VITAL THERAPIES INC

Form S-3

May 25, 2018

As filed with the Securities and Exchange Commission on May

25, 2018

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S 3

REGISTRATION STATEMENT

Under

THE SECURITIES ACT OF 1933

VITAL THERAPIES, INC.

(Exact name of Registrant as specified in its charter)

Delaware 56-2358443

(I.R.S.

(State or other jurisdiction of incorporation or organization)

Employer Identification

Number)

15010

Avenue of Science, Suite 200 San Diego, California 92128 (858) 673-6840

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Russell J.

Cox

Chief

Executive

Officer

Vital

Therapies,

Inc.

15010

Avenue of

Science,

Suite 200

San Diego,

California

(858)673-6840

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

John M. Dunn General Counsel Vital Therapies, Inc.

15010 Avenue of Science, Suite 200 San Diego, California 92128

(858) 673-6840

Martin J. Waters Wilson Sonsini Goodrich & Rosati. Professional Corporation 12235 El Camino Real San Diego, California 92130 (858)350-2300

Approximate date of commencement of proposed sale to the public: From time to time, after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. "

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering."

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box."

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 the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Accelerated Large accelerated filer "

filer x

(Do not

check if a Smaller smaller reporting

Non-accelerated filer " reporting company "

company)

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. x

CALCULATION OF REGISTRATION FEE Title							
of Each Classount of be Stegristicsed to be	Proposed Maximum Offering Price Per Unit of Share	Proposed Maximum Aggregate rOffering Price	Amount of Registration Fee				
Registered Primary Offering: Common Stock, \$0.0001	(3)	(1)	_				
par value per share Preferred							
Stock, \$0.0001 p(alr)(2) value	(3)	(1)	_				
per share Whantants	(3)	(1)	_				
Debt (1)(2) Securities	(3)	(1)	_				
U (h)(3 ()4) Total	(3)	(1)	_				
Primary Offering Secondary	_	\$200,000,000(5)(6))\$11,832.55 (5)(8)				
Offering: Common Stock, \$2,500,000 par value	\$6.19 (7)	\$15,475,000	\$ 1,926.64 (7)				
per share Total Registration Fee		\$215,475,000	\$ 13,759.19 (8)				
(1) With respect to the primary offering, an indeterminate amount or number of the securities of each identified class							

amount or number of the securities of each identified class described in this registration statement is being registered as may from time to time be issued at indeterminate prices in U.S. Dollars. With respect to the primary offering, subject to

Rule 462(b) under the Securities Act of 1933, as amended, or the Securities Act, in no event will the aggregate maximum offering price of all securities sold by the registrant pursuant to this registration statement exceed \$200,000,000 or the equivalent thereof in one or more foreign currencies, foreign currency units or composite currencies.

- (2) Pursuant to Rule 416 under the Securities Act, this registration statement shall also cover any additional shares of the registrant's securities that become issuable by reason of any stock splits, stock dividends or similar transactions.
- (3) The registrant will determine the proposed maximum aggregate offering price per unit or share when it issues the above listed securities.
- (4) Any securities registered hereunder may be sold separately or as units with other securities registered hereunder.
- (5) The proposed maximum aggregate offering price has been estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act.
- (6) Pursuant to Rule 415(a)(6) under the Securities Act, includes \$112,456,567 of unsold securities (the "Unsold Securities") previously registered on the registrant's Form S-3 Registration Statement, filed with the Securities Exchange Commission (the "Commission") on May 12, 2015, (SEC File No. 333-204097) and declared effective by the Commission on May 26, 2015 (the "Prior Registration Statement").
- (7) Pursuant to Rule 457(c) of the Securities Act, the offering price and registration fee are computed based on the average high and low prices reported for the registrant's common stock traded on the Nasdaq Global Market on May 21, 2018.
- (8) Pursuant to Rule 415(a)(6) under the Securities Act, the registrant hereby offsets the total registration fee due under this Registration Statement by the amount of the filing fee associated with the \$112,456,567 of the Unsold Securities to be sold by the registrant. The associated filing fee of \$13,067.45 for the Unsold Securities under the Prior Registration Statement is hereby used to offset the current registration fee due.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains two prospectuses:

a base prospectus which covers both (a) the offering, issuance and sale by the registrant of up to a maximum aggregate offering price of \$200,000,000 of the registrant's common stock, preferred stock, debt securities, warrants, and/or units, and (b) the possible offering and sale by selling stockholders from time to time, after we announce topline data for our VTL-308 clinical study, of up to an aggregate of 2,500,000 shares of our common stock in one or more offerings, subject to market conditions and prices, liquidity objectives and other investment considerations; and a sales agreement prospectus supplement covering the offering, issuance and sale by the registrant of up to a maximum aggregate offering price of \$60,000,000 of the registrant's common stock that may be issued and sold under a sales agreement with Cantor Fitzgerald & Co.

The base prospectus immediately follows this explanatory note. The sales agreement prospectus supplement immediately follows the base prospectus. The common stock that may be offered, issued and sold by the registrant under the sales agreement prospectus supplement is included in the \$200,000,000 of securities that may be offered, issued and sold by the registrant under the base prospectus. Any portion of the \$60,000,000 included in the sales agreement prospectus supplement that is not previously sold or included in an active placement notice pursuant to the sales agreement is available for sale in other offerings pursuant to the base prospectus, and if no shares are sold under the sales agreement, the full \$200,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this prospectus is not complete and may be changed. We may not sell the securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 25, 2018 PROSPECTUS
Vital Therapies, Inc.
\$200,000,000
Common Stock, Preferred Stock,
Warrants, Debt Securities, Units
2,500,000 Shares of Common Stock
Offered by Selling Stockholders

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, up to an aggregate maximum amount of \$200,000,000.

In addition, selling stockholders named in this prospectus may from time to time, after we announce topline data for our VTL-308 clinical study, offer and sell up to an aggregate of 2,500,000 shares of our common stock in one or more offerings, subject to market conditions and prices, liquidity objectives and other investment considerations. We will not receive any of the proceeds from the sale of our common stock by the selling stockholders.

Our common stock is listed on The Nasdaq Global Market under the symbol "VTL." On May 21, 2018, the last reported sale price of our common stock on The Nasdaq Global Market was \$6.25 per share. There is currently no market for the other securities we may offer; however, we will provide information in any applicable prospectus supplement regarding any listing of securities other than shares of our common stock on any securities exchange.

This prospectus describes the general terms of the securities we may offer and the general manner in which we may offer these securities. Each time we sell securities described herein, and in certain cases where one or more selling stockholders sell securities pursuant to this prospectus, we or the selling stockholders, as applicable, will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. Such prospectus supplements may also add, update or change information contained in this prospectus. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Market or any other securities market or other exchange with respect to the securities covered by such prospectus supplement. You should carefully read this prospectus and any applicable prospectus supplement, together with the documents we incorporate by reference, before you invest.

We are an "emerging growth company" as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE "RISK FACTORS" ON PAGE 6 OF THIS PROSPECTUS AND IN THE PROSPECTUS SUPPLEMENT, IF APPLICABLE, BEFORE INVESTING IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

These securities may be offered and sold to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis. If underwriters, dealers, or agents are used to sell the securities, we will name them and describe their compensation in a prospectus supplement. In addition, the underwriters may over-allot a portion of the securities.

The date of this prospectus is, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this shelf process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings up to an aggregate dollar amount of \$200,000,000. In addition, the selling stockholders may from time to time, after we announce topline data for our VTL-308 clinical study, sell up to an aggregate amount of 2,500,000 shares of our common stock in one or more offerings, subject to market conditions and prices, liquidity objectives and other investment considerations. This prospectus provides you with a general description of the securities we or the selling stockholders may offer. Each time we sell securities described herein, and in certain cases where one or more selling stockholders sell securities pursuant to this prospectus, we or the selling stockholders, as applicable, will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. The prospectus supplement may also add to, update or change information contained in this prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement. You should carefully read both this prospectus and any accompanying prospectus supplement, together with the information incorporated by reference and any other offering materials. See "Where You Can Find More Information" and "Information Incorporated by Reference."

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or issuer free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related issuer free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related issuer free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits.

You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related issuer free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any issuer free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or issuer free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or issuer free writing prospectus, as applicable. You should assume that the information appearing in this prospectus, any prospectus supplement or any document incorporated by reference is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date. References in this prospectus to the "company," "we," "us" and "our" and similar terms or Vital Therapies refer to Vital Therapies, Inc.

PROSPECTUS SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before deciding to invest in our securities. You should carefully read this entire prospectus and any applicable prospectus supplement, including each of the documents incorporated herein or therein by reference, before making an investment decision. Investors should carefully consider the information set forth under "Risk Factors" on page 6 of this prospectus and incorporated by reference to our annual report on Form 10-K and our quarterly reports on Form 10-Q.

Overview

We are a clinical-stage biotechnology company focusing on the discovery, development and commercialization of cell-based therapies capable of transforming the management of life-threatening conditions. Our initial product candidate, the ELAD® System, or ELAD, is a human-cell-based, bio-artificial liver which is being developed to improve rates of survival among patients with acute forms of liver failure.

We believe that the ELAD System may improve rates of overall survival and transform the management of acute forms of liver failure. Therapy with ELAD consists of a single, up to five-day treatment session, during which a patient's blood plasma is passed continuously through four cartridges containing approximately one pound of VTL C3A cells. These cells, which are grown by us from our proprietary cell banks, are human, liver-derived cells, which have been shown to retain a large number of the liver's synthetic and metabolic functions. During therapy with the ELAD System, we believe that the VTL C3A cells may infuse the patient's plasma with beneficial proteins, including growth factors, cell survival proteins, and anti-inflammatory proteins, and also remove certain harmful substances, such as endotoxin, all of which may better allow the patient's own liver to recover and regenerate, thereby potentially improving patient survival. The ELAD System has been granted orphan drug designation by the U.S. Food and Drug Administration, or FDA, and the European Commission, for the treatment of patients with acute liver failure, including alcoholic hepatitis.

