The following fair value hierarchy table presents information about each major category of our financial assets and liabilities measured at fair value on a recurring basis (in thousands):

<b>Fair Value Measurement at December 31, 2014</b>				
	<b>Fair Value</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Assets</b>				
Money market funds	\$ 101,592	\$ 101,592	\$	\$

<b>Fair Value Measurement at December 31, 2013</b>				
	<b>Fair Value</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Assets</b>				
Money market funds	\$ 37,158	\$ 37,158	\$	\$
<b>Liabilities</b>				
Future purchase rights	\$ 2,600	\$	\$	\$ 2,600

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We report the change in fair value during each period as a non-operating gain or loss. There were no transfers between Level 1, Level 2 or Level 3 for our assets or liabilities during any period presented. The following table summarizes the changes in Level 3 preferred stock warrant liabilities measured at fair value on a recurring basis for the year ended December 31, 2012 (in thousands):

	<b>Fair Value of Preferred Stock Warrant Liabilities</b>
Balance at January 1, 2012	\$ 180
Revaluation of warrants	(180)
Balance at December 31, 2012	\$

The preferred stock warrants were converted to common stock warrants in February 2012 (see Note 2).

The following table summarizes the changes in Level 3 future purchase rights liabilities measured at fair value on a recurring basis for the three years ended December 31, 2014 (in thousands):

	<b>Fair Value of Future Purchase Rights Liabilities</b>
Balance at January 1, 2012	\$
Initial valuation of future purchase rights	3,101
Re-measurement of future purchase rights	(3,101)
Balance at December 31, 2012	
Initial valuation of additional future purchase rights	1,294
Re-measurement of future purchase rights	1,306
Balance at December 31, 2013	2,600
Re-measurement of future purchase rights	(2,600)
Balance at December 31, 2014	\$

We valued the future purchase rights liabilities in the periods ended December 31, 2013 and 2012 using a binomial lattice option pricing model with the following assumptions:

	<b>December 31, 2013</b>	<b>2012</b>
Common stock fair value	\$ 5.93	\$ 1.17
Preferred stock price	\$ 8.00	\$ 8.00
Volatility	85.0%	80.0%

Risk-free interest rate	0.38%	0.36%
Contractual life (years)	2.08	3.08
Number of nodes	25	37
Dividend yield	0.0%	0.0%

## 7. Redeemable Convertible Preferred Stock

### *Junior Convertible Preferred Stock*

In February 2012, we entered into a securities purchase agreement for the sale of junior convertible preferred stock. In conjunction with the junior preferred stock financing, previously issued shares of redeemable convertible Series A, Series B, Series C, and Series D preferred stock and related preferred stock warrants converted into shares of common stock and common stock warrants, respectively. As a result, we reclassified the aggregate value of the Series A, Series B, Series C, and Series D preferred stock of \$54.7 million to stockholders' equity (deficit).

The junior preferred stock financing totaled \$1.5 million of convertible, but not redeemable, preferred stock at approximately \$0.43 a share, for an aggregate of 3,501,400 shares. During February and March 2012, we received proceeds of \$1.3 million, net of issuance costs of \$40,000. In conjunction with the completion of our IPO in April 2014, all shares of our junior convertible preferred stock were converted into common stock on a one-to-one basis and the remaining unamortized issuance costs of \$31,000 were recognized as accretion to redemption value of the junior convertible preferred stock in the statement of operations.

### *Senior Redeemable Convertible Preferred Stock*

In September 2012, we entered into the Senior Preferred Purchase Agreement that authorized the multi-stage issuance of 14,765,632 shares of our senior redeemable convertible preferred stock for \$8.00 per share. Prior to termination upon the completion of our IPO in April 2014, 10,767,007 shares were issued under the Senior Preferred Purchase. Pursuant to the Senior Preferred Purchase Agreement, we granted the investors in the senior preferred stock financing the right, subject to the satisfaction of certain conditions, to purchase additional shares of senior preferred stock for a purchase price of \$8.00 per share at multiple subsequent closings in accordance with a schedule provided in the Senior Preferred Purchase Agreement, referred to as the future stock purchase rights. Where applicable, the purchase price under the Senior Preferred Stock Purchase Agreement was allocated to the future purchase rights and any related stock options at their estimated fair value, as described under *Future Purchase Rights* below.

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In connection with the senior preferred stock financing, we have entered into a Fourth Amended and Restated Investors Rights Agreement in August 2013 (the Senior Preferred IRA ). The Senior Preferred IRA contains customary registration rights and related provisions, including customary market standoff provisions.

From September to October 2012, we issued 2,606,250 shares of senior preferred stock for proceeds of \$19.8 million, net of issuance costs of \$240,000. We also issued 911,949 shares of senior preferred stock upon the conversion of a loan entered into during 2012 that included \$7.2 million of principal and \$146,000 of accrued interest.

