

PROSPECTUS SUPPLEMENT
(To Prospectus dated August 2, 2018)



1,632,652 Shares of Common Stock Warrants to Purchase 816,326 Shares of Common Stock

We are offering 1,632,652 shares of our common stock, par value \$0.001 per share (the "Common Stock") and warrants to purchase up to 816,326 shares of Common Stock, representing 50% of the shares of Common Stock purchased in this offering (the "Warrants"), at an offering price of \$2.45 per share of Common Stock and associated Warrant, to certain accredited investors pursuant to this prospectus supplement and the accompanying prospectus. Each Warrant is exercisable at an exercise price of \$2.90 per share, is exercisable immediately upon issuance and will expire five years from the issuance date.

In a concurrent registered direct offering, we are also offering 24,906,134 shares of Common Stock and warrants to purchase 12,453,067 shares of Common Stock to certain institutional investors on the same terms as this offering.

Our Common Stock is listed on The Nasdaq Capital Market under the symbol "CLBS." The closing price of our Common Stock on February 12, 2021, as reported by Nasdaq, was \$2.33 per share. There is no established public trading market for the Warrants and we do not intend to list the Warrants on any national securities exchange or nationally recognized trading system.

Investing in our securities involves significant risks. See "Risk Factors" beginning on page S-5 of this prospectus supplement and on page 4 of the accompanying prospectus and the documents incorporated by reference herein.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	<u>Per Share</u>	<u>Total</u>
Offering price for Common Stock and associated Warrants	\$ 2.45	\$ 3,999,9
Proceeds, before expenses, to us (1)	\$ 2.45	\$ 3,999,9

(1) The amount of the offering proceeds to us presented in this table does not include proceeds from the exercise of the Warrants issued in the offering.

Delivery of the shares of Common Stock and Warrants will be made on or about February 17, 2021.

The date of this prospectus supplement is February 12, 2021.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”), under the Securities Act, using a “shelf” registration or continuous offering process. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and certain other matters and may add, update or change information in the accompanying prospectus, including the documents incorporated by reference into this prospectus supplement. The second part is the accompanying prospectus dated August 2, 2018, including the documents incorporated by reference therein, which provides you with general information about securities we may offer from time to time, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. 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 prospectus, on the other hand, you should rely on the information in this prospectus supplement. These documents contain important information you should consider when making your investment decision.

You should rely only on the information provided in this prospectus supplement and the accompanying prospectus, including any information incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with any other information. The information contained in this prospectus supplement and the accompanying prospectus speaks only as of the date set forth on the cover page and may not reflect subsequent changes in our business, financial condition, results of operations and prospects.

We are not, making offers to sell these securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to any person to whom it is unlawful to make such an offer or solicitation. You should read this prospectus supplement, the accompanying prospectus, including any information incorporated by reference, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference”.

Unless otherwise stated or the context requires otherwise, references in this prospectus to “Caladrius Biosciences,” the “company,” or the “Company,” “we,” “us,” or “our” refer to Caladrius Biosciences, Inc. and our subsidiaries, taken together. The Caladrius Biosciences logo and other trademarks or service marks of the Company appearing in this prospectus are the property of Caladrius Biosciences, Inc. All other brand names or trademarks appearing in this prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated by reference into this prospectus. It does not contain all the information you should consider before investing in our securities. Important information is incorporated by reference into this prospectus. To understand this offering fully, you should read carefully the entire prospectus, including "Risk Factors" and "Special Note Regarding Forward-Looking Statements," together with the additional information described under "Information Incorporated by Reference."

Company Overview

We are a clinical-stage biopharmaceutical company dedicated to the development and commercialization of cellular therapies designed to reverse disease and/or promote the regeneration of damaged tissue. We are developing first-in-class therapeutics based on the characteristics of naturally occurring CD34+ cells and their ability to stimulate the growth of new microvasculature. Our technology leverages these cells to enable the body's natural repair mechanisms using formulations unique to each medical indication.

Our leadership team has decades of collective biopharmaceutical development experience. Its goal is to develop and commercialize products that address important unmet medical needs based on a broad and versatile portfolio of candidates. Our current product candidates include HONEDRA[®] (formerly known as CLBS12), recipient of SAKIGAKE designation and eligible for early conditional approval in Japan for the treatment of critical limb ischemia ("CLI") and Buerger's Disease (a subset of CLI with an orphan population) based on the results of an ongoing clinical trial; OLOGO[™] (formerly known as CLBS14), a Regenerative Medicine Advanced Therapy ("RMAT") designated therapy for which we remain in discussion with the U.S. Food and Drug Administration (the "FDA") regarding the size and scope of a protocol for a Phase 3 confirmatory trial in subjects with no-option refractory disabling angina ("NORDA"); CLBS16, the subject of a recently initiated Phase 2b clinical trial in the U.S. (FREEDOM trial) for the treatment of coronary microvascular dysfunction ("CMD"); and CLBS201, a CD34+ cell therapy being explored as a potential treatment for moderate to severe chronic kidney disease ("CKD").

Ischemic Repair (CD34 Cell Technology)

The CD34+ cell was discovered as a result of the deliberate search for a stem cell capable of stimulating the development and/or repair of blood vessels. All tissues in the body maintain their function by replacing cells over time. In addition to the maintenance function, the body must also be capable of building new blood vessels after injury. A CD34+ cell is a stem cell that has the ability to stimulate new blood vessel formation at the level of the microvasculature. No other native cell discovered to date has demonstrated this same capability.

Our proprietary CD34+ cell technology has led to the development of therapeutic product candidates designed to address diseases and conditions caused by ischemia. Ischemia occurs when the supply of oxygenated blood to healthy tissue is restricted. Through the administration of CD34+ cells, we seek to promote the development and formation of new microvasculature and thereby increase blood flow to the impacted area. We believe that a number of conditions caused by underlying ischemic injury can be improved through our CD34+ cell technology, including but not limited to, CLI, CMD, NORDA and CKD.

HONEDRA[®] for Treatment of Critical Limb Ischemia

Our randomized and open-label, registration-eligible study of HONEDRA[®] in Japan for the treatment of CLI, a disease with limited therapeutic options and a higher combined incidence and mortality rate than all cancers but lung cancer, has shown strong results to date. The initial responses observed in the subjects who have reached an endpoint in this open label study are consistent with a positive therapeutic effect and safety profile as reported by previously published clinical trials in Japan. Although the study's enrollment has been slowed by the pandemic's impact in Japan, we are encouraged by the patient pre-screening pipeline that has been identified and hopes to conclude trial enrollment during the second quarter of 2021. While the final outcome of the trial will depend on all data from all subjects, data, to date, are very encouraging.

OLOGO™ for Treatment of No Option Refractory Disabling Angina

We acquired the rights to data and regulatory filings for a CD34+ cell therapy program for refractory angina that had been advanced to Phase 3 by a previous sponsor.

Based on the clinical evidence from the completed studies that a single administration of OLOGO™ reduces mortality, improves angina and increases exercise capacity in patients with otherwise untreatable angina, this product received Regenerative Medicine Advanced Therapy ("RMAT") designation from the FDA. We remain in discussion with the FDA regarding the size and scope of a phase 3 trial which, in combination with previously filed Phase 1, 2 and 3 data, will be considered for the registration of OLOGO™. Notably, the RMAT designation affords the product a 6-month review time for a biologics license application ("BLA"), once submitted.

CLBS16 for Treatment of Coronary Microvascular Dysfunction

In 2017, with the assistance of a \$1.9 million grant from the National Institutes of Health (Award Number R44HL135889), we initiated our program for CLBS16 for the treatment of coronary microvascular dysfunction ("CMD"), a disease that afflicts millions of patients with no current targeted treatment options. That study, the ESCaPE-CMD trial, was a Phase 2a proof-of-concept study that enrolled patients at the Mayo Clinic in Rochester, MN and Cedars-Sinai Medical Center in Los Angeles, CA. In June 2019, we announced the completion of enrollment in this study. Results of the first 17 of 20 patients enrolled in this trial who reached 6-month follow-up were presented as a rapid fire oral presentation on November 16, 2019 at the annual meeting of the American Heart Association in Philadelphia, PA by one of the principal investigators, Dr. Noel Bairey Merz, FACC, FAHA, FESC, the director of the Barbra Streisand Women's Heart Center at Cedars-Sinai in Los Angeles, CA. That data set showed a positive therapeutic effect with a statistically significant improvement in angina frequency, coronary flow reserve, Canadian Cardiovascular Society Angina Class and Seattle Questionnaire score, as well as an acceptable safety profile. The full data set from that study was presented at the SCAI 2020 Scientific Sessions Virtual Conference on May 14, 2020 by Dr. Timothy Henry FACC of the Christ Hospital in Cincinnati, Ohio. In December 2020, we commenced enrollment in our Phase 2b FREEDOM trial of CLBS16 as a therapy for CMD. The first patient in the study was subsequently treated in January 2021 at The Christ Hospital Health Network in Cincinnati, Ohio. This 105-patient double-blind randomized and placebo-controlled clinical trial (FREEDOM trial) is designed to further evaluate the efficacy and safety of intracoronary delivery of autologous CD34+ cells in subjects with CMD and without obstructive coronary artery disease.