In May 2016, we commenced our pivotal VTL-308 clinical study. This is a randomized and controlled study comparing the efficacy and safety of the ELAD System plus standard-of-care to standard-of-care alone in adults, under the age of 50 and without secondary organ failure, with liver failure from severe alcoholic hepatitis, or sAH. VTL-308 was designed to enroll at least 150 subjects, and the study's primary endpoint is a Kaplan-Meier analysis of overall survival to be performed after the last subject to be enrolled has been followed for at least ninety days. The secondary endpoints are to evaluate the proportion of survivors at study days 28 and 91, as well as the proportion of subjects achieving a certain threshold of bilirubin reduction and surviving without transplant. In March 2018, we completed enrollment in VTL-308, and we expect to announce topline data in the third quarter of 2018, likely September. If the data is positive, these results are expected to form the basis for a marketing application to the FDA and other global health regulatory authorities for the approval of the ELAD System for the treatment of sAH. We anticipate performing follow-on studies in other acute forms of liver failure.

Results from a prior study, VTI-208, informed the design of the VTL-308 study and guided its focus on subjects under the age of 50 without secondary organ failure. The VTI-208 study enrolled 203 subjects between 2013 and 2015 with alcohol-induced liver decompensation, most of whom were experiencing liver failure as a result of sAH. In August 2015, we learned that the Kaplan-Meier analysis of overall survival was not statistically different between groups in the intention-to-treat, or ITT, population. However, in a pre-specified subset of 120 subjects with Model for End-stage Liver Disease, or MELD, scores <28, the Kaplan-Meier analysis of overall survival did approach statistical significance. A subject's MELD score is a tool for characterizing the severity of liver disease and degree of secondary organ dysfunction, and also provides a prognosis for survival at 90 days. In another pre-specified exploratory analysis of 101 subjects with less than the median age of 46.9 years, the Kaplan-Meier analysis of overall survival also favored the ELAD-treated subjects.

Earlier studies, prior to VTI-208, were primarily designed to identify patient populations and clinical trial designs that were appropriate to pursue in pivotal clinical studies. Two randomized controlled trials (VTI-201 and VTI-206) were conducted primarily in U.S. subjects to help better define the population that would be appropriate for study in pivotal clinical trials. The outcomes of these studies suggested that subjects in whom alcohol was the predominant factor leading to their acute liver failure were a particularly suitable population for study in pivotal clinical trials. Additionally, a 69-subject randomized, controlled clinical trial (VTIC-301) was performed at two hospital centers in Beijing, China, primarily in subjects with an acute form of liver failure caused by viral hepatitis B. Data showed a statistically significant improvement in transplant-free survival rates in the ELAD-treated group as compared with the control group, while data from a subset comprising the first 49 subjects in this clinical trial revealed a statistically significant difference in overall transplant-free survival.

In the United States, we estimate that at least 40,000 patients annually experience an acute form of liver failure that may be addressed by the ELAD System. These include liver failure from sAH, post-surgical liver failure, and fulminant hepatic failure. Except for liver transplant, which is severely limited by the availability of organs or not advisable for many patients under current guidelines, the current standard-of-care is primarily focused on the management of complications, which does not restore lost liver function and is associated with a high rate of mortality.

In addition to the ELAD System, we are also exploring the use of proteins produced by our VTL C3A cells to resuscitate donated livers prior to transplantation into patients as there is a need to increase the number and quality of livers available for transplant. Our pre-clinical research in this field is being done in collaboration with leading research centers in the U.S. and the UK.

We currently retain worldwide rights to the ELAD System free of royalties. If we receive marketing authorization for our products, we intend to establish targeted commercialization and marketing capabilities for our products in the United States and Europe by developing a sales force that would focus on academic medical centers and other centers of excellence treating liver failure. In the United States, for instance, we believe that the approximately 125 active liver transplant centers, as well as a few dozen other specialized liver centers, represent appropriate sites for the placement of the ELAD System. As such, we believe a small, targeted sales force could effectively cover these institutions and successfully commercialize our ELAD System, if approved. We believe a similar sized sales force would be appropriate for Europe. For commercialization of the ELAD System, if approved, outside of the United States and Europe, we may enter into collaborations or license agreements with strategic partners. Corporate Information

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, California 92128. Our telephone number is (858) 673-6840. Our website address is http://www.vitaltherapies.com. Information contained on the website is not incorporated by reference into this prospectus, and should not be considered to be part of this prospectus.

"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 trade names referred to in this prospectus are the property of their respective owners. Except as set forth above and solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and TM 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. Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We may remain an "emerging growth company" until December 31, 2019 (the fiscal year-end following the fifth anniversary of the completion of our initial public offering), although we may cease to be an "emerging growth company" earlier under

certain circumstances, including (i) if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30, in which case we would cease to be an "emerging growth company" as of the following December 31, or (ii) if our gross revenue exceeds \$1.07 billion in any 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.

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 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 currently plan to take advantage of these reporting exemptions until we are no longer an "emerging growth company." The Securities We May Offer

We may offer up to \$200,000,000 of common stock, preferred stock, warrants, debt securities, and/or units in one or more offerings and in any combination. In addition, the selling stockholders may sell, from time to time, after we announce topline data for our VTL-308 clinical study, up to an aggregate of 2,500,000 shares of our common stock in one or more offerings, subject to market conditions and prices, liquidity objectives and other investment considerations. This prospectus provides you with a general description of the securities we and the selling stockholders may offer. Each time we sell securities described herein, and in certain cases where one or more selling stockholders sell securities pursuant to this prospectus, we or the selling stockholders, as applicable, will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered.

We or the selling stockholders may sell the securities to or through underwriters, dealers or agents, directly to purchasers or through a combination of any of these methods of sale or as otherwise set forth below under "Plan of Distribution." We and the selling stockholders, as well as any agents acting on our or their behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Any prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

Each holder of our common stock is entitled to one vote for each share on all matters to be voted upon by the stockholders, and there are no cumulative rights. Subject to any preferential rights of any outstanding preferred stock, holders of our common stock are entitled to receive ratably the dividends, if any, as may be declared from time to time by the board of directors out of legally available funds. If there is a liquidation, dissolution or winding up of our company, holders of our common stock would be entitled to share ratably in our net assets legally available for distribution to stockholders after the payment of all our debts and liabilities and any preferential rights of any

Preferred Stock

outstanding preferred stock.

Common Stock

Our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including dividend rights, conversion rights, voting rights, redemption privileges and liquidation preferences, of each series of preferred stock.

Each series of preferred stock will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or

winding up, voting rights and rights to convert into common stock. We have no present plans to issue any shares of preferred stock nor are any shares of our preferred stock presently outstanding.

Warrants

We may issue warrants for the purchase of common stock or preferred stock. We may issue warrants independently or together with other securities.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the "debt securities." The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may issue debt securities that are convertible into shares of our common stock.

The senior and subordinated debt securities will be issued under separate indentures between us and a trustee. We have summarized the general features of the debt securities to be governed by the indentures. These indentures have been filed as exhibits to the registration statement of which this prospectus forms a part. We encourage you to read these indentures. Instructions on how you can get copies of these documents are provided under the heading "Where You Can Find More Information."

Units

We may issue units comprised of one or more of the other classes of securities issued by us as described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under "Part II—Item 1A—Risk Factors," in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and "Part II—Item 1A—Risk Factors" in our Quarterly Reports on Form 10-Q, all of which are incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each applicable prospectus supplement, and the information incorporated by reference in this prospectus and each applicable prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, referred to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, referred to as the Exchange Act. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Those statements may appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business." Forward-looking statements include, but are not limited to, information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities and the effects of competition. 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," "plans," "potential," "predishould," "can," "would," "continue," "will" or similar expressions and the negatives of those terms.

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

the cost, timing, and results of our clinical programs for the ELAD® System, including statements related to our VTL-308 phase 3 clinical trial;

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, including our anticipated gross margins if commercialized;

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 or explore future uses of 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, projected cash runway and needs for additional financing; and

our ability to 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 prospectus and the documents incorporated by reference into this prospectus. 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 prospectus or the date of the documents incorporated by reference herein. You should read this prospectus and the documents that we have filed as exhibits to the registration statement, of which this prospectus is a part, 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.

This prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference may also contain estimates and other information concerning our industry that are based on government and industry publications. This information involves a number of assumptions and limitations, and you are cautioned not to give undue weight to these estimates. These government and industry publications generally indicate that their information has been obtained from sources believed to be reliable.

RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS

Our earnings have been inadequate to cover fixed charges and preference dividends. The following table sets forth the dollar amount of the coverage deficiency for each of the years ended December 31, 2015, 2016 and 2017, and the three-month period ended March 31, 2018. We have derived the deficiency of earnings to cover fixed charges and preference dividends from our historical financial statements. The following should be read in conjunction with our financial statements, including the notes thereto, included in our annual report on Form 10-K for the year ended December 31, 2017 and our quarterly report on Form 10-Q for the period ended March 31, 2018, both of which are incorporated by reference in this prospectus. See Exhibit 12.1 hereto for additional detail regarding the computation of the deficiency of earnings to cover fixed charges and preference dividends.

		Tillee	
Eigael Vae	Months Ended		
riscai i ea			
			March 31,
2015	2016	2017	2018
\$(52,023)	\$(40,969)	\$(52,078)	\$(14,388)

Deficiency of earnings available to cover combined fixed charges and preference dividends

As of the date of this prospectus, we have no shares of preferred stock outstanding, and consequently, our ratio of earnings to combined fixed charges and preferred share dividends and ratio of earnings to fixed charges would be identical.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, which may include working capital, capital expenditures and other corporate expenses. We may also use a portion of the net proceeds for the licensing or acquisition of complementary products, technologies or businesses. However, we have no present plans, agreements or commitments with respect to any potential acquisition, investment or license.