In February 2013, we closed another senior preferred stock financing and issued 305,571 shares of senior preferred stock for proceeds of \$2.3 million, net of issuance costs of \$134,000 incurred by us for services rendered by a third-party professional services firm that is also utilized by certain of our investors.

In May 2013, we closed an additional senior preferred stock financing and issued 158,150 shares of senior preferred stock for proceeds of \$1.2 million, net of issuance costs of \$28,000.

In June 2013, we closed a further senior preferred stock financing and issued 3,830,050 shares of senior preferred stock for proceeds of \$30.6 million, net of issuance costs of \$90,000.

In December 2013, we amended the terms of the Senior Preferred Stock Purchase Agreement to provide for a partial acceleration of existing future preferred stock financing closings under the Senior Preferred Stock Purchase Agreement and the sale of additional shares of senior preferred stock to certain of our existing investors and to certain of our directors and officers (the December 2013 Amendment). Pursuant to the Senior Preferred Stock Purchase Agreement, as amended by the December 2013 Amendment, we issued 2.4 million of senior preferred stock for proceeds of \$19.1 million, net of issuance costs of \$102,000, in December 2013.

Pursuant to the Senior Preferred Stock Purchase Agreement, in January 2014 we issued an additional 555,000 shares of senior redeemable convertible preferred stock for proceeds of \$4.3 million, net of issuance costs of \$135,000. Also in January 2014, we completed the sale of 1.5 million shares of our senior redeemable convertible preferred stock at a price of \$8.00 per share in a private placement to new investors for proceeds of \$12.0 million, net of issuance costs of \$31,000.

In February 2014, we completed a pre-emptive rights offering, triggered by the private placement for 241,016 shares of our senior redeemable convertible preferred stock at a price of \$8.00 per share for proceeds of \$1.9 million, net of issuance costs of \$35,000.

In conjunction with the completion of our IPO on April 2014, all the outstanding shares of our senior redeemable convertible preferred stock were converted into common stock on a one-to-one basis and the remaining unamortized discounts of \$3.8 million and issuance costs of \$727,000 were recognized as a deemed dividend and accretion to redemption value of the redeemable convertible preferred stock, respectively, in the statement of operations.

## ***Future Purchase Rights***

Pursuant to the Senior Preferred Purchase Agreement, we granted to the investors in the senior preferred stock financing the future purchase rights, subject to the satisfaction of certain conditions, to purchase additional shares of senior preferred stock for a purchase price of \$8.00 per share at multiple subsequent closings in accordance with a schedule provided in the Senior Preferred Purchase Agreement. These future purchase rights for additional shares of our senior preferred stock were legally detachable from the shares of the underlying senior preferred stock and, as a result, were considered freestanding instruments accounted for separately from the shares of senior preferred stock. As

the future purchase rights were exercisable for shares of our redeemable convertible preferred stock, the future purchase rights were instruments that embodied obligations to transfer assets and were classified as liabilities under the accounting guidance that distinguishes liabilities from equity.

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The following table summarizes the number of shares subject to purchase under future purchase rights initially granted, the fair value per share of the senior preferred stock subject to the rights as initially granted, the initial grant date fair value recorded, the fair value of our common stock used in determining such value, and beneficial conversion amounts underlying the preferred stock that were recorded in connection with certain purchases of such preferred stock under the Senior Preferred Purchase Agreement and the related stock options granted to certain members of our board of directors (in thousands except share and per share amounts):

<b>Issuance Date</b>	<b>Number of Shares Subject to Future Purchase Rights Granted</b>	<b>Fair Value per Share of Rights</b>	<b>Grant Date Fair Value Recorded</b>	<b>Common Stock Value Used in Determining Fair Value</b>	<b>Beneficial Conversion on Underlying Preferred Stock/ Options</b>
September 25, 2012	3,750,000	\$ 2.80	\$ 3,101	\$ 2.30	\$
February 28, 2013	891,250	\$ 2.83	\$ 864	\$ 6.85	\$ 513
April 30, 2013	461,271	\$ 2.40	\$ 379	\$ 6.85	\$ 192
June 26, 2013	66,250	\$ 0.76	\$ 50	\$ 6.82	\$ 264

In conjunction with the issuance of senior preferred stock during the year ended December 31, 2013, we estimated the fair value of the future purchase rights for the shares issued to be \$1.3 million. The future purchase rights were recorded at their estimated fair value, with the remaining amount of the proceeds allocated to the senior preferred stock, resulting in the senior preferred stock being recorded at an amount per share less than the fair value of our common stock at that time. Accordingly, we recorded an aggregate beneficial conversion amount underlying the senior preferred stock of \$705,000, an amount equal to the number of shares of senior preferred stock sold on that date multiplied by the difference between the estimated fair value of the underlying common stock and the value allocated to the senior preferred stock on that date. The beneficial conversion amount was recorded as an offset to additional paid-in capital and was being amortized as a deemed dividend over the redemption period using an effective interest rate method.