CLBS201 for Treatment of Chronic Kidney Disease

We are planning to file an IND for the clinical study of CLBS201, a CD34+ investigational product for administration into the renal arteries to slow the deterioration or reverse the decline of renal function in patients with chronic kidney disease who exhibit rapidly progressive disease. Progressive kidney failure is associated with attrition of the microcirculation of the kidney. Pre-clinical studies in kidney disease and injury models have demonstrated that protection or replenishment of the microcirculation results in improved kidney function. A Phase 2 proof of concept study that is a randomized, placebo-controlled study is being considered for initiation in the 2nd half of 2021.

Additional Out-licensing Opportunities

Our broad intellectual property portfolio of cell therapy assets includes notable programs available for out-licensing in order to continue their clinical development. Our current long-term strategy focuses on advancing our therapies through development with the ultimate objective of obtaining market authorizations and entering commercialization, either alone or with partners, to provide treatment options to patients suffering from life-threatening medical conditions. We believe that we are well-positioned to realize potentially meaningful value increases within our own proprietary pipeline if we are successful in advancing our product candidates to their next significant development milestones.

Coronavirus Considerations

In December 2019, a novel strain of coronavirus (SARS-CoV-2), which causes COVID-19, was reported to have surfaced in China. In March 2020, the World Health Organization declared the outbreak of COVID-19 to be a pandemic, and the world's economies began to experience pronounced effects. Despite the FDA approval of multiple COVID-19 vaccines in late 2020, there remains uncertainty around the extent and duration of disruption, and any future related financial impact cannot be reasonably estimated at this time.

Corporate Information

We incorporated in 1980 as a Delaware corporation and our principal executive offices are located at 110 Allen Road, Second Floor, Basking Ridge, NJ 07920. Our telephone number is (908) 842-0100 and our corporate website address is www.caladrius.com. We include our website address in this prospectus only as an inactive textual reference and do not intend it to be an active link to our website. The information contained on, connected to or that can be accessed via our website is not part of this prospectus.

Recent Developments

January 2021 Private Placement

On January 21, 2021, we entered into a Securities Purchase Agreement with certain institutional and accredited investors, pursuant to which the Company issued and sold to the purchasers in a private placement (the "Private Placement") an aggregate of (i) 12,500,000 shares of Common Stock and (ii) warrants exercisable for up to an aggregate of 6,250,000 shares of Common Stock at a combined offering price of \$2.00 per share of Common Stock and associated Warrant. The warrants have an exercise price of \$2.90 per share. Each warrant was immediately exercisable and will expire five and one-half years from the issuance date. The Private Placement closed on January 25, 2021. The Company received gross proceeds of \$25.0 million in connection with the Private Placement, before deducting placement agent fees and related offering expenses

THE OFFERING

Common Stock offered by this prospectus supplement	1,632,652 shares of Common Stock
Warrants offered by this prospectus supplement	We are offering Warrants to purchase up to 816,326 shares of Common Stock (and the shares of Common Stock issuable upon the exercise of the Warrants). Each Warrant will be exercisable for one share of our common stock at an exercise price of \$2.90 per share, will be exercisable immediately upon issuance and will have a term of five years from the date of issuance. There is no established public trading market for the Warrants and we do not expect a market to develop. In addition, we do not intend to list the Warrants on the Nasdaq Capital Market, any other national securities exchange or any other nationally recognized trading system.
Offering Price per share and associated Warrant	\$2.45
Common stock to be outstanding after this offering and the concurrent registered direct offering	58,434,763 shares of Common Stock, which does not include any shares of Common Stock issuable upon the exercise of the Warrants or warrants issued in the concurrent registered direct offering.
Concurrent registered direct offering	In a concurrent registered direct offering, we are offering 24,906,134 shares of Common Stock and warrants to purchase 12,453,067 shares of Common Stock to certain accredited investors on the same terms as this offering.
Use of proceeds	We intend to use the net proceeds from the sale of the securities offered by this prospectus and the concurrent registered direct offering for general corporate purposes including, but not limited to the clinical advancement of our CD34+ cell technology platform in various cardiac and kidney indications. See “Use of Proceeds.”
Dividend policy	We do not anticipate paying any cash dividends on our Common Stock.
Nasdaq Capital Market symbol	Our Common Stock is listed on The Nasdaq Capital Market under the symbol “CLBS.”
Risk factors	Investing in our securities involves significant risks. See “Risk Factors” beginning on page S-5 of this prospectus supplement and on page 4 of the accompanying prospectus and the documents incorporated by reference herein.

Unless we indicate otherwise, all information in this prospectus is based on 31,895,977 shares of Common Stock, which includes 19,395,977 shares of Common Stock outstanding as of September 30, 2020, plus 12,500,000 shares of Common Stock that were issued in a private placement offering on January 21, 2021, and excludes:

- 1,105,408 shares of our Common Stock issuable upon exercise of outstanding stock options under our equity incentive plans with exercise prices ranging from \$1.80 to \$174.00 and having a weighted average exercise price of \$14.39 per share;
- 347,905 shares of our Common Stock issuable upon vesting of outstanding restricted stock units under our equity incentive plans;
- 2,638,355 shares of our Common Stock issuable upon the exercise of outstanding warrants, other than the warrants described in the bullet point below, with exercise prices ranging from \$2.06 to \$5.89 and having a weighted average exercise price of \$2.18 per share; and
- an aggregate of 13,269,393 shares of Common Stock issuable upon the exercise of the Warrants to be issued to the investors in this offering and the warrants issued in the concurrent registered direct offering at an exercise price of \$2.90 per share.

Unless we specifically state otherwise, all information in this prospectus supplement assumes that the Warrants offered hereby and the warrants issued in the concurrent registered direct offering are not exercised.

RISK FACTORS

Any investment in our securities involves a high degree of risk. Investors should carefully consider the risks described below and all of the information contained in this prospectus supplement and the accompanying prospectus before deciding whether to purchase the securities offered hereby. Our business, financial condition, results of operations and prospects could be materially and adversely affected by these risks if any of them actually occur. The risks and uncertainties described below are not the only ones we face. Additional risks not currently known to us or other factors not perceived by us to present significant risks to our business at this time also could adversely affect our business, operating results and financial conditions, as well as adversely affect the value of an investment in our securities. This prospectus supplement also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks we face as described below and elsewhere in this prospectus supplement.

Risks Related to this Offering

You will experience immediate and substantial dilution as a result of this offering and the concurrent registered direct offering and may experience additional dilution in the future.

You will incur immediate and substantial dilution as a result of this offering and the concurrent registered direct offering. After giving effect to the sale by us of 1,632,652 shares offered in this offering and 24,906,134 shares in the concurrent registered direct offering, each at an offering price of \$2.45 per share and associated warrant, and after deducting the placement agent fee for the concurrent registered direct offering and estimated offering expenses payable by us, investors in this offering can expect an immediate dilution of \$0.3766 per share. In addition, in the past, we issued options and warrants to acquire shares of Common Stock. To the extent these securities are ultimately exercised, you will sustain additional future dilution. In addition, exercise of the warrants that we issue in our past private placement transactions and the Warrants to be issued in the concurrent registered direct, or exercise of other outstanding options or warrants, could result in there being a significant number of additional shares outstanding and dilution to our stockholders.

Because we will have broad discretion and flexibility in how the net proceeds from this offering are used, we may use the net proceeds in ways in which you disagree.

Our management will have broad discretion as to the application of the net proceeds of this offering and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase the market price of our Common Stock.

The price of our Common Stock may be volatile.

The market price of our Common Stock may fluctuate substantially. For example, from January 1, 2019 through February 12, 2021, the market price of our Common Stock has fluctuated between \$1.05 and \$5.44. The price of our Common Stock that will prevail in the market after this offering may be higher or lower than the price that you have paid, depending on many factors, some of which are beyond our control and may not be related to our operating performance. Stock market volatility may also adversely affect the trading price of our Common Stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

Future sales of substantial amounts of our Common Stock, or the possibility that such sales could occur, could adversely affect the market price of our Common Stock.

Future sales in the public market of our Common Stock, including shares offered by the prospectus supplement or shares issued upon exercise of our outstanding stock options, warrants or convertible securities, or the perception by the market that these issuances or sales could occur, could lower the market price of our Common Stock or make it difficult for us to raise additional capital. As of September 30, 2020, we had 19,395,977 shares of Common Stock issued and outstanding, plus 12,500,000 shares of Common Stock that were issued in a private placement offering on January 21, 2021, substantially all of which we believe may be sold publicly, subject in some cases to volume and other limitations, provisions or limitations in registration rights agreements, or prospectus-delivery or other requirements relating to the effectiveness and use of registration statements registering the resale of such shares.

As of September 30, 2020, we had reserved for issuance 1,105,408 shares of our Common Stock issuable upon the exercise of outstanding stock options under our equity incentive plans at a weighted-average exercise price of \$14.39 per share, 347,905 shares of our Common Stock issuable upon vesting of outstanding restricted stock units under our equity incentive plans and we had outstanding warrants to purchase 2,638,355 shares of Common Stock at a weighted average exercise price of \$2.18 per share, plus warrants to purchase 6,250,000 shares of Common Stock at an exercise price of \$2.90 per share that were issued in a private placement offering on January 21, 2021. Subject to applicable vesting requirements, upon exercise of these options or warrants or vesting of these restricted stock units, the underlying shares may be resold into the public market, subject in some cases to volume and other limitations or prospectus-delivery requirements pursuant to registration statements registering the resale of such shares. In the case of outstanding options or warrants that have exercise prices that are below the market price of our Common Stock from time to time, our stockholders would experience dilution upon the exercise of these options.