The timing and amount of our actual expenditures will be based on many factors, including, but not limited to, the timing of clinical trials, preparation for the timing of any submission of a biologics license application and decisions with respect to building commercial operations. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of all material characteristics of our capital stock as set forth in our amended and restated certificate of incorporation and second amended and restated bylaws. The summary does not purport to be complete and is qualified in its entirety by reference to our amended and restated certificate of incorporation and second amended and restated bylaws and to the applicable provisions of Delaware law.

General

Our authorized capital stock consists of 130,000,000 shares of common stock, par value \$0.0001 per share, and 20,000,000 shares of preferred stock, par value \$0.0001 per share.

Common Stock

Outstanding Shares

As of March 31, 2018, there were 42,368,864 shares of our common stock outstanding, held by approximately 69 stockholders of record, and no shares of our preferred stock outstanding. Our board of directors is authorized, without stockholder approval except as required by the listing standards of The Nasdaq Global Market, to issue additional shares of our capital stock.

Voting

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 second 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. Currently, certain stockholders affiliated with Muneer A. Satter, a member of our board of directors, have the right to nominate some members to our board. See "Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation, Bylaws and Fourth Amended and Restated Investors' Rights Agreement-- Senior Preferred Investors' Rights Agreement" below. 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 the 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 initial public offering, 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.

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

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.

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.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued under this prospectus, when paid for, will be fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without further action by the stockholders, to issue up to 20,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while

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providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock. Stock Options

As of March 31, 2018, we had outstanding options to purchase an aggregate of 7,740,808 shares of our common stock pursuant to our equity plans, at a weighted-average exercise price of \$6.66 per share. As of March 31, 2018, 56,506 shares of our common stock remain available for future grant or issuance under our 2014 Equity Incentive Plan and 261,168 shares are available for grant under our 2017 Inducement Equity Incentive Plan, each as amended. In addition, the number of shares available for issuance under the 2014 Plan was increased by 1,200,000 shares effective April 16, 2018.

Warrants

As of March 31, 2018, we had outstanding warrants to purchase an aggregate of 240,620 shares of our common stock at an exercise price of \$92.99 per share.

Registration Rights

Senior Preferred Investors' Rights Agreement

Pursuant to the Fourth Amended and Restated Investors' Rights Agreement, dated August 28, 2013, as amended (the "Senior Preferred IRA"), certain holders of 11,597,719 shares of common stock, including Muneer A. Satter and various trusts and other entities affiliated with Mr. Satter, are entitled to certain rights with respect to the registration of shares of common stock under the Securities Act. Subject to company-imposed lock-ups and certain limitations in the Senior Preferred IRA, including our ability to delay registration in certain circumstances, the holders of at least 25% of these securities then outstanding may demand on three occasions, that we use our reasonable best efforts to register these securities using a long form registration statement for public resale if the anticipated aggregate offering price, net of underwriting discounts and commissions, would exceed \$15 million. If we register any of our common stock either for our own account or for the account of other security holders, the holders of these securities are entitled to include their shares of common stock in that registration, subject to the ability of the underwriters to limit the number of shares included in the offering. We are obligated to use our reasonable best efforts to make short form registration statements available, and the holders of at least 25% of these securities then outstanding may also demand, but not more than two times in any 12-month period, that we register all or a portion of these securities using a short form registration statement, provided, among other limitations, that the proposed aggregate selling price is at least \$15 million. We will be responsible for paying all registration expenses, including the reasonable fees of legal counsel for the selling holders, and the holders selling their shares will be responsible for paying all selling expenses.

Registration rights under the Senior Preferred IRA terminate, as to a given holder of registration rights, when such holder and such holder's affiliates can sell all of their registrable securities in a three-month period pursuant to Rule 144. Accordingly, only Muneer A. Satter and various trusts and other entities affiliated with Mr. Satter who were parties to the Senior Preferred IRA have existing registration rights.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation, Bylaws and Fourth Amended and Restated Investors' Rights Agreement

Certain provisions of Delaware law, our amended and restated certificate of incorporation, our second amended and restated bylaws and the Senior Preferred IRA contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. We believe

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that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and second amended and restated bylaws include provisions that:

authorize our board of directors to issue, without further action by the 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;

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

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; 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; and

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

Senior Preferred Investors' Rights Agreement

The Senior Preferred IRA also provides that, for so long as Muneer A. Satter and various trusts and other entities affiliated with Mr. Satter, referred to 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

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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.

Although not currently serving as such, the Senior Preferred IRA provides that Mr. Satter can elect to serve as our Lead Director. Currently, Mr. Hasnain is serving as our Chairman.

Delaware Anti-Takeover Statute

We have elected in our amended and restated certificate of incorporation not to be subject to Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination, such as a merger, with a person or group owning 15% or more of the corporation's voting stock for a period of three years following the date the person became an interested stockholder, unless (with certain exceptions) the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner. Accordingly, we are not subject to any anti-takeover effects of Section 203. However, our amended and restated certificate of incorporation contains provisions that have the same effect as Section 203, except that they provide that certain of our current stockholders, including Mr. Satter and entities affiliated with him, and any persons to whom certain of our current stockholders sell their common stock will be deemed to have been approved by our board of directors, and thereby not subject to the restrictions set forth in Section 203.

Listing

Our common stock is listed on the Nasdaq Global Market under the symbol "VTL."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC, or AST. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

DESCRIPTION OF THE WARRANTS

We may issue warrants for the purchase of our preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with our preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of warrants;

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the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants:

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;

the dates on which the right to exercise the warrants shall commence and expire;

•f applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

•f applicable, a discussion of material U.S. federal income tax considerations;

the anti-dilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants;

any adjustments to the terms of the warrants resulting from the occurrence of certain events or from the entry into or consummation by us of certain transactions;

any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and

any additional terms of the warrants, including procedures and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of us.

This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

DESCRIPTION OF THE DEBT SECURITIES

The debt securities may be either secured or unsecured and will either be our senior debt securities or our subordinated debt securities. The debt securities may be issued under one or more separate indentures between us and a trustee to be specified in an accompanying prospectus supplement. Senior debt securities may be issued under a senior

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indenture and subordinated debt securities may be issued under a subordinated indenture. Together, the senior indenture and the subordinated indenture are called indentures in this description. This prospectus, together with the applicable prospectus supplement, will describe the terms of a particular series of debt securities.

The following is a summary of selected provisions and definitions of the indentures and debt securities to which any prospectus supplement may relate. Other specific terms of the applicable indenture and debt securities will be described in the applicable prospectus supplement. The summary of selected provisions of the indentures and the debt securities appearing below is not complete and is subject to, and qualified entirely by reference to, all of the provisions of the applicable indenture and certificates evidencing the applicable debt securities. If any particular terms of the indenture or debt securities described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. For additional information, you should look at the applicable indenture and the certificate evidencing the applicable debt security that is filed as an exhibit to the registration statement that includes the prospectus.

General

Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series.

We are not limited as to the amount of debt securities we may issue under the indentures. Unless otherwise provided in a prospectus supplement, a series of debt securities may be reopened to issue additional debt securities of such series.

The prospectus supplement relating to a particular series of debt securities will set forth:

whether the debt securities are senior or subordinated;

the offering price;

the title:

any limit on the aggregate principal amount;

the person who shall be entitled to receive interest, if other than the record holder on the record date;

the date or dates the principal will be payable;

the interest rate or rates, which may be fixed or variable, if any, the date from which interest will accrue, the interest payment dates and the regular record dates, or the method for calculating the dates and rates;

the place where payments may be made;

any mandatory or optional redemption provisions or sinking fund provisions and any applicable redemption or purchase prices associated with these provisions;

if issued other than in denominations of U.S. \$1,000 or any multiple of U.S. \$1,000, the denominations in which the debt securities shall be issuable:

if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;

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if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or a holder may elect payment to be made in a different currency;

the portion of the principal amount that will be payable upon acceleration of maturity, if other than the entire principal amount;

if the principal amount payable at stated maturity will not be determinable as of any date prior to stated maturity, the amount or method for determining the amount which will be deemed to be the principal amount;

if applicable, whether the debt securities shall be subject to the defeasance provisions described below under

• Satisfaction and Discharge; Defeasance" or such other defeasance provisions specified in the applicable prospectus supplement for the debt securities;

any conversion or exchange provisions;

whether the debt securities will be issuable in the form of a global security;

the deletion, addition or change in any event of default;

any change or modification to the subordination provisions applicable to the subordinated debt securities if different from those described below under "Subordinated Debt Securities;"

any deletion, addition or change in the covenants set forth in Article 10 of the indenture;

any paying agents, authenticating agents, security registrars or other agents for the debt securities, if other than the trustee;

any provisions relating to any security provided for the debt securities, including any provisions regarding the circumstances under which collateral may be released or substituted;

any provisions relating to guaranties for the securities and any circumstances under which there may be additional obligors;

any provisions granting special rights to holders when a specified event occurs;

any special tax provisions that apply to the debt securities;

with respect to the debt securities that do not bear interest, the dates for certain required reports to the applicable trustee;

any and all additional, eliminated or changed terms that will apply to the debt securities; and any other terms of such debt securities.

Unless otherwise specified in the prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at time of issuance is below market rates. The U.S. federal income tax considerations applicable to debt securities sold at a discount will be described in the applicable prospectus supplement.

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Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any partial redemption of debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange, any debt security of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion of the debt security being redeemed in part.

We will appoint the trustee as the initial security registrar. Any transfer agent, in addition to the security registrar initially designated by us, will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;

be deposited with the depositary or nominee or custodian; and

bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

an event of default is continuing with respect to the debt securities of the applicable series; or

any other circumstance described in a prospectus supplement has occurred permitting or requiring the issuance of any such security.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for all purposes under the indentures. Except in the above limited circumstances, owners of beneficial interests in a global security will not be:

entitled to have the debt securities registered in their names;

entitled to physical delivery of certificated debt securities; or

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considered to be holders of those debt securities under the indenture.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as "participants." Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary. The depositary policies and procedures may change from time to time. Neither any trustee nor we will have any responsibility or liability for the depositary's or any participant's records with respect to beneficial interests in a global security.