In connection with the issuance of senior preferred stock in June 2013 discussed above, we also granted to certain members of our board of directors who participated in the senior preferred stock financings one common stock option for each share of preferred stock purchased through June 2013. An aggregate of 86,917 common stock options were granted to these board members, which were valued at \$4.91 per share utilizing the BSM option pricing model. After allocation of the proceeds to the underlying future purchase rights as noted above, the remaining amount of the proceeds were allocated between the common stock options and the senior preferred stock acquired using the relative fair value method. As the allocated value per share of the senior preferred stock acquired was less than the fair value of our common stock on such date, we recorded a beneficial conversion associated with the options granted, on the underlying senior preferred stock of \$264,000. This beneficial conversion was also recorded as an offset to additional paid-in capital and was being amortized as a deemed dividend over the redemption period using an effective interest rate method.

All remaining future purchase rights associated with our preferred stock were terminated and the remaining unamortized beneficial conversion balance of \$878,000 was recognized as a reduction to equity at the effective date of our IPO in April 2014.

***Certificate of Incorporation***

The material terms of our amended restated certificate of incorporation, which became effective as of the closing of our IPO in April 2014, are as follows:

*Authorized Shares*

Our amended and restated certificate of incorporation authorizes the company to issue 150,000,000 shares of stock consisting of 130,000,000 shares of common stock, par value of \$0.0001 per share and 20,000,000 shares of preferred stock, par value \$0.0001 per share.

*Dividends*

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

*Liquidation Preference*

In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preferences that may be granted to the holders of any then outstanding shares of preferred stock.

**Table of Contents***Rights and Preferences*

Holders of common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock, which we may designate and issue in the future.

*Voting Rights*

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and amended and restated bylaws do not provide for cumulative voting rights. Because of this absence of cumulative voting, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. In addition, our amended and restated certificate of incorporation also provides that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the combined voting power of all our stockholders entitled to vote on the election of directors, voting together as a single class.

Subject to supermajority votes for some matters, matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, provided that the holders of our common stock are not allowed to vote on any amendment to our certificate of incorporation that relates solely to the terms of one or more series of preferred stock if the holders of such affected series are entitled, either separately or together with the holders or one or more such series, to approve such amendment. The affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors and, in some cases, the affirmative vote of a majority of minority stockholders entitled to vote in any annual election of directors are required to amend or repeal our bylaws, amend or repeal certain provisions of our certificate of incorporation, approve certain transactions with certain affiliates, or approve the sale or liquidation of the company. The vote of a majority of minority of stockholders applies when an individual or entity and its affiliates or associates together own more than 50% of the voting power of our then outstanding capital stock, excluding any such person that owned 15% or more of our outstanding voting stock immediately prior to our IPO, and such a vote would require the approval of the majority of our voting stock, excluding the voting stock held by such a majority holder.

*Warrants*

We issued warrants to purchase redeemable convertible preferred stock in connection with financing activities or for consulting services. In connection with the junior preferred stock financing in February 2012, all warrants to purchase Series B, Series C, and Series D preferred stock converted to common stock warrants. The common stock warrants outstanding as of December 31, 2014, have a weighted-average exercise price of \$95.21 and expire between February 2016 and September 2019. Our warrant activity is as follows for the three years ended December 31, 2014:

		<b>Number Outstanding</b>	<b>Weighted- average Exercise Price</b>
Balance outstanding	January 1, 2012	252,308	\$ 95.84
Expiration of warrants		(1,662)	\$ 191.69

Balance outstanding and 2014	December 31, 2012, 2013	250,646	\$	95.21
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## 8. Common Stock

In April 2014, we completed an IPO selling 4,500,000 shares of our common stock at \$12.00 per share and received net proceeds of \$50.2 million after underwriters' discounts and commissions. In addition, we incurred \$5.8 million in offering expenses, resulting in total costs of \$9.6 million and net offering proceeds to us of \$44.4 million. In May 2014, the underwriters exercised their option to purchase an additional 675,000 shares of our common stock at \$12.00 per share in full. As a result, we received an additional \$7.5 million in net proceeds after underwriters' discounts and commissions of \$567,000, for total net proceeds of \$51.9 million from the IPO.