Our business has been and may continue to be adversely affected by the COVID-19 pandemic.

The COVID-19 pandemic has affected our operations and may materially affect our business. In response to the pandemic, we have limited operations, including implemented work from home and social distancing policies. For instance, our clinical trials may suffer from lower than anticipated patient recruitment or enrollment and we may be forced to temporarily delay certain ongoing clinical trials. In addition, we risk a delay, default and/or nonperformance under our existing agreements arising from force majeure. The extent to which COVID-19 impacts our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the effectiveness and availability of the COVID-19 vaccines, among others.

In addition, COVID-19 has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions, social distancing and business shutdowns. We have taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily allowing all employees to work remotely. We have already suspended non-essential travel worldwide for our employees and are discouraging employee attendance at other gatherings. These measures could negatively affect our business. For instance, temporarily requiring all employees to work remotely may induce absenteeism, disrupt our operations or increase the risk of a cybersecurity incident. COVID-19 has also caused volatility in the global financial markets and threatened a slowdown in the global economy, which may negatively affect our ability to raise additional capital on attractive terms or at all.

The extent to which COVID-19 may impact our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the severity of COVID-19 or the effectiveness of actions to contain and treat COVID-19, particularly in the geographies where we or our third party suppliers, contract manufacturers, or contract research organizations operate. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operations and financial condition.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements regarding our business, financial condition, results of operations and prospects. Words such as "expects," "anticipates," "intends," "plans," "believes," "seeks," "estimates" and similar expressions or variations thereof are intended to identify forward-looking statements as denoted in this prospectus. Additionally, statements concerning future matters are forward-looking statements. These statements include, among other things, statements regarding:

- our ability to obtain sufficient capital or strategic business arrangements to fund our operations and expansion plans, including meeting our financial obligations under various licensing and other strategic arrangements, the funding of our clinical trials for product candidates, and the commercialization of the relevant technology;
- our ability to build and maintain the management and human resources infrastructure necessary to support the growth of our business;
- whether a market is established for our cell-based products and services and our ability to capture a meaningful share of this market;
- scientific, regulatory and medical developments beyond our control;
- our ability to obtain and maintain, as applicable, appropriate governmental licenses, accreditations or certifications or to comply with healthcare laws and regulations or any other adverse effect or limitations caused by government regulation of our business;
- whether any of our current or future patent applications result in issued patents, the scope of those patents and our ability to obtain and maintain other rights to technology required or desirable for the conduct of our business; and our ability to commercialize products without infringing upon the claims of third party patents;
- whether any potential strategic or financial benefits of various licensing agreements will be realized;
- the results of our development activities;
- our ability to complete our other planned clinical trials (or initiate other trials) in accordance with our estimated timelines due to delays associated with enrolling patients due to the novelty of the treatment, the size of the patient population and the need of patients to meet the inclusion criteria of the trial or otherwise;
- the extent to which the COVID-19 coronavirus may impact our business, including our clinical trials and financial condition; and
- other factors discussed in "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on March 5, 2020.

The words "believe," "anticipate," "believe," "design," "estimate," "forecast," "outlook," "plan," "predict," "seek," "expect," "intend," "may," "could," "should," "potential," "likely," "project," "continue," "will," and "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed in our forward-looking statements and you should not place undue reliance on these statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those discussed under the heading "Risk Factors" contained or incorporated in this prospectus supplement and the accompanying prospectus and any free writing prospectus we may authorize for use in connection with a specific offering. These factors and the other cautionary statements made in this prospectus supplement and the accompanying prospectus should be read as being applicable to all related forward-looking statements whenever they appear in this prospectus supplement and the accompanying prospectus. Except as required by law, we do not assume any obligation to update any forward-looking statement. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Although forward-looking statements in this prospectus reflect the good faith judgment of our management, such statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties and actual results and outcomes may differ materially from the results and outcomes discussed in or anticipated by the forward-looking statements. Factors that could cause or contribute to such differences in results and outcomes include, without limitation, those specifically addressed under the heading “Risks Factors” above, as well as those discussed elsewhere in this prospectus. Readers are urged not to place undue reliance on these forward-looking statements, which speak only as of the date of this prospectus. We file reports with the SEC and our electronic filings with the SEC (including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, and any amendments to these reports) are available free of charge on the SEC’s website at <http://www.sec.gov>. You can also read and copy any materials we file with the SEC at the SEC’s Public Reference Room at 100 F Street, NE, Washington, DC 20549. You can obtain additional information about the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330.

We undertake no obligation to revise or update any forward-looking statements in order to reflect any event or circumstance that may arise after the date of this prospectus, except as required by law. Readers are urged to carefully review and consider the various disclosures made throughout the entirety of this prospectus, which are designed to advise interested parties of the risks and factors that may affect our business, financial condition, results of operations and prospects.

USE OF PROCEEDS

We estimate that the net proceeds from the offering and the concurrent registered direct offering will be approximately \$60.4 million, after deducting the placement agent fees for the concurrent registered direct offering and estimated offering expenses payable by us and excluding any proceeds we may receive upon exercise of the Warrants and the warrants being offered in the concurrent registered direct offering.

We intend to use the proceeds from this offering for working capital and general corporate purposes, including the advancement of its CD34+ technology-based clinical programs.

Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

DILUTION

If you invest in our securities, your interest will be diluted immediately to the extent of the difference between the offering price and the as adjusted net tangible book value per share of our Common Stock after this offering and the concurrent registered direct offering.

Our net tangible book value as of September 30, 2020 was approximately \$37.5 million or \$1.9327 per share of Common Stock. Net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of Common Stock outstanding. Our pro forma net tangible book value as of September 30, 2020 was \$60.7 million, or \$1.9031 per share of Common Stock. Pro forma net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of Common Stock outstanding as of September 30, 2020, after giving effect to the issuance of 12,500,000 shares of Common Stock in a private placement offering on January 21, 2021.

After giving effect to the sale of 1,632,652 shares of Common Stock and associated Warrants in this offering and 24,906,134 shares of Common Stock and associated warrants in the concurrent registered direct offering, each at an offering price of \$2.45 per share and associated warrant, and after deduction of the placement agent fees for the concurrent registered direct offering and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2020, would have been approximately \$121.2 million, or \$2.0734 per share. This represents an immediate increase in net tangible book value of \$0.1703 per share to existing stockholders and an immediate dilution in the pro forma as adjusted net tangible book value of \$0.3766 per share to purchasers of Common Stock in this offering.

The following table illustrates this calculation on a per share basis.

Offering price per share	\$	2.4500
Net tangible book value per share as of September 30, 2020 ⁽¹⁾	\$	1.9327
Pro forma net tangible book value per share after giving effect to January 21, 2021 private placement offering	\$	1.9031
Increase per share attributable to the offering and concurrent registered direct offering	\$	0.1703
Pro forma as adjusted net tangible book value per share after giving effect to this offering and concurrent registered direct offering	\$	2.0734
Dilution in net tangible book value to new investors	\$	0.3766

⁽¹⁾The calculation of net tangible book value as of September 30, 2020 is based on 19,395,977 shares of Common Stock outstanding. The calculation of pro forma net tangible book value is based on 58,434,763 shares of Common Stock outstanding. Each calculation excludes the following:

- 1,105,408 shares of our Common Stock issuable upon exercise of outstanding stock options under our equity incentive plans with exercise prices ranging from \$1.80 to \$174.00 and having a weighted average exercise price of \$14.39 per share;
- 347,905 shares of our Common Stock issuable upon vesting of outstanding restricted stock units under our equity incentive plans;
- 2,638,355 shares of our Common Stock issuable upon the exercise of outstanding warrants, other than the warrants described in the bullet point below, at a weighted average exercise price of \$2.18 per share; and
- an aggregate of 13,269,393 shares of Common Stock issuable upon the exercise of the Warrants to be issued to the investors in this offering and the warrants issued in the concurrent registered direct offering at an exercise price of \$2.90 per share.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors will experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of Common Stock, other equity securities or convertible debt securities in the future.

DESCRIPTION OF SECURITIES

The shares of Common Stock and the Warrants (and the shares of Common Stock issuable upon the exercise of the Warrants) offered in this offering will be issued pursuant to a securities purchase agreement between the investors and us. We urge you to review the form securities purchase agreement and the form of Warrant, which will be included as exhibits to a current report on Form 8-K filed with the SEC in connection with this offering, for a complete description of the terms and conditions applicable to these securities.

The following brief summary of the material terms and provisions of the Warrants is subject to, and qualified in its entirety by, the form of Warrant.

Common Stock

The material terms and provisions of our Common Stock are described under the heading “Description of Capital Stock” starting on page 7 of the accompanying prospectus.