Payment and Paying Agents

Unless otherwise indicated in a prospectus supplement, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in a prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

40 business days prior to the date the money would be turned over to the applicable state; or

at the end of two years after such payment was due,

will be repaid to us thereafter. The holder may look only to us for such payment.

No Protection in the Event of a Change of Control

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly-leveraged transaction, whether or not such transaction results in a change in control.

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Covenants

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any financial or restrictive covenants.

Consolidation, Merger and Sale of Assets

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, we may not consolidate with or merge into any other person (other than one of our subsidiaries), in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person (other than a subsidiary of Vital Therapies, Inc.), unless:

the successor entity, if any, is a U.S. corporation, limited liability company, partnership, trust or other business entity; the successor entity assumes our obligations on the debt securities and under the indentures;

immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and

certain other conditions specified in the indenture are met.

Events of Default

Unless we indicate otherwise in a prospectus supplement, the following will be events of default for any series of debt securities under the indentures:

- (1) we fail to pay principal of or any premium on any debt security of that series when due;
- (2) we fail to pay any interest on any debt security of that series for 30 days after it becomes due;
- (3) we fail to deposit any sinking fund payment when due;
- (4) we fail to perform any other covenant in the indenture and such failure continues for 90 days after we are given the notice required in the indentures; and
- (5) certain events involving our bankruptcy, insolvency or reorganization.

Additional or different events of default applicable to a series of debt securities may be described in a prospectus supplement. An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

The trustee may withhold notice to the holders of any default, except defaults in the payment of principal, premium, if any, interest, any sinking fund installment on, or with respect to any conversion right of, the debt securities of such series. However, the trustee must consider it to be in the interest of the holders of the debt securities of such series to withhold this notice.

Unless we indicate otherwise in a prospectus supplement, if an event of default, other than an event of default described in clause (5) above, shall occur and be continuing with respect to any series of debt securities, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount and premium, if any, of the debt securities of that series, or if any debt securities of that series are

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original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, to be due and payable immediately. Unless we indicate otherwise in a prospectus supplement, if an event of default described in clause (5) above shall occur, the principal amount and premium, if any, of all the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, will automatically become immediately due and payable. Any payment by us on the subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under "Subordinated Debt Securities." Notwithstanding the foregoing, each indenture will provide that we may, at our option, elect that the sole remedy for an event of default relating to our failure to comply with our obligations described under the section entitled "Reports" below or our failure to comply with the requirements of Section 314(a)(1) of the Trust Indenture Act will for the first 180 days after the occurrence of such an event of default consist exclusively of the right to receive additional interest on the relevant series of debt securities at an annual rate equal to (i) 0.25% of the principal amount of such series of debt securities for the first 90 days after the occurrence of such event of default and (ii) 0.50% of the principal amount of such series of debt securities from the 91st day to, and including, the 180th day after the occurrence of such event of default, which we call "additional interest." If we so elect, the additional interest will accrue on all outstanding debt securities from and including the date on which such event of default first occurs until such violation is cured or waived and shall be payable on each relevant interest payment date to holders of record on the regular record date immediately preceding the interest payment date. On the 181st day after such event of default (if such violation is not cured or waived prior to such 181st day), the debt securities will be subject to acceleration as provided above. In the event we do not elect to pay additional interest upon any such event of default in accordance with this paragraph, the debt securities will be subject to acceleration as provided above.

In order to elect to pay the additional interest as the sole remedy during the first 180 days after the occurrence of any event of default relating to the failure to comply with the reporting obligations in accordance with the preceding paragraph, we must notify all holders of debt securities and the trustee and paying agent of such election prior to the close of business on the first business day following the date on which such event of default occurs. Upon our failure to timely give such notice or pay the additional interest, the debt securities will be immediately subject to acceleration as provided above.

After acceleration, the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amounts or interest, have been cured or waived. Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee reasonable indemnity. Generally, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee.

A holder of debt securities of any series will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

- (1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;
- (2) the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and

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the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request (3) from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 60 days after the original request.

Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security (if the debt security is convertible) without following the procedures listed in (1) through (3) above.

We will furnish the trustee an annual statement from our officers as to whether or not we are in default in the performance of the conditions and covenants under the indenture and, if so, specifying all known defaults.

Modification and Waiver

Unless we indicate otherwise in a prospectus supplement, the applicable trustee and we may make modifications and amendments to an indenture with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

We may also make modifications and amendments to the indentures for the benefit of holders without their consent, for certain purposes including, but not limited to:

to evidence the succession of another person to Vital Therapies, or successive successions, and the assumption by any such successor of the covenants of Vital Therapies in the indentures in compliance with Article 8 of the indentures; adding covenants;

adding events of default;

making certain changes to facilitate the issuance of the debt securities;

to add to, change or eliminate any of the provisions of the indentures or series of securities, provided that any such addition, change or elimination (A) shall neither (i) apply to any security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (ii) modify the rights of the holder of any such security with respect to such provision or (B) shall become effective only when there is no such security outstanding;

securing the debt securities;

providing for guaranties of, or additional obligors on, the debt securities;

to establish the form or term of debt securities as permitted by Sections 2.1 and 3.1 of the indenture;

providing for a successor trustee or additional trustees;

conforming the indenture to the description of the securities set forth in this prospectus or the accompanying prospectus supplement;

curing any ambiguity, defect or inconsistency; provided that such action shall not adversely affect the interest of the holders in any material respect;

permitting or facilitating the defeasance and discharge of the debt securities;

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make such other provisions in regard to matters or questions arising under the indentures or under any supplemental indentures as our board of directors may deem necessary or desirable, and which does not in each case adversely affect the interests of the holders of the debt securities of a series; and

comply with requirements of the SEC in order to effect or maintain the qualifications of the indentures under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act").

However, neither the trustee nor we may make any modification or amendment without the consent of the holder of each outstanding security of that series affected by the modification or amendment if such modification or amendment would:

change the stated maturity of the principal of, or any installment of principal or interest on, any debt security; reduce the principal, premium, if any, or interest on any debt security or any amount payable upon redemption or repurchase, whether at our option or the option of any holder, or reduce the amount of any sinking fund payments; reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;

change the place of payment or the currency in which any debt security is payable;

impair the right to enforce any payment after the stated maturity or redemption date;

•f subordinated debt securities, modify the subordination provisions in a materially adverse manner to the holders; •adversely affect the right to convert any debt security if the debt security is a convertible debt security; or

change the provisions in the indenture that relate to modifying or amending the indenture.

Satisfaction and Discharge; Defeasance

We may be discharged from our obligations on the debt securities, subject to limited exceptions, of any series that have matured or will mature or be redeemed within one year if we deposit enough money with the trustee to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities. Each indenture contains a provision that permits us to elect either or both of the following:

we may elect to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding. If we make this election, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities. we may elect to be released from our obligations under some or all of any financial or restrictive covenants applicable to the series of debt securities to which the election relates and from the consequences of an event of default resulting from a breach of those covenants.

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To make either of the above elections, we must irrevocably deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities. This amount may be made in cash and/or U.S. government obligations or, in the case of debt securities denominated in a currency other than U.S. dollars, cash in the currency in which such series of securities is denominated and/or foreign government obligations. As a condition to either of the above elections, for debt securities denominated in U.S. dollars, we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the action.

With respect to debt securities of any series that are denominated in a currency other than United States dollars, "foreign government obligations" means:

direct obligations of the government that issued or caused to be issued the currency in which such securities are denominated and for the payment of which obligations its full faith and credit is pledged, or, with respect to debt securities of any series which are denominated in Euros, direct obligations of certain members of the European Union for the payment of which obligations the full faith and credit of such members is pledged, which in each case are not callable or redeemable at the option of the issuer thereof; or

obligations of a person controlled or supervised by or acting as an agency or instrumentality of a government described in the bullet above the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which are not callable or redeemable at the option of the issuer thereof.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing Law

The indentures and the debt securities will be governed by, and construed under, the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

No Personal Liability of Directors, Officers, Employees and Stockholders

No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours, or because of the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as a consideration for, the execution of such indentures and the issuance of the debt securities.

Regarding the Trustee

The indentures limit the right of the trustee, should it become our creditor, to obtain payment of claims or secure its claims.

The trustee will be permitted to engage in certain other transactions with us. However, if the trustee acquires any conflicting interest, and there is a default under the debt securities of any series for which it is trustee, the trustee must eliminate the conflict or resign.

Subordinated Debt Securities

The following provisions will be applicable with respect to each series of subordinated debt securities, unless otherwise stated in the prospectus supplement relating to that series of subordinated debt securities.

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The indebtedness evidenced by the subordinated debt securities of any series is subordinated, to the extent provided in the subordinated indenture and the applicable prospectus supplement, to the prior payment in full, in cash or other payment satisfactory to the holders of senior debt, of all senior debt, including any senior debt securities. Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, whether voluntary or involuntary, marshalling of assets, assignment for the benefit of creditors, or in bankruptcy, insolvency, receivership or other similar proceedings, payments on the subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt. In the event of any acceleration of the subordinated debt securities of any series because of an event of default with respect to the subordinated debt securities of that series, holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt before the holders of subordinated debt securities are entitled to receive any payment or distribution.

In addition, the subordinated debt securities will be structurally subordinated to all indebtedness and other liabilities of our subsidiaries, including trade payables and lease obligations. This occurs because our right to receive any assets of our subsidiaries upon their liquidation or reorganization, and your right to participate in those assets, will be effectively subordinated to the claims of that subsidiary's creditors, including trade creditors, except to the extent that we are recognized as a creditor of such subsidiary. If we are recognized as a creditor of that subsidiary, our claims would still be subordinate to any security interest in the assets of the subsidiary and any indebtedness of the subsidiary senior to us.

We are required to promptly notify holders of senior debt or their representatives under the subordinated indenture if payment of the subordinated debt securities is accelerated because of an event of default.