In October 2014, we completed a follow-on public offering selling 2,000,000 shares of our common stock at \$17.50 per share and received net proceeds of \$32.6 million after underwriters' discounts and commissions. In addition, we incurred \$511,000 in offering expenses, resulting in total costs of \$3.0 million and net offering proceeds to us of \$32.0 million. In November 2014, the underwriters exercised a portion of their option and purchased an additional 50,000 shares of our common stock at \$17.50 per share. As a result, we received an additional \$814,000 in net proceeds after underwriters' discounts and commissions, for total net proceeds from the follow-on public offering of \$32.9 million, net of discounts, commissions and costs, from the offering.

**Table of Contents*****Stock Reserved for Future Issuance***

Shares reserved for future issuance at December 31, 2014 are as follows:

	<b>Number of Shares</b>
Exercise of common stock warrants	250,646
Common stock options outstanding	3,210,693
Common stock options available for future grant	373,803
 Total common shares reserved for future issuance	 3,835,142

**9. Stock Compensation Plans*****Equity Incentive Plans***

Our 2014 Equity Incentive Plan, or the 2014 Plan, became effective in April 2014 and replaced our 2012 Stock Option Plan, or the 2012 Plan, with respect to future awards. The 2014 Plan provides for the grant of stock options, restricted stock, restricted stock units, stock appreciation rights, performance awards and performance units to employees, directors, and consultants. Option grants under the 2014 Plan generally have a ten-year term and vest over four years. Shares available for grant under the 2014 Plan include any shares remaining available or becoming available in the future under the 2012 Plan due to cancellation or forfeiture. In addition, the 2014 Plan provides for annual increases in the number of shares available for issuance thereunder beginning upon its effective date in April 2014, and on each annual anniversary, equal to the lower of:

1,200,000 shares of our common stock;

3% of the outstanding shares of our common stock on the second-to-the-last day prior to each anniversary date of the effectiveness date of our IPO; or

an amount as our board of directors may determine.

Our 2012 Stock Option Plan, or the 2012 Plan, provided for the grant of stock options, restricted stock, restricted stock units, stock purchase rights, and performance awards to employees, directors, and consultants. Option grants under the 2012 Plan generally have a ten-year term, vest over four years and are exercisable immediately, subject to a repurchase right that lapses as the option vests. Options to purchase 55,516 shares of our common stock had been exercised prior to vesting under the 2012 Plan, of which 24,444 shares were unvested and subject to repurchase as of December 31, 2014. During 2014, 20,715 shares vested resulting in a release of the repurchase liability of \$104,000. We have not repurchased any shares related to these early exercises for which our repurchase liability was \$123,000 as of December 31, 2014.

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Prior to the adoption of the 2012 Plan, we granted incentive awards under the 2004 Stock Option Plan. In February 2012 and in connection with the junior preferred stock financing, 27,230 outstanding options from the 2004 Stock Option Plan were canceled, which represented all options outstanding at the time of cancellation. In conjunction with the cancellation of options, we expensed previously unrecognized compensation cost of \$27,000.

As of December, 2014, the aggregate number of shares outstanding or available for grant under the 2012 and 2014 Plans was 3,584,496 shares.

The following table summarizes stock option activity:

	<b>Options</b>	<b>Weighted-Average Exercise Price</b>	<b>Weighted-Average Remaining Contractual Term (Years)</b>	<b>Aggregate Intrinsic Value (In thousands)</b>
Outstanding as of January 1, 2014	3,098,573	\$ 6.71		
Granted	326,324	\$ 16.85		
Exercised	(142,041)	\$ 6.00		
Forfeited	(72,163)	\$ 8.11		
Outstanding as of December 31, 2014	3,210,693	\$ 7.54	8.0	\$ 55,845
Options vested and expected to vest as of December 31, 2014	3,129,706	\$ 7.45	7.9	\$ 54,722
Options exercisable as of December 31, 2014	2,981,319	\$ 6.64	7.9	\$ 54,529

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The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of our common stock for those shares that had exercise prices lower than the fair value of our common stock as of December 31, 2014. The number of options vested and expected to vest is calculated as the total number of options vested plus the number of unvested options remaining after applying our estimated forfeiture rate. As of December 31, 2014, there was \$5.8 million of total compensation cost related to unvested stock option awards not yet recognized, which is expected to be recognized over a remaining weighted-average vesting period of 2.2 years.

The following table summarizes information about stock options (in thousands):

	<b>Year Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Aggregate intrinsic value of options exercised	\$ 1,972	\$ 633	\$

We have not capitalized or recognized an income tax benefit from the exercise of any stock options as we continue to record a full valuation allowance on our deferred tax assets.