Warrants

The material terms and provisions of the Warrants being offered pursuant to this prospectus supplement and the accompanying prospectus are summarized below. This summary is subject to and qualified in its entirety by the form of Warrant, which will be provided to each investor in this offering and will be filed with the SEC on a current report on Form 8-K in connection with this offering.

General Terms of the Warrants. The Warrants to be issued in this offering represent the rights to purchase up to an aggregate of 816,326 shares of Common Stock at an exercise price of \$2.90 per share. Each Warrant will be exercisable immediately upon issuance and will have a term of five years from the date of issuance.

Exercise. Holders of the Warrants may exercise their Warrants to purchase shares of our Common Stock at any time prior to the expiration date by delivering (i) notice of exercise, appropriately completed and duly signed, and (ii) if such holder is not utilizing the cashless exercise provisions with respect to the Warrants, payment of the exercise price for the number of shares with respect to which the Warrant is being exercised. Warrants may be exercised in whole or in part, but only for full shares of Common Stock. We provide certain rescission and buy-in rights to a holder if we fail to deliver the shares of Common Stock issuable upon exercise of the Warrants by the date on which delivery of the stock certificate is required by the Warrant. With respect to the rescission rights, the holder has the right to rescind the exercise if stock certificates are not timely delivered. The buy-in rights apply if after the date on which delivery of the stock certificate is required by the Warrant, the holder purchases (in an open market transaction or otherwise) shares of our Common Stock to deliver in satisfaction of a sale by the holder of the Warrant shares that the holder anticipated receiving from us upon exercise of the Warrant. In this event, we will:

- pay in cash to the holder the amount equal to the excess (if any) of the total buy-in price over the product of (A) such number of Warrant shares that we were required to deliver to the holder times (B) the price at which the sell order giving rise to holder’s purchase obligation was executed; and
- at the election of holder, either (A) reinstate the portion of the Warrant as to such number of shares of Common Stock, or (B) deliver to the holder a certificate or certificates representing such number of shares of Common Stock

In addition, the Warrant holders are entitled to a “cashless exercise” option if, at the time of exercise, there is no effective registration statement registering, or no current prospectus available for, the issuance or resale of the shares of Common Stock issuable upon exercise of the Warrants. This option entitles the Warrant holders to elect to receive fewer shares of Common Stock without paying the cash exercise price. The number of shares to be issued would be determined by a formula set forth in the Warrant.

The shares of Common Stock issuable on exercise of the Warrants will be, when issued and paid for in accordance with the Warrants, duly and validly authorized, issued and fully paid and non-assessable. We will authorize and reserve at least that number of shares of Common Stock equal to the number of shares of Common Stock issuable upon exercise of all outstanding Warrants.

Fundamental Transactions. If, at any time while this Warrant is outstanding, (i) we, directly or indirectly, in one or more related transactions effect any merger or consolidation, (ii) we, directly or indirectly, effect any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer is completed pursuant to which holders

of our Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock, (iv) we, directly or indirectly, in one or more related transactions, effect any reclassification, reorganization or recapitalization of our Common Stock or any compulsory share exchange pursuant to which the our Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) we, directly or indirectly, in one or more related transactions consummate a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another person or entity that acquires more than 50% of the outstanding shares of our Common Stock (each a "Fundamental Transaction"), then, upon any subsequent exercise of this Warrant, the Holder shall have the right to receive, for each Warrant Share that would have been issuable upon such exercise immediately prior to the occurrence of such Fundamental Transaction, at the option of the Holder, the number of shares of Common Stock of the surviving corporation, and/or any additional consideration (the "Alternate Consideration ") receivable as a result of such Fundamental Transaction by a holder of the number of shares of Common Stock for which the Warrant is exercisable immediately prior to such Fundamental Transaction.

Subsequent Rights Offerings. If, at any time while the Warrants are outstanding, we issue rights, options or warrants to all holders of our Common Stock entitling them to purchase our Common Stock, warrants, securities or other property, then the holders of the Warrants will be entitled to acquire those rights, options and warrants on the basis of the number of shares of Common Stock acquirable upon complete exercise of the Warrants (without regard to any limitations on exercise thereof, including without limitation, the beneficial ownership limitation).

Pro Rata Distributions. If, at any time while the Warrants are outstanding, we make a dividend or distribution of assets or rights to acquire assets to all holders of our Common Stock, the holders of the Warrants will be entitled to participate in the dividend or distribution of assets or rights to acquire assets on the basis of the number of shares of Common Stock acquirable upon complete exercise of the Warrants (without regard to any limitations on exercise thereof, including without limitation, the beneficial ownership limitation).

Certain Adjustments. The exercise price and the number of shares of Common Stock purchasable upon the exercise of the Warrants are subject to adjustment upon the occurrence of specific events, including stock dividends, stock splits, combinations and reclassifications of our Common Stock.

Delivery of Shares. Upon the holder's exercise of a Warrant, we will promptly, but in no event later than two trading days or the standard settlement period after the delivery to us of the notice of exercise and no later than one trading date after the delivery to us of the aggregate exercise price, issue and deliver, or cause to be issued and delivered, the shares of Common Stock issuable upon exercise of the Warrant. In addition, we will, if the holder provides the necessary information to us, issue and deliver the shares electronically through The Depository Trust Corporation through its Deposit or Withdrawal at Custodian system (DWAC) or another established clearing corporation performing similar functions. If we fail for any reason to timely deliver to the investor the Warrant shares, we will pay to the investor, in cash, as liquidated damages and not as a penalty, for each \$1,000 of Warrant shares subject to such exercise, \$10 per trading day (increasing to \$20 per trading day on the fifth trading day after such liquidated damages begin to accrue) for each trading day after the trading day on which the Warrant shares were required to be delivered, until such Warrant shares are delivered or the investor rescinds such exercise.

Notice of Corporate Action. We will provide notice to holders of the Warrants to provide them with the opportunity to exercise their Warrants and hold Common Stock in order to participate in or vote on the following corporate events:

- if we shall take a record of the holders of our Common Stock for the purpose of entitling them to receive a dividend or other distribution, or a redemption of Common Stock, or any warrant or right to subscribe for or purchase any shares of stock of any class or any other right;
- any reclassification of our capital stock or any consolidation or merger with, or any sale, transfer or other disposition of all or substantially all of our property, assets or business to, or any compulsory share exchange with, another corporation; or
- a voluntary or involuntary dissolution, liquidation or winding up of our Company.

Limitations on Exercise. Subject to limited exceptions, a holder of Warrants will not have the right to exercise any portion of its Warrants if the holder, together with its affiliates, would beneficially own in excess of 4.99% (or, 9.99% at the election of the holder prior to issuance) of the number of shares of our Common Stock outstanding immediately after giving effect to such exercise, provided that the holder may increase or decrease the beneficial ownership limitation up to 9.99%. Any increase in the beneficial ownership limitation shall not be effective until 61 days following notice of such change to us.

PLAN OF DISTRIBUTION

We have entered into a securities purchase agreement with certain accredited investors pursuant to which we have agreed to issue and sell directly to such investors, and such investors have agreed to purchase directly from us, an aggregate of 1,632,652 shares of Common Stock and Warrants to purchase an aggregate of 816,326 shares of Common Stock, at a combined offering price of \$2.45 per share of Common Stock and associated Warrant.

The shares of Common Stock and Warrants are being offered and sold by us directly to the investors without a placement agent, underwriter, broker or dealer. We are not paying underwriting discounts or commissions in connection with this offering.

We expect to deliver the shares of our Common Stock and Warrants being offered pursuant to this prospectus supplement on or about February 17, 2021.

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C., New York, New York.

EXPERTS

The consolidated financial statements incorporated in this Prospectus by reference from the Company's Annual Report on Form 10-K have been audited by Grant Thornton LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference (which report expresses an unqualified opinion on the consolidated financial statements). Such consolidated financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. The address for the SEC's website is <http://www.sec.gov>.

We have filed a registration statement, of which this prospectus supplement is a part, covering the securities offered hereby. As allowed by SEC rules, this prospectus supplement does not include all of the information contained in the registration statement and the included exhibits, financial statements and schedules. You are referred to the registration statement, the included exhibits, financial statements and schedules for further information. This prospectus supplement is qualified in its entirety by such other information.

We are subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information are available at the website of the SEC referred to above. We maintain a website at www.caladrius.com. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our Common Stock.

INFORMATION INCORPORATED BY REFERENCE

We are “incorporating by reference” specific documents that we file with the SEC, which means that we can disclose important information to you by referring you to those documents that are considered part of this prospectus. Information that we file subsequently with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below, and any documents that we file with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of this prospectus until the termination of the offering of all of the securities registered pursuant to the registration statement of which this prospectus is a part (excluding any portions of such documents that have been “furnished” but not “filed” for purposes of the Exchange Act):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 5, 2020 (including information specifically incorporated by reference therein for our Proxy Statement filed with the SEC on April 29, 2020);

- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020, filed with the SEC on May 7, 2020;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2020, filed with the SEC on August 13, 2020;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2020, filed with the SEC on November 5, 2020;
- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 29, 2020;
- our Current Reports on Form 8-K filed with the SEC on April 22, 2020, April 24, 2020, May 26, 2020, June 18, 2020, July 10, 2020, July 28, 2020, August 5, 2020, November 5, 2020, November 17, 2020 and January 25, 2021; and
- the description of our Common Stock contained in our Registration Statement on Form 8-A, filed with the SEC on August 2, 2013 (including any amendment or report filed with the SEC for the purpose of updating such description).