Under the subordinated indenture, we may not make payment on the subordinated debt securities if:

a default in our obligations to pay principal, premium, if any, interest or other amounts on our senior debt occurs and the default continues beyond any applicable grace period, which we refer to as a payment default; or any other default occurs and is continuing with respect to designated senior debt that permits holders of designated senior debt to accelerate its maturity, which we refer to as a non-payment default, and the trustee receives a payment blockage notice from us or some other person permitted to give the notice under the subordinated indenture.

in case of a payment default, when the default is cured or waived or ceases to exist, and

We will resume payments on the subordinated debt securities:

in case of a non-payment default, the earlier of when the default is cured or waived or ceases to exist or 179 days after the receipt of the payment blockage notice.

No new payment blockage period may commence on the basis of a non-payment default unless 365 days have elapsed from the effectiveness of the immediately prior payment blockage notice. No non-payment default that existed or was continuing on the date of delivery of any payment blockage notice to the trustee shall be the basis for a subsequent payment blockage notice.

As a result of these subordination provisions, in the event of our bankruptcy, dissolution or reorganization, holders of senior debt may receive more, ratably, and holders of the subordinated debt securities may receive less, ratably, than our other creditors. The subordination provisions will not prevent the occurrence of any event of default under the subordinated indenture.

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The subordination provisions will not apply to payments from money or government obligations held in trust by the trustee for the payment of principal, interest and premium, if any, on subordinated debt securities pursuant to the provisions described under the section entitled "Satisfaction and Discharge; Defeasance," if the subordination provisions were not violated at the time the money or government obligations were deposited into trust.

If the trustee or any holder receives any payment that should not have been made to them in contravention of subordination provisions before all senior debt is paid in full in cash or other payment satisfactory to holders of senior debt, then such payment will be held in trust for the holders of senior debt.

Senior debt securities will constitute senior debt under the subordinated indenture.

Additional or different subordination provisions may be described in a prospectus supplement relating to a particular series of debt securities.

Definitions

"Designated senior debt" means our obligations under any particular senior debt in which the instrument creating or evidencing the same or the assumption or guarantee thereof, or related agreements or documents to which we are a party, expressly provides that such indebtedness shall be designated senior debt for purposes of the subordinated indenture. The instrument, agreement or other document evidencing any designated senior debt may place limitations and conditions on the right of such senior debt to exercise the rights of designated senior debt.

Indebtedness" means the following, whether absolute or contingent, secured or unsecured, due or to become due, outstanding on the date of the indenture for such series of securities or thereafter created, incurred or assumed: our indebtedness evidenced by a credit or loan agreement, note, bond, debenture or other written obligation; all of our obligations for money borrowed;

all of our obligations evidenced by a note or similar instrument given in connection with the acquisition of any businesses, properties or assets of any kind,

our obligations:

as lessee under leases required to be capitalized on the balance sheet of the lessee under generally accepted accounting principles, or

as lessee under leases for facilities, capital equipment or related assets, whether or not capitalized, entered into or leased for financing purposes;

all of our obligations under interest rate and currency swaps, caps, floors, collars, hedge agreements, forward contracts or similar agreements or arrangements;

all of our obligations with respect to letters of credit, bankers' acceptances and similar facilities, including reimbursement obligations with respect to the foregoing;

all of our obligations issued or assumed as the deferred purchase price of property or services, but excluding trade accounts payable and accrued liabilities arising in the ordinary course of business;

all obligations of the type referred to in the above clauses of another person, the payment of which, in either case, we have assumed or guaranteed, for which we are responsible or liable, directly or indirectly, jointly or severally, as obligor, guarantor or otherwise, or which are secured by a lien on our property; and

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renewals, extensions, modifications, replacements, restatements and refundings of, or any indebtedness or obligation issued in exchange for, any such indebtedness or obligation described in the above clauses of this definition. "Senior debt" means the principal of, premium, if any, and interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-petition interest is allowable as a claim in any such proceeding, and rent payable on or in connection with, and all fees and other amounts payable in connection with, our indebtedness. However, senior debt shall not include:

expressly provide that it shall not be senior in right of payment to the subordinated debt securities or expressly provide that such indebtedness is on the same basis or "junior" to the subordinated debt securities; or debt to any of our subsidiaries, a majority of the voting stock of which is owned, directly or indirectly, by us. "Subsidiary" means a corporation more than 50% of the outstanding voting stock of which is owned, directly or indirectly, by us or by one or more of our other subsidiaries or by a combination of us and our other subsidiaries. For purposes of this definition, "voting stock" means stock or other similar interests which ordinarily has or have voting power for the election of directors, or persons performing similar functions, whether at all times or only so long as no senior class of stock or other interests has or have such voting power by reason of any contingency.

DESCRIPTION OF THE UNITS

We may issue units comprised of one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be held or transferred separately;

- a description of the terms of any unit agreement governing the units;
- a description of the provisions for the payment, settlement, transfer or exchange of the units;
- a discussion of material federal income tax considerations, if applicable; and
- whether the units if issued as a separate security will be issued in fully registered or global form.

The descriptions of the units in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable agreements. These descriptions do not restate those agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable agreements because they, and not the summaries, define your rights as holders of the units. For more information, please review the forms of the relevant agreements, which will be filed with the SEC promptly after the offering of units and will be available as described in the section titled "Where You Can Find More Information."

SELLING STOCKHOLDERS

This prospectus also relates to the possible resale from time to time, after we announce topline data for our VTL-308 clinical study, by the stockholders named herein, who we refer to in this prospectus as the "selling

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stockholders," of up to an aggregate maximum amount of 2,500,000 shares of our common stock in one or more offerings, subject to market conditions and prices, liquidity objectives and other investment considerations. Such shares of common stock were issued and outstanding prior to the original filing date of the registration statement of which this prospectus forms a part. The selling stockholders originally acquired the shares of our common stock included in this prospectus through (i) our directed share program at our initial public offering, our follow-on public offerings, or otherwise on the open market, and (ii) several private placements of our common stock or convertible preferred stock prior to our initial public offering, with all such shares of convertible preferred stock converted into shares of our common stock in connection with our initial public offering. Additional information about the selling stockholders, where applicable, will be set forth in an applicable prospectus supplement, documents incorporated by reference in this prospectus or in a free writing prospectus we file with the SEC.

The following table sets forth the information about the selling stockholders, including the number of shares of our common stock beneficially owned by such selling stockholders immediately prior to the date of this prospectus, the number of shares offered hereby and registered by the registration statement of which this prospectus is a part, and the number of shares of our common stock to be beneficially owned by such selling stockholders after this offering. The number of shares to be owned after this offering assumes that all shares covered by this prospectus will be sold by the selling stockholders and that no additional shares of our common stock are subsequently bought or sold by the selling stockholders.

Name	Shares Benefic Owned Prior to the Da Prospectus	•	Shares Subject to Sale Pursuant to this Prospectus	Shares Beneficially Owned After Sale of All Shares Subject to Sale Pursuant to this Prospectus	
	Number of Shares	Percent		Number of Shares	Percent
Satter Medical Technology Partners, L.P.	4,250,000 (1)(3)	10.0	933,469	3,316,531	7.8
Trusts and Other Entities Affiliated with Muneer A. Satter	7,347,719 (2)(3)	17.3	1,566,531	5,781,188	13.6

- (1) Muneer A. Satter has sole voting and dispositive power over all such shares. Mr. Satter disclaims beneficial ownership of all such shares, except to the extent of his pecuniary interest.
- (2) Includes (a) 4,202,930 shares that are held by the Muneer A. Satter Revocable Trust for which Mr. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such shares and (b) 2,929,347 shares that are held by various other trusts and other entities for which Mr. Satter serves as trustee, investment adviser or manager and, in such capacity, has sole voting and dispositive power over all such shares. Also includes (i) warrants to acquire 60,639 shares of common stock that are held by the Muneer A. Satter Revocable Trust, (ii) warrants to acquire 61,533 shares of common stock that are held by various trusts and other entities for which Mr. Satter serves as trustee, investment adviser or manager, and (iii) stock options to purchase 93,270 shares of common stock held by Mr. Satter. Excludes a stock option to purchase 29,538 shares of common stock, which vests and becomes exercisable on the earlier of May 23, 2019 or the date immediately prior to our 2019 annual meeting of stockholders. Mr. Satter disclaims beneficial ownership of all shares included in clauses (b) and (ii) above, except to the extent of his pecuniary interest.
- (3) Shares may also be sold, transferred or otherwise disposed of at any time and from time to time, after we announce topline data for our VTL-308 clinical study, in transactions exempt from the registration requirements of the Securities Act. The address for each selling stockholder is c/o Satter Management Co., L.P., 676 N. Michigan Avenue, Suite

4000, Chicago, IL 60611.

No selling stockholder has had any material relationship with us or any of our affiliates within the past three fiscal years, other than Muneer A. Satter is a member of our Board of Directors and the selling stockholders are entitled to the board and registration rights described in this prospectus under "Description of Capital Stock."

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PLAN OF DISTRIBUTION

We and/or the selling stockholders, if applicable, may sell the securities offered through this prospectus and any accompanying prospectus supplement, if required, in any of the following ways: (1) to or through underwriters or dealers, (2) directly to purchasers, including our affiliates, (3) through agents, or (4) through a combination of any these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices.

We or the selling stockholders may use any one or more of the following methods when selling securities: underwritten transactions;

privately negotiated transactions;

sales through the Nasdaq Global Market or on any national securities exchange or quotation service on which the shares of common stock may be listed or quoted at the time of sale;

sales in the over-the-counter market;

ordinary brokerage transactions and transactions in which the broker solicits purchasers;

broker-dealers may agree with the selling stockholders to sell a specified number of such securities at a stipulated price per share;

a block trade (which may involve crosses) in which the broker-dealer so engaged will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;

• 'at-the-market offerings" to or through a market maker or into an existing trading market, on an exchange or otherwise; exchange distributions and/or secondary distributions;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

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If required, a prospectus supplement with respect to a particular offering will set forth the terms of the offering, including the following:

the names of any underwriters or agents;

the name or names of any managing underwriter or underwriters;

the name or names of any selling stockholders;

the sales price of the securities;

the net proceeds from the sale of the securities;

any delayed delivery arrangements;

any underwriting discounts, commissions or agency fees and other item constituting underwriters' or agents' compensation;

any initial price to public;

any discounts or concessions allowed or reallowed or paid to dealers; and

any commissions paid to agents.