***Stock-based Compensation Expense***

The weighted-average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2014, 2013 and 2012 was \$11.87, \$5.53, \$0.47, respectively. The following are the ranges of underlying assumptions used to determine the fair value of stock options granted to employees and non-employees:

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Employees and Directors:			
Risk-free interest rate	1.53% - 1.89%	0.76% - 1.10%	0.76% - 0.99%
Expected dividend yield	0%	0%	0%
Expected volatility	80% - 85%	90% - 100%	100%
Expected term of options (years)	6 - 6.2	5 - 5.5	5 - 6
Range of common stock value	\$ 7.55 - \$24.04	\$ 6.77 - \$9.94	\$ 0.43 - \$1.17

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Non-Employees:			
Risk-free interest rate	0.11% - 1.27%	0.13% - 0.86%	0.17% - 0.57%
Expected dividend yield	0%	0%	0%
Expected volatility	73% - 85%	90% - 100%	100%
Expected term of options (years)	1 - 4	1 - 4	1 - 4
Range of common stock value	\$ 11.31 - \$27.24	\$ 5.93 - \$9.94	\$ 1.17

***December 31, 2012 Valuation Analysis***

During the first quarter of 2013, we commenced an analysis of the enterprise value of our company and the fair value of our common stock as of December 31, 2012, which utilized an Option Pricing Model, or OPM. OPM is appropriate to use when the range of possible future outcomes is so difficult to predict that any such forecast would be highly

speculative, or there is a substantially contemporaneous sale of stock to a third party. OPM treats common stock and convertible preferred stock as call options on the enterprise value, with exercise prices based on the liquidation preference of the convertible preferred stock. Therefore, the common stock has value only if the funds available for distribution to the stockholders exceed the value of the liquidation preference to be received by holders of our redeemable convertible preferred stock at the time of a liquidity event, such as a merger, sale or an initial public offering, or IPO, assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the stockholders. The common stock is modeled to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the convertible preferred stock is liquidated. OPM uses the BSM option pricing model to price the call option.

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The OPM considered the relative rights and preferences of the various securities, including the seniority of the liquidation preferences for preferred equity, and the potential for dilution caused by the conversion of the preferred equity. Additionally, our preferred stockholders have various rights that give them greater control and influence over future liquidity, financing and other decisions relating to our company than the holders of our common stock. The OPM applied a percentage of participation for each class of shares for each valuation interval based on BSM option pricing models and a 25.4% discount for lack of marketability was applied for the common stockholders. The resulting implied per share value of our common stock was \$1.17 per share as of December 31, 2012, which was utilized to determine the BSM fair value for the purpose of calculating stock-based compensation expense related to the options granted in September and December 2012 at an exercise price of \$8.00 per share.

### *2013 and 2014 Valuation Analyses*

Due to our management's and board of directors' decision to pursue an IPO, coupled with our belief that we could reasonably estimate the form and timing of potential liquidity events, we utilized a Probability Weighted Expected Return Method, or PWERM, for our 2013 and 2014 valuations prior to the completion of our IPO in April 2014. Under this method, the implied fair value of our common stock is estimated based upon an analysis of future values assuming various outcomes. The value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available to us as well as the rights of each share class. The possible outcomes considered are based upon an analysis of future scenarios as described below:

closing of an initial public offering;

sale to a strategic acquirer;

continuation as a private company with subsequent liquidation event; and

dissolution.

Critical assumptions required to perform the PWERM include the following:

Scenarios: Expected future events were identified.

Scenario probabilities: Estimates of the probability of occurrence of each event were identified.

Valuation: Expected future values under each scenario were estimated.

Timing: Expected timing to the event under each scenario were estimated.

Risk adjusted discount rates: Risk-adjusted discount rates were selected for each equity class based on the rights and preferences of each equity class and market data.

Discounts: Appropriate minority or marketability discounts, if any, required to estimate the per share value of the various equity classes were determined.

In determining the implied fair value of our common stock in the IPO scenario, we assumed that the redeemable convertible preferred stock then outstanding would be converted into common stock. In allocating value to our common stock in the merger or sale scenario, we first allocated to our outstanding shares of redeemable convertible preferred stock the greater of the liquidation preference of the redeemable convertible preferred stock and the amount that would have been payable had all such shares of redeemable convertible preferred stock been converted to common stock.

There is inherent uncertainty in these estimates and, if we had made different assumptions, the fair value of the underlying common stock and amount of our stock-based compensation expense, net loss and net loss per share amounts would have differed.

#### *March 31, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by December 31, 2013	25%
Sale by December 31, 2013	20%
Private company	30%
Dissolution	25%

A 13% discount for lack of marketability was applied for common stockholders. The resulting implied fair value of \$6.85 per share was utilized to determine the BSM fair value for the purpose of calculating stock-based compensation expense related to the options granted in March 2013 at an exercise price of \$8.00 per share.