You may request, and we will provide you with, a copy of these filings, at no cost, by calling us at (212) 584-4178 or by writing to us at the following address:

Caladrius Biosciences, Inc.
800 Westchester Ave., Ste. N341
Rye Brook, New York 10573
Attention: Corporate Secretary

We maintain a website at <http://www.caladrius.com>. You may access our definitive proxy statements on Schedule 14A, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and periodic amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or therein, in any other subsequently filed document that also is or is deemed to be incorporated by reference herein and in this prospectus, modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified and superseded, to constitute a part of this prospectus.

Any statement made in this prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified by reference to the actual document.

PROSPECTUS

\$150,000,000

CALADRIUS BIOSCIENCES, INC.

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$150,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock or preferred stock or debt securities upon the exercise of warrants.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is traded on The Nasdaq Capital Market under the symbol "CLBS." On August 1, 2018, the last reported sale price of our common stock on The Nasdaq Capital Market was \$5.08 per share.

Investing in our securities involves risks. See "Risk Factors" at page 3 of this prospectus.

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

This prospectus may not be used to consummate sales of securities unless it is accompanied by a prospectus supplement.

The date of this prospectus is August 2, 2018.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, using a “shelf” registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$150,000,000. We have provided to you in this prospectus a general description of the securities we may offer. Each time we sell securities under this shelf registration process, we will provide a prospectus supplement that will contain specific information about the terms of the offering. We may also add, update or change any of the information contained in this prospectus in the prospectus supplement or any “free writing prospectus” we may authorize to be delivered to you. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement or any free writing prospectus we may authorize to be delivered to you, you should rely on the information in the prospectus supplement or free writing prospectus, as the case may be, provided that 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 or any prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement. This prospectus, together with the applicable prospectus supplements and any free writing prospectus we may authorize to be delivered to you, includes all material information relating to a particular offering.

An investment in our securities involves certain risks that should be carefully considered by prospective investors. See “Risk Factors.”

You should read this prospectus and any prospectus supplement as well as additional information described under “Incorporation of Certain Documents by Reference” and “Where You Can Find More Information” on pages 25 and 25, respectively.

ABOUT CALADRIUS

Overview

Caladrius Biosciences, Inc. (“we,” “us,” “our,” “Caladrius” or the “Company”) is a company developing cellular therapeutics to treat select cardiovascular and autoimmune diseases. We leverage specialized development expertise to advance our therapies through development with the aim of eventually obtaining market authorization and commercializing, either alone or with partners, and providing treatment options to patients suffering from life-threatening medical conditions. Our product candidates include autologous CD34 cell-based therapies for ischemic repair that are in phase 2 of clinical development as well as an autologous, ex vivo expanded and activated, polyclonal regulatory T cell (“Treg”) therapy completing a phase 2 study targeting recent-onset type 1 diabetes mellitus (“T1D”) in children aged 8-17. We also have acquired the rights to data and regulatory filings for a CD34-based cell therapy program for refractory angina, which had advanced to phase 3 under the previous owner. We have designated this program CLBS14-RfA.

Ischemic Repair (CD34 Cell Technology)

Our CD34 cell technology has led to the development of therapeutic product candidates designed to address diseases and conditions caused by ischemia. Ischemia occurs when the supply of oxygenated blood to healthy tissue is restricted. Through the administration of CD34 cells, we seek to promote the development and formation of new blood vessels and thereby increase blood flow to the impacted area. We believe that a number of conditions caused by underlying ischemic injury can be improved through our CD34 cell technology, including critical limb ischemia (“CLI”), coronary microvascular dysfunction (“CMD”) and refractory angina (“RfA”). Published reports in *Circulation Cardiovascular Interventions*, *Atherosclerosis*, *Stem Cells* and *Circulation Journal*, provide preliminary evidence that CD34 cell therapy is safe and can exert significant therapeutic effects in patients with CLI, a condition in which blood flow to the legs is severely impaired, causing pain and non-healing ulcers and, ultimately, potentially resulting in the need for amputation. Our Clinical Trial Notification for a pivotal Phase 2 trial investigating our product candidate in CLI, CLBS12, was submitted to the Japanese Pharmaceutical and Medical Device Agency (“PMDA”) and was cleared to proceed. The protocol design was agreed to with PMDA, the study was opened for enrollment in December 2017 and treatment of the first patient was announced in March 2018. Based on our discussions with the PMDA, we expect that a successful outcome of this trial will qualify CLBS12 for consideration of early conditional approval in Japan, thereby effectively making our phase 2 trial a registration trial. In addition, Japan’s Ministry of Health, Labour and Welfare (“MHLW”) recently assigned CLBS12 “SAKIGAKE” designation (a Japanese regulatory status similar to “breakthrough” designation awarded by FDA in the USA) reflecting its expectation of “prominent effectiveness” based on data of mechanism of action from non-clinical and early phase clinical trials. The SAKIGAKE Designation System promotes research and development in Japan, driving early practical application for innovative pharmaceutical products, medical devices and regenerative medicines. As a designated therapy under the system, CLBS12 should have the benefits of prioritized consultation, a dedicated review system to support the development and review process, as well as reduced review time from the normal 12 months down to 6 months. In anticipation of a successful trial outcome and the possibility of conditional approval, we continue to seek a local partner for CLBS12 in Japan. We also have acquired the rights to data and regulatory filings for a CD34-based cell therapy program for refractory angina, which had advanced to phase 3 under the previous investigational new drug application (“IND”) holder. We have designated this program CLBS14-RfA and recently reactivated the IND with the U.S. Food and Drug Administration (“FDA”). Furthermore, we submitted grant applications in an effort to seek non-dilutive financing to investigate the CD34 technology for additional clinical indications in the United States. In October 2017 we announced the award of a \$1.9 million grant from the National Institutes of Health to support a clinical study of CD34 cells in patients with coronary microvascular dysfunction. The first patient has been enrolled in this study of CLBS14-CMD.

Immunomodulation (Treg Technology)

We are developing strategically, through the utilization of our core development expertise, a product candidate (CLBS03) that has the potential to be an innovative therapy for T1D. This therapy is based on a proprietary platform technology for immunomodulation. We have selected, as an initial target, the unmet medical need of patients who are newly diagnosed with T1D, most of whom will be under the age of 18. This program is based on the use of Tregs to treat diseases caused by imbalances in an individual's immune system. This novel approach seeks to restore immune balance by enhancing Treg number and function. Tregs are a natural part of the human immune system and regulate the activity of effector T cells, the cells that are responsible for protecting the body from pathogens and foreign antigens. When Tregs function properly, only harmful foreign materials are attacked by effector T cells. In autoimmune disease, however, it is thought that deficient Treg activity and numbers permit the effector T cells to attack the body's own beneficial cells. In the case of T1D, the beta cells in the pancreas are attacked, thereby reducing and/or eliminating over time the patient's ability to produce insulin. Insulin is necessary to regulate sugar metabolism and maintain proper sugar levels in the blood. Inconsistent or unnatural insulin levels can lead to

many complications, including blindness, vascular disease and, if no insulin supplement is provided, even death. There are currently no curative treatments for T1D, only lifelong insulin therapy, which often does not prevent serious co-morbidities. Two Phase 1 clinical trials of Treg technology in T1D, taken together demonstrated safety and tolerance, feasibility of manufacturing, an implied durability of effect as well as an early indication of potential therapeutic effect through the preservation of beta cell function. In the first quarter of 2016, we commenced patient enrollment in the first of two cohorts in The Sanford Project: T-Rex Study, a Phase 2 prospective, randomized, placebo-controlled, double-blind clinical trial (the "TRex Study") to evaluate the safety and efficacy of CLBS03 in adolescents with recent onset T1D. We entered into a strategic collaboration with Sanford Research to support the execution of this trial. Sanford Research is a U.S.-based non-profit research organization that supports an emerging translational research center focused on finding a cure for T1D.

CLBS03 has been granted Fast Track and orphan drug designations from the U.S. Food and Drug Administration ("FDA") as well as Advanced Therapeutic Medicinal Product ("ATMP") classification from the European Medicines Agency ("EMA"). In October 2016, we received a satisfactory safety evaluation by our independent Data Safety Monitoring Board based on safety data then available from the first 19 patients enrolled in the trial. A subsequent interim analysis was conducted after approximately 50% of patients reached the six-month follow-up milestone, the results of which were publicly released in March 2018 that the therapy continued to be well tolerated and was deemed non-futile for therapeutic effect. In January 2018, we announced completion of enrollment (110 patients) of the TRex Study.

In February 2017, the California Institute for Regenerative Medicine ("CIRM") awarded us funds of up to \$12.2 million to support the T-Rex Study. The funding is based upon the achievement of certain milestones related to the proportion of subjects enrolled in California, as well as manufacturing and development costs incurred in California. In March 2018, CIRM calculated the precise amount of the funding award as \$8.6 million, based on the actual number of subjects enrolled in California. We have received total funding of \$7.9 million through March 31, 2018.