A selling stockholder that is an entity may elect to make a pro rata in-kind distribution of shares of our common stock to its members, partners or stockholders pursuant to the registration statement of which this prospectus forms a part by delivering a prospectus. To the extent that such members, partners or stockholders are not affiliates of such selling stockholder, such members, partners or stockholders would thereby receive freely tradeable shares of our common stock pursuant to the distribution through a registration statement.

Sale through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers. The prospectus supplement will include the names of the principal underwriters the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time

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without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

If dealers are used in the sale of securities offered through this prospectus, we or the selling stockholders will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

To our knowledge, there are currently no plans, arrangements or understandings between the selling stockholders and any underwriter, dealer or agent regarding the sale of the shares covered by this prospectus by such selling stockholders. If any selling stockholder notifies us that a material arrangement has been entered into with an underwriter, dealer or other agent for the sale of shares through a block trade, special offering or secondary distribution, we may be required to file a prospectus supplement pursuant to applicable SEC rules promulgated under the Securities Act.

Direct Sales and Sales through Agents

We or the selling stockholders may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. Any required prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us or the selling stockholders. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We or the selling stockholders may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

At-the-Market Offerings

We or the selling stockholders may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4). To the extent that we or the selling stockholders make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us or the selling stockholders, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such agreement, we or the selling stockholders will sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we or the selling stockholders may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined as of the date of this prospectus. Pursuant to the terms of the agreement, we or the selling stockholders may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our common stock or other securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus or prospectus supplement.

Delayed Delivery Contracts

If the prospectus supplement indicates, we or the selling stockholders may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

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Market Making, Stabilization and Other Transactions

Unless the applicable prospectus supplement states otherwise, each series of offered securities will be a new issue and will have no established trading market. We may elect to list any series of offered securities on an exchange. Any underwriters that we or the selling stockholders use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

Any underwriter may also engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 under the Securities Exchange Act of 1934, as amended. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may make the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic Auctions

We or the selling stockholders may also make sales through the Internet or through other electronic means. Since we or the selling stockholders may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you should pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called "real-time" basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder's individual bids would be accepted, prorated or rejected. For example, in the case of a debt security, the clearing spread could be indicated as a number of "basis points" above an index treasury note. Of course, many pricing methods can and may also be used. Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

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General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us or the selling stockholders against certain liabilities, including liabilities under the Securities Act. Agents, dealers, and underwriters may engage in transactions with or perform services for us in the ordinary course of their businesses. The selling stockholders and any agents, underwriters or dealers that are involved in selling shares of our common stock may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such agents, underwriters or dealers and any profit on the resale of shares of our common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

There can be no assurance that any selling stockholder will sell any or all of the shares of our common stock registered pursuant to the registration statement of which this prospectus forms a part. The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than pursuant to the registration statement of which this prospectus forms a part. If sold under the registration statement of which this prospectus forms a part, the securities will be freely tradable in the hands of persons other than our affiliates.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, San Diego, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2017 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's requirement for additional financing to fund future operations as described in Note 1 to the consolidated financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Incorporation by Reference" are also available on our Internet website, www.vitaltherapies.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

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INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC; provided, however, that we are not incorporating any information furnished under any of Item 2.02 or Item 7.01 of any current report on Form 8-K (and exhibits filed on such form that are related to such items):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed on March 13, 2018, as amended on March 14, 2018;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, filed on May 8, 2018; and the description of our common stock contained in our Registration Statement on Form 8-A as filed with the SEC on November 15, 2013 pursuant to Section 12(b) of the Exchange Act.

We also incorporate by reference into this prospectus additional documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering of the securities described in this prospectus, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding those documents or portions of those documents deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus is deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

You should rely only on the information incorporated by reference or provided in this prospectus. Neither we nor the selling stockholders have authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Vital Therapies, Inc. Attn: Investor Relations 15010 Avenue of Science, Suite 200 San Diego, California 92128 (858) 673-6840

You may also access the documents incorporated by reference in this prospectus through our website at www.vitaltherapies.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

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The information in this prospectus is not complete and may be changed. We may not sell the securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 25, 2018

PROSPECTUS SUPPLEMENT

Vital Therapies, Inc.

Up to \$60,000,000

Common Stock

We have previously entered into a Controlled Equity OfferingSM sales agreement with Cantor Fitzgerald & Co., or the sales agreement, relating to shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$60,000,000 from time to time through Cantor Fitzgerald & Co., acting as agent.

Our common stock is listed on the Nasdaq Global Market under the symbol "VTL." On May 21, 2018, the last reported sale price of our common stock on the Nasdaq Global Market was \$6.25 per share.

Sales of our common stock, if any, under this prospectus supplement may be made in sales deemed to be "at-the-market offerings" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cantor Fitzgerald & Co. is not required to sell any specific number or dollar amount of securities, but will act as sales agent and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald & Co. and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Except as otherwise described in the sales agreement, Cantor Fitzgerald & Co. will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold. In connection with the sale of our common stock on our behalf, Cantor Fitzgerald & Co. will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cantor Fitzgerald & Co. will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cantor Fitzgerald & Co. with respect to certain liabilities, including liabilities under the Securities Act and The Securities Exchange Act of 1934, as amended, or Exchange Act.

We are an "emerging growth company" as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

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INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE "RISK FACTORS" ON PAGE S-6 OF THIS PROSPECTUS AND UNDER SIMILAR HEADINGS IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS BEFORE INVESTING IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this sales agreement prospectus supplement, referred to generally herein as the prospectus supplement, and the accompanying base prospectus, we may offer shares of our common stock having an aggregate offering price of up to \$60,000,000 from time to time at prices and on terms to be determined by market conditions at the time of offering.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this sales agreement prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both documents combined. If information in this sales agreement prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date, for example, a document incorporated by reference in this prospectus supplement, the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying base prospectus or in any document incorporated by reference in this prospectus supplement having an earlier date than the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. You should also read and consider the additional information under the captions "Information Incorporated by Reference" and "Where You Can Find More Information" in this prospectus supplement.

In making your investment decision, you should rely only on the information contained or incorporated by reference in this prospectus supplement, in the accompanying base prospectus and in any free writing prospectus with respect to this offering filed by us with the SEC. We have not, and Cantor Fitzgerald & Co., or Cantor, has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information you should not rely on it. You should assume that the information appearing in this prospectus supplement, the accompanying base prospectus, any free writing prospectus with respect to the offering filed by us with the SEC and the documents incorporated by reference herein and therein is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying base prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying base prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying base prospectus outside the United States. This prospectus supplement and the accompanying base prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying base prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

References in this prospectus supplement to the "company," "Vital Therapies," "we," "us" and "our" and similar terms refer to Vital Therapies, Inc.

We have filed or incorporated by reference exhibits to the registration statement of which this prospectus forms a part. You should read the exhibits carefully for provisions that may be important to you.

PROSPECTUS SUMMARY

This summary description about us, our business and this offering highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before deciding to invest in our common stock. You should carefully read this entire prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including each of the documents incorporated herein or therein by reference, before making an investment decision. Investors should carefully consider the information set forth under "Risk Factors" on page S-6 and incorporated by reference to our annual report on Form 10-K and our quarterly reports on Form 10-Q.

Overview

We are a clinical-stage biotechnology company focusing on the discovery, development and commercialization of cell-based therapies capable of transforming the management of life-threatening conditions. Our initial product candidate, the ELAD® System, or ELAD, is a human-cell-based, bio-artificial liver which is being developed to improve rates of survival among patients with acute forms of liver failure.

We believe that the ELAD System may improve rates of overall survival and transform the management of acute forms of liver failure. Therapy with ELAD consists of a single, up to five-day treatment session, during which a patient's blood plasma is passed continuously through four cartridges containing approximately one pound of VTL C3A cells. These cells, which are grown by us from our proprietary cell banks, are human, liver-derived cells, which have been shown to retain a large number of the liver's synthetic and metabolic functions. During therapy with the ELAD System, we believe that the VTL C3A cells may infuse the patient's plasma with beneficial proteins, including growth factors, cell survival proteins, and anti-inflammatory proteins, and also remove certain harmful substances, such as endotoxin, all of which may better allow the patient's own liver to recover and regenerate, thereby potentially improving patient survival. The ELAD System has been granted orphan drug designation by the U.S. Food and Drug Administration, or FDA, and the European Commission, for the treatment of patients with acute liver failure, including alcoholic hepatitis.

In May 2016, we commenced our pivotal VTL-308 clinical study. This is a randomized and controlled study comparing the efficacy and safety of the ELAD System plus standard-of-care to standard-of-care alone in adults, under the age of 50 and without secondary organ failure, with liver failure from severe alcoholic hepatitis, or sAH. VTL-308 was designed to enroll at least 150 subjects, and the study's primary endpoint is a Kaplan-Meier analysis of overall survival to be performed after the last subject to be enrolled has been followed for at least ninety days. The secondary endpoints are to evaluate the proportion of survivors at study days 28 and 91, as well as the proportion of subjects achieving a certain threshold of bilirubin reduction and surviving without transplant. In March 2018, we completed enrollment in VTL-308, and we expect to announce topline data in the third quarter of 2018, likely September. If the data is positive, these results are expected to form the basis for a marketing application to the FDA and other global health regulatory authorities for the approval of the ELAD System for the treatment of sAH. We anticipate performing follow-on studies in other acute forms of liver failure.