**Table of Contents***June 30, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by November 15, 2013	35%
Sale by November 15, 2013	10%
Private company	30%
Dissolution	25%

A 9% discount for lack of marketability was applied for common stockholders. The resulting implied fair value of \$6.82 per share was utilized to determine the BSM fair value for the purpose of calculating stock-based compensation expense related to the options granted in May, June, and July 2013 at an exercise price of \$8.00 per share. The decrease in implied fair value of our common stock from March 31, 2013 was primarily due to dilution from the issuance of substantially more shares of our redeemable convertible senior preferred stock during the second quarter of 2013 that have superior rights to our common stock.

*September 3, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by November 15, 2013	50%
Sale by November 15, 2013	10%
Private company	25%
Dissolution	15%

A 7% discount for lack of marketability was applied for common stockholders. The resulting implied fair value of \$9.94 per share was utilized to determine the BSM fair value for the purpose of calculating stock-based compensation expense related to the options granted in September 2013 at an exercise price of \$10.50 per share. The implied fair value of our common stock increased from June 30, 2013 primarily due to the increased likelihood of an IPO scenario as a result of progress made toward a public offering. In addition, we decreased our discount for lack of marketability reflecting a decrease in the expected time to liquidity.

*September 30, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by November 15, 2013.	50%
Sale by November 15, 2013	10%
Private company	25%
Dissolution	15%

A 6% discount for lack of marketability was applied for common stockholders, which resulted in an implied fair value of \$10.02 per share. This increase in implied fair value of our common stock from September 3, 2013 was associated with a slight decrease in our discount for lack of marketability due to a decrease in the expected time to liquidity. There were no changes to our probability-weighted scenarios as no significant changes occurred from our September 3, 2013 valuation analysis.

*December 1, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

Scenario	Weight
IPO by May 15, 2014	20%
Sale by September 30, 2015	10%
Private company	50%
Dissolution	20%

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A discount for lack of marketability was applied for common stockholders of 10%, 21% and 28% for the IPO, sale and private company scenarios, respectively. The resulting implied fair value of \$6.77 per share was utilized to determine the BSM fair value for the purpose of calculating stock-based compensation expense related to the options granted in December 2013 at an exercise price of \$8.00 per share. The decrease in fair value of our common stock from September 30, 2013 was primarily related to the increases in discount for lack of marketability due to an increase in the expected time to a liquidity event associated with the projected timing of an IPO or a sale of our company.

*December 31, 2013 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by May 15, 2014	20%
Sale by September 30, 2015	10%
Private company	50%
Dissolution	20%

A discount for lack of marketability was applied for common stockholders of 9%, 20% and 28% for the IPO, sale and private company scenarios, respectively, which resulted in an implied fair value of \$5.93 per share. The decrease in fair value of our common stock from December 1, 2013 was primarily related to dilution from the issuance of additional shares of our redeemable convertible senior preferred stock in December 2013, partially offset by a slight decrease in discount for lack of marketability for the IPO and sale scenarios reflecting a decrease in the expected time to liquidity.

*February 12, 2014 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by May 15, 2014	25%
Sale by September 30, 2015	10%
Private company	50%
Dissolution	15%

A discount for lack of marketability was applied for common stockholders of 8%, 20% and 28% for the IPO, sale and private company scenarios, respectively, which resulted in an implied fair value of \$7.55 per share. The increase in fair value of our common stock from December 31, 2013 was primarily related to the increase in likelihood of an IPO scenario based on progress toward a public offering, coupled with a slight decrease in discount for lack of marketability for the IPO and sale scenarios. These were partially offset by dilution from the issuance of additional shares of our senior redeemable convertible preferred stock in January 2014.

*March 31, 2014 Valuation Analysis*

Our analysis considered the following probability-weighted scenarios:

<b>Scenario</b>	<b>Weight</b>
IPO by April 15, 2014	65%
Sale by September 30, 2015	10%
Private company	15%
Dissolution	10%

A discount for lack of marketability was applied for common stockholders of 2%, 17% and 27% for the IPO, sale and private company scenarios, respectively, which resulted in an implied fair value of \$11.30 per share. The increase in fair value of our common stock from December 31, 2013 and February 12, 2014, was related to the increase in likelihood of an IPO scenario as significant progress had been completed toward a public offering and the decrease in discount for lack of marketability for the IPO scenario that reflected the proximity to the projected time to liquidity. These were slightly offset by dilution from the issuance of additional shares of our senior redeemable convertible preferred stock in January and February 2014, as applicable.