Additional Out-licensing Opportunities

Our broad intellectual property portfolio of cell therapy assets includes notable programs available for out-licensing in order to continue their clinical development. These include additional indications for our Treg product and additional indications for our CD34 cell technology.

Our current long-term strategy focuses on advancing our therapies through development with the aim of eventually obtaining market authorization and commercializing, either alone or with partners, to provide treatment options to patients suffering from life-threatening medical conditions. We believe that we are positioned to realize potentially meaningful value increases within our own proprietary pipeline if we are successful in advancing our product candidates to their next significant development milestones.

Discontinued Operations

On May 18, 2017, we completed the previously announced sale of our remaining 80.1% membership interest in PCT, LLC, a Caladrius company ("PCT") to Hitachi Chemical Co. America, Ltd. ("Hitachi"), pursuant to the Interest Purchase Agreement (the "Purchase Agreement") dated as of March 16, 2017, by and among us, PCT and Hitachi (the "2017 Hitachi Transaction"), for \$75.0 million in cash plus an additional cash adjustment of \$4.4 million based on PCT's cash and outstanding indebtedness as of the closing date and a potential future milestone payment. The sale of PCT represented a strategic shift that has had a major effect on our operations, and therefore, all periods presented were adjusted to reflect PCT as discontinued operations. PCT is now known as Hitachi Chemical Advanced Therapeutic Systems.

RISK FACTORS

Investing in our securities involves risk. Please see the risk factors set forth under the heading "Risk Factors" beginning on page 14 of our Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission (the "SEC") on March 22, 2018, as amended on April 2, 2018 (our "2017 Form 10-K"), which documents are on file with the Securities and Exchange Commission and incorporated by reference into this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any prospectus supplement. The risks and uncertainties we have described are not the only ones facing our Company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, any prospectus supplement and the documents we incorporate by reference in this prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical facts, that we include in this prospectus, any prospectus supplement, and in the documents we incorporate by reference in this prospectus, may be deemed forward-looking statements for purposes of the Securities Act and the Exchange Act. We use the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "project," "will," "would" and similar expressions to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and, accordingly, you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from anticipated results expressed or implied by such forward-looking statements, including among others:

- our ability to obtain sufficient capital or strategic business arrangements to fund our operations and expansion plans, including meeting our financial obligations under various licensing and other strategic arrangements, the funding of our clinical trials for product candidates, and the commercialization of the relevant technology;
- our ability to build and maintain the management and human resources infrastructure necessary to support the growth of our business;
- whether a market is established for our cell-based products and services and our ability to capture a meaningful share of this market;
- scientific, regulatory and medical developments beyond our control;
- our ability to obtain and maintain, as applicable, appropriate governmental licenses, accreditations or certifications or comply with healthcare laws and regulations or any other adverse effect or limitations caused by government regulation of our business;
- whether any of our current or future patent applications result in issued patents, the scope of those patents and our ability to obtain and maintain other rights to technology required or desirable for the conduct of our business; and our ability to commercialize products without infringing the claims of third party patents;
- whether any potential strategic or financial benefits of various licensing agreements will be realized;
- the results of our development activities; and
- our ability to complete our other planned clinical trials (or initiate other trials) in accordance with our estimated timelines due to delays associated with enrolling patients due to the novelty of the treatment, the size of the patient population and the need of patients to meet the inclusion criteria of the trial or otherwise.

The factors discussed herein, including those risks described in "Item 1A. Risk Factors" in the 2017 Form 10-K and in the Company's other periodic filings with the SEC, which are available for review at www.sec.gov under "Search for Company Filings," could cause actual results and developments to be materially different from those expressed or implied by such statements. All forward-looking statements attributable to us are expressly qualified in their entirety by these and other factors. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they

were made. Except as required by law, the Company undertakes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read these factors and the other cautionary statements made in the documents we incorporate by reference as being applicable to all related forward-looking statements wherever they appear in this prospectus, any prospectus supplement, and any document incorporated by reference. We caution you that we do not undertake any obligation to update forward-looking statements made by us, except as required by law.

USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for working capital, including research and development of cell therapeutic product candidates, expansion of our business, strategic transactions and other general corporate purposes. We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of any securities. Pending the use of the net proceeds, we may use the net proceeds to invest in investment-grade, interest-bearing securities.

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize all the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time, in one or more offerings:

- common stock;
- preferred stock;
- debt securities;
- warrants to purchase any of the securities listed above; and
- units consisting of any combination of the securities listed above.

In this prospectus, we refer to the common stock, preferred stock, debt securities, warrants and units collectively as “securities.” The total dollar amount of all securities that we may sell will not exceed \$150,000,000.

If we issue debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of all material characteristics of our capital stock as set forth in our certificate of incorporation and bylaws, and our outstanding warrants. The summary does not purport to be complete and is qualified in its entirety by reference to our certificate of incorporation and bylaws, which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and to the provisions of the General Corporation Law of the State of Delaware, as amended.

Common Stock

We are authorized to issue 500,000,000 shares of common stock, par value \$0.001 per share (“Common Stock”). Holders of our Common Stock are entitled to one vote per share in the election of directors and on all other matters on which stockholders are entitled or permitted to vote. Holders of our Common Stock are not entitled to cumulative voting rights. Therefore, holders of a majority of the shares voting for the election of directors can elect all of the directors. Subject to the terms of any outstanding series of preferred stock, the holders of our Common Stock are entitled to dividends in the amounts and at times as may be declared by the Board of Directors out of funds legally available. Upon liquidation or dissolution, holders of our Common Stock are entitled to share ratably in all net assets available for distribution to stockholders after payment of any liquidation preferences to holders of our preferred stock. Holders of our Common Stock have no redemption, conversion or preemptive rights.

As of July 23, 2018, we had 9,724,281 shares of Common Stock issued and outstanding, exclusive of existing convertible preferred stock, options and warrants and the shares and warrants to be issued pursuant to the registration statement of which this prospectus is a part.

Preferred Stock

We are authorized to issue up to 20,000,000 shares of preferred stock, par value \$0.01 per share, with such designations, rights, and preferences as may be determined from time to time by our Board of Directors. Accordingly, our Board of Directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting, or other rights that could adversely affect the voting power or other rights of the holders of our Common Stock. The issuance of preferred stock could have the effect of restricting dividends on our Common Stock, diluting the voting power of our Common Stock, impairing the liquidation rights of our Common Stock, or delaying or preventing a change in control of our company, all without further action by our stockholders.

As of July 23, 2018, there were 10,000 shares of our Series B Convertible Redeemable Preferred Stock, \$0.01 par value per share (“Series B Preferred Stock”), issued and outstanding.

Series B Preferred Stock

The Series B Preferred Stock ranks *pari passu* with our Common Stock with respect to the payment of dividends and to the distribution of assets upon liquidation, dissolution or winding up.

So long as any shares of the Series B Preferred Stock are outstanding, no dividend shall be declared or paid or set aside for payment or other distribution declared or made upon our Common Stock or upon any other stock ranking junior to, or on a parity with, the Series B Preferred Stock as to dividends or upon liquidation, dissolution or winding up, unless, in the case of our preferred stock, the same dividend is declared, paid or set aside for payment on all outstanding shares of the Series B Preferred Stock or in the case of our Common Stock, ten times such dividend per share is declared, paid or set aside for payment on each outstanding share of the Series B Preferred Stock.

Except as otherwise provided by law, each share of the Series B Preferred Stock has the same voting rights as ten shares of our Common Stock and the holders of the Series B Preferred Stock and the Common Stock shall vote together as one class on all matters.

The holder of any share of Series B Preferred Stock has the right, at such holder’s option, to convert such share into one one-hundredth of a fully paid and non-assessable share of our Common Stock, subject to adjustment.

In the event of any voluntary or involuntary dissolution, liquidation or winding up of our Company, after any distribution of assets is made to the holders of any other class or series of stock that ranks prior to the Series B Preferred Stock in respect of distributions upon the liquidation of the Company, the holder of each share of Series B Preferred Stock then outstanding shall be entitled to be paid out of our assets available for distribution to our stockholders, an amount on a *pari passu* basis equal to ten times the amount per share distributed to the holders of our Common Stock. After payment of the full amount of the distribution to which they are entitled, the holders of shares of the Series B Preferred Stock will not be entitled to any further participation in any distribution of assets by the Company.

Shares of Series B Preferred Stock issued and reacquired by us shall have the status of authorized and unissued shares of preferred stock, undesignated as to series, subject to later issuance.

Holders of shares of Series B Preferred Stock are not entitled to any preemptive or subscription rights in respect of any securities of the corporation.

Options

As of July 23, 2018, we had outstanding options to purchase an aggregate of 1,073,216 shares of our Common Stock with exercise prices ranging from \$3.30 to \$303.00 per share, with an approximate weighted average exercise price of \$31.49 per share. The shares of our Common Stock underlying all such options are registered with the SEC.

Warrants

As of July 23, 2018, we had outstanding warrants to purchase an aggregate of 48,654 shares of our Common Stock with exercise prices ranging from \$5.89 to \$146.60, with an approximate weighted average exercise price of \$59.84 per share. The shares of Common Stock underlying the vast majority of such warrants have been registered for resale.