Results from a prior study, VTI-208, informed the design of the VTL-308 study and guided its focus on subjects under the age of 50 without secondary organ failure. The VTI-208 study enrolled 203 subjects between 2013 and 2015 with alcohol-induced liver decompensation, most of whom were experiencing liver failure as a result of sAH. In August 2015, we learned that the Kaplan-Meier analysis of overall survival was not statistically different between groups in the intention-to-treat, or ITT, population. However, in a pre-specified subset of 120 subjects with Model for End-stage Liver Disease, or MELD, scores <28, the Kaplan-Meier analysis of overall survival did approach statistical significance. A subject's MELD score is a tool for characterizing the severity of liver disease and degree of secondary organ dysfunction, and also provides a prognosis for survival at 90 days. In another pre-specified exploratory analysis of 101 subjects with less than the median age of 46.9 years, the Kaplan-Meier analysis of overall survival also favored the ELAD-treated subjects.

Earlier studies, prior to VTI-208, were primarily designed to identify patient populations and clinical trial designs that were appropriate to pursue in pivotal clinical studies. Two randomized controlled trials (VTI-201 and VTI-206) were conducted primarily in U.S. subjects to help better define the population that would be appropriate for study in pivotal clinical trials. The outcomes of these studies suggested that subjects in whom alcohol was the predominant factor leading to their acute liver failure were a particularly suitable population for study in pivotal clinical trials. Additionally, a 69-subject randomized, controlled clinical trial (VTIC-301) was performed at two hospital centers in Beijing, China, primarily in subjects with an acute form of liver failure caused by viral hepatitis B. Data showed a statistically significant improvement in transplant-free survival rates in the ELAD-treated group as compared with the control group, while data from a subset comprising the first 49 subjects in this clinical trial revealed a statistically significant difference in overall transplant-free survival.

In the United States, we estimate that at least 40,000 patients annually experience an acute form of liver failure that may be addressed by the ELAD System. These include liver failure from sAH, post-surgical liver failure, and fulminant hepatic failure. Except for liver transplant, which is severely limited by the availability of organs or not advisable for many patients under current guidelines, the current standard-of-care is primarily focused on the management of complications, which does not restore lost liver function and is associated with a high rate of mortality.

In addition to the ELAD System, we are also exploring the use of proteins produced by our VTL C3A cells to resuscitate donated livers prior to transplantation into patients as there is a need to increase the number and quality of livers available for transplant. Our pre-clinical research in this field is being done in collaboration with leading research centers in the U.S. and the UK.

We currently retain worldwide rights to the ELAD System free of royalties. If we receive marketing authorization for our products, we intend to establish targeted commercialization and marketing capabilities for our products in the United States and Europe by developing a sales force that would focus on academic medical centers and other centers of excellence treating liver failure. In the United States, for instance, we believe that the approximately 125 active liver transplant centers, as well as a few dozen other specialized liver centers, represent appropriate sites for the placement of the ELAD System. As such, we believe a small, targeted sales force could effectively cover these institutions and successfully commercialize our ELAD System, if approved. We believe a similar sized sales force would be appropriate for Europe. For commercialization of the ELAD System, if approved, outside of the United States and Europe, we may enter into collaborations or license agreements with strategic partners. Corporate Information

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. Information contained on the website is not incorporated by reference into this prospectus, and should not be considered to be part of this prospectus.

"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 trade names referred to in this prospectus are the property of their respective owners. Except as set forth above and solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and TM 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. Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We may remain an "emerging growth company" until as late as December 31, 2019 (the fiscal year-end following the fifth anniversary of the completion of our initial public offering), although we may cease to be an "emerging growth

company" earlier under certain circumstances, including (i) if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30, in which case we would cease to be an "emerging growth company" as of the following December 31, or (ii) if our gross revenue exceeds \$1.07 billion in any 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.

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 currently plan to take advantage of these reporting exemptions until we are no longer an "emerging growth company."

THE OFFERING

Common Stock Offered by Us

Shares of our common stock having an aggregate offering price of up to \$60,000,000.

Plan of Distribution

"At-the-market offering" that may be made from time to time through our sales agent, Cantor Fitzgerald & Co. See "Plan of Distribution" on page S-15 of this prospectus supplement. We currently intend to use the net proceeds from this offering, if any, for general corporate

Use of Proceeds

purposes and working capital requirements. See "Use of Proceeds" on page S-12 of this prospectus

supplement.

Nasdaq Global

VTL

Market Symbol

Investing in our common stock involves significant risks. Please see "Risk Factors" on page S-6 of

Risk Factors

this prospectus supplement and in the documents incorporated by reference herein, to read about

factors you should consider before deciding to purchase shares of our common stock.

RISK FACTORS

You should consider carefully the risks described below and discussed under the section captioned "Risk Factors" contained in our most recent Annual Report on Form 10-K, as revised or supplemented by our Quarterly Reports on Form 10-Q since the filing of our most recent Annual Report on Form 10-K, each of which is incorporated by reference in this prospectus in their entirety, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus and any free writing prospectus with respect to this offering filed by us with the SEC, before you make a decision to invest in our common stock. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of these risks actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered may be higher than the book value per share of our common stock, you may suffer immediate substantial dilution in the net tangible book value of the common stock you purchase in this offering. See "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

You may experience significant dilution as a result of future financings and the exercise of outstanding options or warrants.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including offerings pursuant to the accompanying base prospectus. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

In addition, we have a significant number of securities convertible into, or allowing the purchase of, our common stock. As of March 31, 2018, 317,674 shares of common stock were reserved for future issuance under our incentive stock plans. As of that date, there were also options to purchase 7,740,808 shares of our common stock outstanding and warrants to purchase 240,620 shares of our common stock outstanding. The exercise of outstanding options or warrants having an exercise price per share that is less than the offering price per share in this offering will increase dilution to investors in this offering.

We will have broad discretion in the use of the net proceeds from this offering and may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the use of the net proceeds, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and delay the development of the ELAD System. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments. These investments may not yield a favorable return to our stockholders.

If we sell additional equity or debt securities to fund our operations, it may impose restrictions on our business. In order to raise additional funds to support our operations, we may sell additional equity or debt securities, which may impose restrictive covenants that adversely impact our business. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities due to such restrictions, our business, financial condition and results of operations could be materially adversely affected.

Future sales of our common stock in the public market or other financings could cause our stock price to fall. Sales of a substantial number of shares of our common stock in the public market, the perception that these sales might occur or other financings, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. A substantial majority of the outstanding shares of our common stock are, and all of the shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless these shares are owned or purchased by "affiliates" as that term is defined in Rule 144 under the Securities Act. In addition, shares of common stock issuable upon exercise of outstanding options and shares reserved for future issuance under our incentive stock plan will be eligible for sale in the public market to the extent permitted by applicable vesting requirements and, in some cases, subject to compliance with the requirements of Rule 144. As a result, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws. Because we do not intend to declare cash dividends on our shares of common stock in the foreseeable future, stockholders must rely on appreciation of the value of our common stock for any return on their investment. We have never declared or paid cash dividends on our common stock and do not anticipate declaring or paying any cash dividends in the foreseeable future. In addition, the terms of any existing or future debt agreements may preclude us from paying dividends. As a result, we expect that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for the foreseeable future.

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.

The market price of our common stock has been, and may continue to be volatile and fluctuate significantly, and you may not be able to sell the shares you purchase in this offering at or above the offering price.

The market price of our common stock has been and is likely to continue to be highly volatile. Since our initial public offering in April 2014 at a price of \$12.00 per share, the sale price of stock as reported on The Nasdaq Global Market has ranged from \$2.25 to \$35.20 through May 10, 2018. Our announcement that the VTI-208 clinical trial failed to meet its primary or secondary endpoints resulted in a significant decline in the market price of our common stock. In addition, as with any public company, some investors hold a short position in our common stock. Such investors have published and distributed information about our company including on current and past clinical trials. Activities by these investors may increase the volatility of the market price of our common stock, and may affect our ability to raise additional funds and to complete our clinical trials.

Our stock price could be subject to wide fluctuations due to all disclosed risk factors but also including, without limitation:

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 potential 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.

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; 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information incorporated by reference in this prospectus supplement, the accompanying base prospectus and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, referred to as the Securities Act, and Section 21E of the Exchange Act of 1934. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Those statements may appear in this prospectus supplement, the accompanying base prospectus and the documents incorporated herein and therein by reference, particularly in the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business." Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities and the effects of competition. 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," "plans," "pote "predicts," "projects," "should," "can," "would," "continue," "will," or similar expressions and the negatives of those terms. These forward-looking statements include, among other things, statements about:

the cost, timing, and results of our clinical programs for the ELAD® System, including statements related to our VTL-308 phase 3 clinical trial;

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, including our anticipated gross margins if commercialized;

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 or explore future uses of 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, projected cash runway and needs for additional financing; and

our ability to 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 prospectus supplement and the documents incorporated by reference in this prospectus supplement and the accompanying base prospectus. 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 prospectus or the date of the documents incorporated by reference herein. You should read this prospectus and the documents that we have filed as exhibits to the registration statement, of which this prospectus is a part, 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.

This prospectus and the documents incorporated herein by reference may also contain estimates and other information concerning our industry, which are based on government and industry publications. This information involves a number of assumptions and limitations, and you are cautioned not to give undue weight to these estimates. These government and industry publications generally indicate that their information has been obtained from sources believed to be reliable.

USE OF PROCEEDS

The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Cantor as a source of financing.

Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include working capital, capital expenditures and other corporate expenses. We may also use a portion of the net proceeds for the licensing or acquisition of complementary products, technologies or businesses. However, we have no present plans, agreements or commitments with respect to any potential acquisition, investment or license. The timing and amount of our actual expenditures will be based on many factors, including but not limited to the timing of clinical trials, preparation for the timing of any submission of a biologics license application and decisions with respect to building commercial operations. As a result, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock upon closing of this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our historical net tangible book value as of March 31, 2018 was \$37.3 million, or \$0.88 per share, based on 42,368,864 shares of common stock outstanding as of March 31, 2018.