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The following table summarizes the allocation of stock-based compensation expense to employees and non-employees (in thousands):

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Employees and Directors:			
Research and development	\$ 763	\$ 262	\$ 45
General and administrative	937	503	94
Totals	\$ 1,700	\$ 765	\$ 139

	<b>Years Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Non-Employees:			
Research and development	\$ 757	\$ 149	\$ 5
General and administrative	53	34	
Totals	\$ 810	\$ 183	\$ 5

**10. Income Taxes**

Our net loss before income tax was subject to tax in the following jurisdictions for the following periods (in thousands):

	<b>Year Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
United States	\$ (47,482)	\$ (32,524)	\$ (6,321)
Foreign	(185)	(194)	(380)
	\$ (47,667)	\$ (32,718)	\$ (6,701)

Our rate reconciliation consists of the following:

	<b>Year Ended December 31,</b>		
	<b>2014</b>	<b>2013</b>	<b>2012</b>
Federal statutory rate	35.0%	35.0%	35.0%
State tax (net of federal benefit)	5.4%	5.3%	5.8%
Research and development credits	3.8%	3.9%	1.8%

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Warrants/purchase rights liabilities	2.2%	(1.6%)	19.9%
Foreign net operating losses	(0.4%)	(1.2%)	(0.6%)
382 limited net operating losses and credits		(0.6%)	(415.2%)
Change in valuation allowance	(45.1%)	(40.0%)	355.5%
Other	(0.9%)	(0.8%)	(2.2%)
Effective tax rate	0.0%	0.0%	0.0%

Significant components of our deferred tax assets are shown below. A valuation allowance has been established as realization of such deferred tax assets has not met the more likely-than-not threshold requirement. If our judgment changes and it is determined that we will be able to realize these deferred tax assets, the tax benefits relating to any reversal of the valuation allowance on deferred tax assets will be accounted for as a reduction to income tax expense.

	<b>December 31,</b>	
	<b>2014</b>	<b>2013</b>
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	\$ 33,517	\$ 15,073
Research and development tax credits	3,269	1,426
Stock compensation	879	181
Foreign net operating loss carryforwards	377	504
Other, net	1,715	1,066
Total deferred tax assets	39,757	18,250
Less valuation allowance	(39,757)	(18,250)
	\$	\$



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We have a history of incurring net operating losses each year since inception that is due to our history as a development stage company with no realized revenues from our planned principal operations. These cumulative operating losses provide significant negative evidence in the determination of whether or not we will be able to realize our deferred tax assets such as our net operating losses and other favorable temporary differences. As a result, we have maintained a full valuation allowance against the entire balance of deferred tax assets since the date of inception. The valuation allowance increased by \$21.5 million and \$13.1 million for the years ended December 31, 2014 and 2013, respectively.

As of December 31, 2014, we had available net operating loss, or NOL, carryforwards of approximately \$84.8 million and \$79.4 million for federal and state income tax purposes, respectively. The federal and state NOLs begin to expire in 2023 and 2015, respectively. As of December 31, 2014, we have federal and state research and development tax credits available for income tax purposes of approximately \$2.3 million and \$1.4 million, respectively. The federal research and development credits begin to expire in 2023 and the state research and development tax credits do not expire. These carryforwards are net of the Section 382 and 383 limitations discussed below.

As of December 31, 2014, we also have available NOLs from our Chinese subsidiary of approximately \$1.5 million. The Chinese NOLs begin to expire in 2015.

Sections 382 and 383 of the Internal Revenue Code (the IRC) limit a company's ability to utilize certain net operating losses and tax credit carryforwards in the event of a cumulative change in ownership in excess of 50%, as defined. We experienced changes in ownership, as defined in Section 382, in February 2012 and in December 2013. As a result, the deferred tax asset associated with our federal and state net operating loss carryforwards and federal and state research credits have been reduced based on the Section 382 limitations. The amount of the reduction in our deferred tax assets is based on the estimated amount of the NOL carryforwards and federal and state research credits we believe cannot be used based on the estimated amount of our Section 382 annual limitation. We have reduced our deferred tax assets by \$23.8 million and have estimated that approximately \$58.7 million and \$56.2 million of our federal and state NOLs, respectively, cannot be used in future years as a result of this change in ownership. Additionally, we have estimated that approximately \$2.2 million and \$1.6 million of our federal and state research credits, respectively, cannot be used in future years. We have not experienced any additional changes as defined in Section 382 through December 31, 2014. If additional Section 382 changes occur, limitations against the utilization of net operating losses and credits could further impact our future cash flows, but would not impact our 2014 consolidated financial statements, due to the existence of a full valuation allowance against our deferred tax assets.

Approximately \$1.8 million of both the federal and state NOL carryforwards reflected above relate to excess tax deductions for stock compensation, the income tax benefit of which will be recorded as additional paid-in capital if and when realized.