Series AMO Warrants

General. Upon closing the Amorcyte Merger on October 17, 2011, as a portion of the merger consideration we issued Series AMO Warrants to purchase shares of our Common Stock (the "Series AMO Warrants"), of which 18,654 shares remain outstanding as of July 23, 2018. The Series AMO Warrants are evidenced by a "Global Warrant" and were delivered in book entry form to the former stockholders of Amorcyte. Each Series AMO Warrant entitles the holder to purchase one share of our Common Stock at an exercise price of \$146.60 per share. The exercise price per share of each Warrant will be subject to adjustment upon the occurrence of certain events as provided in the form of global warrant certificate and summarized below. The Series AMO Warrants may be exercised at any time during their seven year term, unless redeemed; provided, however, that transfer of any shares of our Common Stock issuable upon exercise of the Series AMO Warrants was restricted until the one year anniversary of the closing date of the Amorcyte Merger. The Series AMO Warrants will expire at the end of their seven-year term. A Series AMO Warrant holder will not be deemed to be a holder of the underlying Common Stock for any purpose until the Series AMO Warrant is exercised.

Redemption. In the event our Common Stock is trading at a per share price equal to or exceeding the redemption threshold of \$346.60 per share for twenty (20) out of thirty (30) consecutive trading days, we have the option to call the Series AMO Warrants. If the holders of Series AMO Warrants have not exercised their warrants within 14 days of the redemption notice, we may redeem the Series AMO Warrants at \$0.0001 per warrant. We will send the redemption notice by first class mail to Series AMO Warrant holders at their last known addresses appearing on the registration records maintained by the transfer agent of the Series AMO Warrants. No other form of notice by publication or otherwise will be required. If we call any Series AMO Warrants for redemption, they will be exercisable until close of business on the business day next preceding the specified redemption date.

Adjustments of Exercise Price. The exercise price and redemption price of the Series AMO Warrants is subject to adjustment in specified circumstances, including in the event (i) there is a merger or consolidation and we are not the surviving corporation; (ii) there is subdivision, combination or reclassification of securities, recapitalization, automatic conversion, or other similar event affecting the number or character of outstanding shares of our Common Stock; or (iii) we declare any stock dividend to stockholders or effect any split or reverse split with respect to our Common Stock. The Series AMO Warrants do not contain provisions protecting against dilution resulting from the sale of additional shares of our Common Stock for less than the exercise price of the Series AMO Warrants or the current market price of our Common Stock.

No Voting and Dividend Rights. Until exercised, the Series AMO Warrants have no voting, dividend or other stockholder rights.

Registration Rights. We shall use commercially reasonable efforts to maintain the effectiveness of the Registration Statement on Form S-4 which covers the shares of our Common Stock underlying the Series AMO Warrants or file and maintain the effectiveness of another registration statement covering the shares of our Common Stock issuable upon exercise of the Series AMO Warrants at any time that both (a) the Series AMO Warrants are exercisable and (b) the exercise price of the Series AMO Warrants is less than 105% of the price at which our Common Stock is trading on the NYSE MKT (or if our Common Stock is no longer trading on the NYSE MKT, such other stock exchange on which such shares trade). In no event will any holder of a Series AMO Warrant be entitled to receive a "net cash settlement" in lieu of physical settlement in shares of our Common Stock regardless of whether we comply with our obligation described in the preceding sentence.

The description of the Series AMO Warrants contained herein does not purport to be complete and is qualified in its entirety by reference to the Warrant Agreement and the Form of Global Series AMO Warrant attached thereto, which is filed as Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on October 17, 2011.

Warrants Issued in Connection of an Amendment to Loan and Security Agreement

On March 11, 2016, we entered into a Consent and Third Amendment to Loan and Security Agreement (the “Amendment”) with Oxford Finance, LLC (the “Lender”). In connection with the Amendment, we issued to the Lender warrants to purchase an aggregate of 30,000 shares of Common Stock (the “Lender Warrants”), which are exercisable for a period of 7 years from the issuance date at an exercise price of \$5.89 per share.

Anti-Takeover Effects of Certain Provisions of Delaware Law and Our Certificate of Incorporation and Bylaws

Our Amended and Restated Certificate of Incorporation and bylaws contain some provisions that could make our acquisition by means of a tender or exchange offer, a proxy contest or otherwise more difficult. These provisions are summarized below.

Special Meetings. Our bylaws provide that special meetings of our stockholders may, unless otherwise prescribed by law, be called by our Chairman of the Board (if any), our Board of Directors or our Chief Executive Officer and shall be held at such place, on such date and at such time as shall be fixed by our Board of Directors or the person calling the meeting. Business transacted at any special meeting shall be limited to matters relating to the purpose or purposes stated in the notice of the meeting.

Undesignated Preferred Stock. The ability to authorize undesignated preferred stock makes it possible for our Board of Directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us. The ability to issue preferred stock may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Delaware Anti-Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, owned 15% or more of a corporation’s outstanding voting securities. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our Board of Directors does not approve in advance. We also anticipate that Section 203 may discourage attempted acquisitions that might result in a premium over the market price for the shares of our Common Stock held by stockholders.

The provisions of Delaware law, our Amended and Restated Certificate of Incorporation and our bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These

provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Potential Effects of Authorized but Unissued Stock

We have shares of Common Stock and preferred stock available for future issuance without stockholder approval. We may utilize these additional shares for a variety of corporate purposes, including future public offerings to raise additional capital, to facilitate corporate acquisitions or payment as a dividend on the capital stock.

The existence of unissued and unreserved Common Stock and preferred stock may enable our Board of Directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third-party attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, the Board of Directors has the discretion to determine designations, rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences of each series of preferred stock, all to the fullest extent permissible under the Delaware General Corporation Law and subject to any limitations set forth in our certificate of incorporation. The purpose of authorizing the Board of Directors to issue preferred stock and to determine the rights and preferences applicable to such preferred stock is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing desirable flexibility in connection with possible financings, acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from acquiring, a majority of our outstanding voting stock.

Limitations of Director Liability and Indemnification of Directors, Officers and Employees

Section 145 of the Delaware General Corporation Law, permits indemnification of directors, officers, agents and controlling persons of a corporation under certain conditions and subject to certain limitations. Section 145 empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative, by reason of the fact that he or she is or was a director, officer or agent of the corporation or another enterprise if serving at the request of the Company. Depending on the character of the proceeding, a corporation may indemnify against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding if the person indemnified 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. In the case of an action by or in the right of the corporation, no indemnification may be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine that despite the adjudication of liability such person is fairly and reasonably entitled to indemnity for such expenses which the court shall deem proper. Section 145 further provides that to the extent a present or former director or officer of a corporation has been successful in the defense of any action, suit or proceeding referred to above or in the defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.

Litigation Forum Selection Clause

Our bylaws provides that, unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company to the Company or its stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or our bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine shall be the Court of Chancery in the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware).

Indemnification Agreements

We have entered into indemnification agreements with each of our Chief Executive Officer, Chief Financial Officer, General Counsel, certain other employees and each of our directors pursuant to which we have agreed to indemnify such party to the full extent permitted by law, subject to certain exceptions, if such party becomes subject to an action because such party is our director, officer, employee, agent or fiduciary.

Transfer Agent

The transfer agent and registrar for our Common Stock is Continental Stock Transfer & Trust Company. Its address is 17 Battery Place, New York, New York, 10004 and its telephone number is (212) 509-4000.

The Nasdaq Capital Market

Our Common Stock is traded on the The Nasdaq Capital Market under the symbol “CLBS.”

DESCRIPTION OF DEBT SECURITIES

We summarize below some of the provisions that will apply to the debt securities unless the applicable prospectus supplement provides otherwise. This summary may not contain all information that is important to you. The complete terms of the debt securities will be contained in the applicable notes. The notes will be included or incorporated by reference as exhibits to the registration statement of which this prospectus is a part. You should read the provisions of the notes. You should also read the prospectus supplement, which will contain additional information and which may update or change some of the information below.

General

This prospectus describes certain general terms and provisions of the debt securities. The debt securities will be issued under an indenture between us and a trustee to be designated prior to the issuance of the debt securities. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus. The prospectus supplement will also indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue, from time to time, debt securities, in one or more series, that will consist of either our senior debt (“senior debt securities”), our senior subordinated debt (“senior subordinated debt securities”), our subordinated debt (“subordinated debt securities”) or our junior subordinated debt (“junior subordinated debt securities”) and, together with the senior subordinated debt securities and the subordinated debt securities, the “subordinated securities”). Debt securities, whether senior, senior subordinated, subordinated or junior subordinated, may be issued as convertible debt securities or exchangeable debt securities.

We have summarized herein certain terms and provisions of the form of indenture (the “indenture”). The summary is not complete and is qualified in its entirety by reference to the actual text of the indenture. The indenture is an exhibit to the registration statement of which this prospectus is a part. You should read the indenture for the provisions which may be important to you. The indenture is subject to and governed by the Trust Indenture Act of 1939, as amended.