On a pro forma basis, after giving effect to our receipt of \$58.0 million of estimated net proceeds (after deducting commissions and estimated offering expenses payable by us) from our sale of \$60.0 million of common stock in this offering at an assumed public offering price of \$6.25 per share (the last reported sale price of our common stock on the Nasdaq Global Market on May 21, 2018), our as adjusted net tangible book value as of March 31, 2018 would have been \$95.3 million, or \$1.83 per share. This amount would represent an immediate increase in net tangible book value of \$0.95 per share of our common stock to existing stockholders and an immediate and substantial dilution in net tangible book value of \$4.42 per share of our common stock to new investors purchasing shares of common stock in this offering at the assumed public offering price.

The following table illustrates this hypothetical dilution on a per share basis:

Assumed public offering price per share \$6.25

Historical net tangible book value per share \$0.88

Increase per share attributable to new investors 0.95

As adjusted net tangible book value per share after this offering Dilution per share to new investors \$4.42

The table above assumes for illustrative purposes that an aggregate of 9,600,000 shares of our common stock are sold at a price of \$6.25 per share, the last reported sale price of our common stock on the Nasdaq Global Market on May 21, 2018, for aggregate gross proceeds of \$60.0 million. The shares sold in this offering, if any, will be sold from time to time at various prices.

The information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing and will also be affected by any securities sold by us, if any, pursuant the accompanying base prospectus. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$6.25 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$60.0 million is sold at that price, would increase our as adjusted net tangible book value per share after the offering to \$1.88 per share and would increase the dilution in net tangible book value per share to new investors to \$5.37 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$6.25 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$60.0 million is sold at that price, would decrease our as adjusted net tangible book value per share after the offering to \$1.77 per share and would decrease the dilution in net tangible book value per share to new investors to \$3.48 per share, after deducting commissions and estimated aggregate offering expenses payable by us.

The above table is based on 42,368,864 shares of common stock outstanding as of March 31, 2018, and excludes: 240,620 shares of our common stock issuable upon the exercise of outstanding warrants, at a weighted average exercise price of \$92.99 per share;

- 7,740,808 shares of our common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of \$6.66 per share; and
- 317,674 shares of our common stock available for future issuance pursuant to our equity incentive plans, which may be increased by the board of directors from time to time.

To the extent that outstanding stock options or warrants are exercised, investors purchasing our common stock in this offering will experience further dilution. In addition, to the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have previously entered into a Controlled Equity OfferingSM sales agreement with Cantor under which we may issue and sell shares of our common stock from time to time through Cantor acting as agent. We may issue and sell shares through this prospectus supplement having an aggregate gross sales price of up to \$60,000,000. The following summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. The sales agreement has been incorporated by reference as an exhibit to our Registration Statement on Form S-3 of which this prospectus forms a part.

Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cantor may sell our common stock by any method permitted by law deemed to be an "at-the-market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act, including sales made directly on The Nasdaq Global Market, or on any other existing trading market for our common stock. We may instruct Cantor not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Cantor may suspend the offering of common stock upon notice and subject to other conditions.

Except as otherwise described in the sales agreement, we will pay Cantor commissions, in cash, for its services in acting as agent in the sale of our common stock. Cantor will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Cantor under the terms of the sales agreement, will be approximately \$175,500. Settlement for sales of common stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of The Depository Trust Company or by such other means as we and Cantor may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the common stock shares under the terms and subject to the conditions set forth in the sales agreement. In connection with the sale of the common stock on our behalf, Cantor will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cantor will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the termination of the sales agreement as permitted therein. We and Cantor may each terminate the sales agreement at any time upon ten days' prior notice.

Any portion of the \$60,000,000 included in this sales agreement prospectus supplement that is not previously sold or included in an active placement notice pursuant to the sales agreement is available for sale in other offerings pursuant to the base prospectus, and if no further shares are sold under the sales agreement, the full \$200,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement. Cantor and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Cantor will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

This prospectus in electronic format may be made available on a website maintained by Cantor, and Cantor may distribute this prospectus and the accompanying base prospectus electronically.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, San Diego, California. Cantor is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2017 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's requirement for additional financing to fund future operations as described in Note 1 to the consolidated financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Incorporation by Reference" are also available on our Internet website, www.vitaltherapies.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC; provided, however, that we are not incorporating any information furnished under any of Item 2.02 or Item 7.01 of any current report on Form 8-K (and exhibits filed on such form that are related to such items):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed on March 13, 2018, as amended on March 14, 2018;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, filed on May 8, 2018; and the description of our common stock contained in our Registration Statement on Form 8-A as filed with the SEC on November 15, 2013 pursuant to Section 12(b) of the Exchange Act.

We also incorporate by reference into this prospectus additional documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering of the securities described in this prospectus, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding those documents or portions of those documents deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus is deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

You should rely only on the information incorporated by reference or provided in this prospectus. Neither we nor the selling stockholders have authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Vital Therapies, Inc. Attn: Investor Relations 15010 Avenue of Science, Suite 200 San Diego, California 92128 (858) 673-6840

You may also access the documents incorporated by reference in this prospectus through our website at www.vitaltherapies.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

Up to \$60,000,000

Common Stock

PROSPECTUS SUPPLEMENT

, 2018

Part II

Information Not Required in Prospectus

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the estimated costs and expenses (other than the actual SEC registration fee), other than underwriting discounts and commissions, payable by the registrant in connection with the sale of the securities being registered.

Securities and Exchange Commission registration fee	\$13,759
Accounting fees and expenses	6,000
Legal fees and expenses	135,500
Transfer agent fees and expenses	15,000
Miscellaneous	5,241
Total	\$175,500

Item 15. Indemnification of Directors and Officers

The Registrant's amended and restated certificate of incorporation contains provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, the personal liability of the Registrant's directors and executive officers for monetary damages for breach of their fiduciary duties as directors or officers. The Registrant's amended and restated certificate of incorporation and amended and restated bylaws provide that the Registrant must indemnify its directors and executive officers and may indemnify its employees and other agents to the fullest extent permitted by the General Corporation Law of the State of Delaware.

Sections 145 and 102(b)(7) of the General Corporation Law of the State of Delaware provide that a corporation may indemnify any person made a party to an action by reason of the fact that he or she was a director, executive officer, employee or agent of the corporation or is or was serving at the request of a corporation against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action if he or she acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of an action by or in right of the corporation, no indemnification may generally be made in respect of any claim as to which such person is adjudged to be liable to the corporation.

The Registrant has entered into indemnification agreements with its directors and executive officers, in addition to the indemnification provided for in its amended and restated certificate of incorporation and amended and restated bylaws, and intends to enter into indemnification agreements with any new directors and executive officers in the future.

The Registrant has purchased and intends to maintain insurance on behalf of any person who is or was a director or officer of the Registrant against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

See also the undertakings set out in response to Item 17 herein.

Item 16. Exhibits

A list of exhibits filed herewith is contained in the exhibit index that immediately precedes such exhibits and is incorporated herein by reference.

Item 17. Undertakings

- (a) The undersigned registrant hereby undertakes:
- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
 - To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or
- decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.
- That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective (2) amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
- Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As
- (B) provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated

by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to the effective date.

That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities

- of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer and sell such securities to such purchaser:
- Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding), is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.
- (d) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.

Exhibit Index

		Incorporated by Reference			
Exhibit Number	Exhibit Title	Form	File No.	Exhibi	tFiling Date
1.1*	Form of Underwriting Agreement.				
	Controlled Equity OfferingSM Sales Agreement, dated May 12,				
1.2	2015, by and between Vital Therapies, Inc. and Cantor	S-3	333-204097	1.2	May 12, 2015
	Fitzgerald & Co.				
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 Vital Therapies, Inc.	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
4.5*	Form of Certificate of Designation.				
4.6*	Form of Preferred Stock Certificate.				
4.7	Form of Senior Indenture.	S-3	333-204097	4.7	May 12, 2015
4.8*	Form of Senior Note.				
4.9	Form of Subordinated Indenture.	S-3	333-204097	4.9	May 12, 2015
4.10*	Form of Subordinated Note.				
4.11*	Form of Warrant.				
4.12*	Form of Unit Agreement.				
5.1**	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.				
12.1**	Statement re Computation of Ratio of Earnings to Fixed Charges and Preference Dividends.				
23.1**	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.				
23.2**	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).				
24.1**	Power of Attorney (included on the signature page).				

*To be filed by amendment or as an exhibit to a report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and incorporated herein by reference.

**Filed herewith.

Signatures

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on May 25, 2018.

Vital Therapies, Inc.

By: /s/ Russell J. Cox

Russell J. Cox

Chief Executive Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Russell J. Cox and Michael V. Swanson, and each of them acting individually, as his or her true and lawful attorneys-in-fact and agents, with full power of each to act alone, with full powers of substitution and re-substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this registration statement on Form S-3 with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, with full power of each to act alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Russell J. Cox Russell J. Cox	Director and Chief Executive Officer (Principal Executive Officer)	May 25, 2018
/s/ Michael V. Swanson Michael V. Swanson	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	May 25, 2018
/s/ Faheem Hasnain Faheem Hasnain	Chairman	May 25, 2018
/s/ Jean-Jacques Bienaimé Jean-Jacques Bienaimé	Director	May 25, 2018
/s/ Cheryl L. Cohen Cheryl L. Cohen	Director	May 25, 2018
/s/ Douglas E. Godshall	Director	May 25, 2018
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Douglas E. Godshall

/s/ Errol R. Halperin Errol R. Halperin

Director May 25, 2018

/s/ J. Michael Millis, M.D. Director May 25, 2018

J. Michael Millis, M.D.

/s/ Muneer A. Satter Muneer A. Satter

Director May 25, 2018

/s/ Lowell E. Sears Lowell E. Sears

Director May 25, 2018