The following table summarizes the activity related to our unrecognized tax benefits (in thousands):

	<b>Year Ended December 31,</b>	
	<b>2014</b>	<b>2013</b>
Balance at beginning of year	\$ 407	\$
Additions based on tax positions related to the current year	533	337
Changes for prior period tax positions	(2)	70

Balance at end of year	\$ 938	\$ 407
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We do not anticipate any significant changes in the amount of unrecognized tax benefits over the next twelve months. Due to the full valuation allowance we have on our net deferred tax asset balance, there are no unrecognized tax benefits that would impact the effective tax rate if recognized.

We are subject to U.S. federal, California and various other states and Chinese income taxes. We are no longer subject to U.S. federal or state income tax examination by tax authorities for tax returns filed for the years ended on or before December 31, 2009. However, to the extent allowed by law, the taxing authorities may have the right to examine the period from 2003 through 2014 where NOLs were generated and carried forward, and make adjustments to the amount of the NOL carryforward. We are not currently under examination by any federal or state jurisdictions.

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**Table of Contents****11. Related Party Transactions*****Directors***

During the years ended December 31, 2014, 2013 and 2012, we paid an aggregate of \$33,500, \$39,000, and \$7,000, respectively, to a member of our board of directors for consulting services and services rendered as chair of our Clinical Advisory Board.

One member of our board of directors was a partner and is no longer practicing law as of the end of 2013 with a firm that provides certain legal services to us. For the years ended December 31, 2013 and 2012, we incurred an aggregate of \$100,000 and \$73,000, respectively, in fees for these services.

***Clinical Advisory Board and Scientific Advisory Board***

Certain members of our Clinical Advisory Board and Scientific Advisory Board hold positions at medical institutions where we conduct business. During the years ended December 31, 2014 and 2013, we incurred an estimated aggregate of \$1.7 million and \$824,000, respectively, in fees to these institutions, primarily for clinical trial costs. As of December 31, 2014 and 2013, accounts payable and accrued expenses combined included \$1.6 million and \$643,000, respectively, due to these institutions.

**12. Selected Quarterly Data (unaudited)**

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2014 and 2013 are as follows (in thousands, except per share data):

	<b>For the Quarters Ended</b>				
	<b>March 31</b>	<b>June 30</b>	<b>September 30</b>	<b>December 31</b>	<b>Total Year</b>
<b>2014:</b>					
Operating expenses	\$ 11,876	\$ 11,638	\$ 12,810	\$ 14,018	\$ 50,342
Net loss	\$ (10,748)	\$ (10,167)	\$ (12,798)	\$ (13,954)	\$ (47,667)
Net loss attributable to common stockholders	\$ (13,818)	\$ (16,251)	\$ (12,798)	\$ (13,954)	\$ (56,821)
Basic and diluted net loss per share attributable to common stockholders (1)	\$ (24.49)	\$ (0.91)	\$ (0.59)	\$ (0.59)	
<b>2013:</b>					
Operating expenses	\$ 4,926	\$ 7,063	\$ 9,165	\$ 10,248	\$ 31,402
Net loss	\$ (9,358)	\$ (6,144)	\$ (6,977)	\$ (10,239)	\$ (32,718)
Net loss attributable to common stockholders	\$ (10,331)	\$ (7,267)	\$ (9,034)	\$ (12,453)	\$ (39,085)
Basic and diluted net loss per share attributable to common stockholders (1)	\$ (22.11)	\$ (14.33)	\$ (16.31)	\$ (22.28)	

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per share calculations will not necessarily equal the annual per share calculation.



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Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Vital Therapies, Inc.

Date: March 19, 2015

By: /s/ Terence E. Winters, Ph.D.  
Terence E. Winters, Ph.D.  
*Chief Executive Officer*

**POWER OF ATTORNEY**

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Terence E. Winters and Michael V. Swanson, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ TERENCE E. WINTERS, Ph.D. Terence E. Winters, Ph.D.	Co-Chairman and Chief Executive Officer (Principal Executive Officer)	March 19, 2015
/s/ MICHAEL V. SWANSON Michael V. Swanson	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 19, 2015
/s/ MUNEER A. SATTER Muneer A. Satter	Co-Chairman and Lead Director	March 19, 2015
/s/ JEAN-JACQUES BIENAIMÉ Jean-Jacques Bienaimé	Director	March 19, 2015
/s/ PHILIP M. CROXFORD Philip M. Croxford	Director	March 19, 2015

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/s/ DOUGLAS E. GODSHALL	Director	March 19, 2015
Douglas E. Godshall		
/s/ ERROL R. HALPERIN	Director	March 19, 2015
Errol R. Halperin		
/s/ J. MICHAEL MILLIS, M.D.	Director	March 19, 2015
J. Michael Millis, M.D.		
/s/ LOWELL E. SEARS	Director	March 19, 2015
Lowell E. Sears		
/s/ RANDOLPH C. STEER, M.D., PH.D.	Director	March 19, 2015
Randolph C. Steer, M.D., Ph.D.		