The indenture does not limit the amount of debt securities which we may issue. We may issue debt securities up to an aggregate principal amount as we may authorize from time to time which securities may be in any currency or currency unit designated by us. The terms of each series of debt securities will be established by or pursuant to (a) a supplemental indenture, (b) a resolution of our board of directors, or (c) an officers’ certificate pursuant to authority granted under a resolution of our board of directors. The prospectus supplement will describe the terms of any debt securities being offered, including:

- the title of the debt securities;
- the limit, if any, upon the aggregate principal amount or issue price of the debt securities of a series;
- ranking of the specific series of debt securities relative to other outstanding indebtedness, including any debt of any of our subsidiaries;
- the price or prices at which the debt securities will be issued;
- the designation, aggregate principal amount and authorized denominations of the series of debt securities;
- the issue date or dates of the series and the maturity date of the series;

- whether the securities will be issued at par or at a premium over or a discount from their face amount;
- the interest rate, if any, and the method for calculating the interest rate and basis upon which interest shall be calculated;
- the right, if any, to extend interest payment periods and the duration of the extension;
- the interest payment dates and the record dates for the interest payments;
- any mandatory or optional redemption terms or prepayment, conversion, sinking fund or exchangeability or convertibility provisions;
- the currency of denomination of the securities;
- the place where we will pay principal, premium, if any, and interest, if any, and the place where the debt securities may be presented for transfer;
- if payments of principal of, premium, if any, or interest, if any, on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- if other than denominations of \$1,000 or multiples of \$1,000, the denominations the debt securities will be issued in;
- whether the debt securities will be issued in the form of global securities or certificates;
- the applicability of and additional provisions, if any, relating to the defeasance of the debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the entire principal amount;
- the currency or currencies, if other than the currency of the United States, in which principal and interest will be paid;
- the dates on which premium, if any, will be paid;
- any addition to or change in the “Events of Default” described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to or change in the covenants described in the prospectus or in the indenture with respect to the debt securities;
- our right, if any, to defer payment of interest and the maximum length of this deferral period; and
- other specific terms, including any additional events of default or covenants.

We may issue debt securities at a discount below their stated principal amount. Even if we do not issue the debt securities below their stated principal amount, for United States federal income tax purposes the debt securities may be deemed to have been issued with a discount because of certain interest payment characteristics. We will describe in any applicable prospectus supplement the United States federal income tax considerations applicable to debt securities issued at a discount or deemed to be issued at a discount, and will describe any special United States federal income tax considerations that may be applicable to the particular debt securities.

Senior Debt

Senior debt securities will rank equally and *pari passu* with all of our other unsecured and unsubordinated debt from time to time outstanding.

Subordinated Debt

The indenture does not limit our ability to issue subordinated debt securities. Any subordination provisions of a particular series of debt securities will be set forth in the supplemental indenture, board resolution or officers' certificate related to that series of debt securities and will be described in the relevant prospectus supplement.

If this prospectus is being delivered in connection with a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated by reference in this prospectus will set forth the approximate amount of senior indebtedness outstanding as of the end of the most recent fiscal quarter.

Conversion or Exchange Rights

Debt securities may be convertible into or exchangeable for our other securities or property. The terms and conditions of conversion or exchange will be set forth in the supplemental indenture, board resolution or officers' certificate related to that series of debt securities and will be described in the relevant prospectus supplement. The terms will include, among others, the following:

- the conversion or exchange price;
- the conversion or exchange period;
- provisions regarding our ability or the ability of the holder to convert or exchange the debt securities;
- events requiring adjustment to the conversion or exchange price; and
- provisions affecting conversion or exchange in the event of our redemption of the debt securities.

Merger, Consolidation or Sale of Assets

The indenture prohibits us from merging into or consolidating with any other person or selling, leasing or conveying substantially all of our assets and the assets of our subsidiaries, taken as a whole, to any person, unless:

- either we are the continuing corporation or the successor corporation or the person which acquires by sale, lease or conveyance substantially all our or our subsidiaries' assets is a corporation organized under the laws of the United States, any state thereof, or the District of Columbia, and expressly assumes the due and punctual payment of the principal of, and premium, if any, and interest, if any, on all the debt securities and the due performance of every covenant of the indenture to be performed or observed by us, by supplemental indenture satisfactory to the trustee, executed and delivered to the trustee by such corporation;
- immediately after giving effect to such transactions, no Event of Default described under the caption "Events of Default and Remedies" below or event which, after notice or lapse of time or both would become an Event of Default, has happened and is continuing; and
- we have delivered to the trustee an officers' certificate and an opinion of counsel each stating that such transaction and such supplemental indenture comply with the indenture provisions relating to merger, consolidation and sale of assets.

Upon any consolidation or merger with or into any other person or any sale, conveyance, lease, or other transfer of all or substantially all of our or our subsidiaries' assets to any person, the successor person shall succeed, and be substituted for, us under the indenture and each series of outstanding debt securities, and we shall be relieved of all obligations under the indenture and each series of outstanding debt securities to the extent we were the predecessor person.

Events of Default and Remedies

When we use the term “Event of Default” in the indenture with respect to the debt securities of any series, we mean:

- i. default in paying interest on the debt securities when it becomes due and the default continues for a period of 30 days or more;
- ii. default in paying principal, or premium, if any, on the debt securities when due;
- iii. default is made in the payment of any sinking or purchase fund or analogous obligation when the same becomes due, and such default continues for 30 days or more;
- iv. default in the performance, or breach, of any covenant or warranty in the indenture (other than defaults specified in clause (1), (2) or (3) above) and the default or breach continues for a period of 60 days or more after we receive written notice of such default from the trustee or we and the trustee receive notice from the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the series;
- v. certain events of bankruptcy, insolvency, reorganization, administration or similar proceedings with respect to us have occurred; and
- vi. any other Event of Default provided with respect to debt securities of that series that is set forth in the applicable prospectus supplement accompanying this prospectus.

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness that we may have outstanding from time to time. Unless otherwise provided by the terms of an applicable series of debt securities, if an Event of Default under the indenture occurs with respect to the debt securities of any series and is continuing, then the trustee or the holders of not less than 51% of the aggregate principal amount of the outstanding debt securities of that series may by written notice require us to repay immediately the entire principal amount of the outstanding debt securities of that series (or such lesser amount as may be provided in the terms of the securities), together with all accrued and unpaid interest and premium, if any. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

After a declaration of acceleration, the holders of a majority in aggregate principal amount of outstanding debt securities of any series may rescind this accelerated payment requirement if all existing Events of Default, except for nonpayment of the principal on the debt securities of that series that has become due solely as a result of the accelerated payment requirement, have been cured or waived and if the rescission of acceleration would not conflict with any judgment or decree. The holders of a majority in aggregate principal amount of the outstanding debt securities of any series also have the right to waive past defaults, except a default in paying principal or interest on any outstanding debt security, or in respect of a covenant or a provision that cannot be modified or amended without the consent of all holders of the debt securities of that series.

No holder of any debt security may seek to institute a proceeding with respect to the indenture unless such holder has previously given written notice to the trustee of a continuing Event of Default, the holders of not less than 51% in aggregate principal amount of the outstanding debt securities of the series have made a written request to the trustee to institute proceedings in respect of the Event of Default, the holder or holders have offered reasonable indemnity to the trustee and the trustee has failed to institute such proceeding within 60 days after it received this notice. In addition, within this 60-day period the trustee must not have received directions inconsistent with this written request by holders of a majority in aggregate principal amount of the outstanding debt securities of that series. These limitations do not apply, however, to a suit instituted by a holder of a debt security for the enforcement of the payment of principal, interest or any premium on or after the due dates for such payment.

During the existence of an Event of Default actually known to a responsible officer of the trustee, the trustee is required to exercise the rights and powers vested in it under the indenture and use the same degree of care and skill in its exercise as a prudent person would under the circumstances in the conduct of that person's own affairs. If an Event of Default has occurred and is continuing, the trustee is not under any obligation to exercise any of its rights or powers at the request or direction of any of the holders unless the holders have offered to the trustee security or indemnity reasonably satisfactory to the trustee. Subject to certain provisions, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series 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.

The trustee will, within 90 days after receiving notice of any default, give notice of the default to the holders of the debt securities of that series, unless the default was already cured or waived. Unless there is a default in paying principal, interest or any premium when due, the trustee can withhold giving notice to the holders if it determines in good faith that the withholding of notice is in the interest of the holders. In the case of a default specified in clause (4) above describing Events of Default, no notice of default to the holders of the debt securities of that series will be given until 60 days after the occurrence of the event of default.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if it in good faith determines that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

The indenture may be amended or modified without the consent of any holder of debt securities in order to:

- evidence a successor to the trustee;
- cure ambiguities, defects or inconsistencies;
- provide for the assumption of our obligations in the case of a merger or consolidation or transfer of all or substantially all of our assets that complies with the covenant described under “- Merger, Consolidation or Sale of Assets”;
- make any change that would provide any additional rights or benefits to the holders of the debt securities of a series;
- add guarantors or co-obligors with respect to the debt securities of any series;
- secure the debt securities of a series;
- establish the form or forms of debt securities of any series;
- add additional Events of Default with respect to the debt securities of any series;
- add additional provisions as may be expressly permitted by the Trust Indenture Act;
- maintain the qualification of the indenture under the Trust Indenture Act; or
- make any change that does not adversely affect in any material respect the interests of any holder.

Other amendments and modifications of the indenture or the debt securities issued may be made with the consent of the holders of not less than a majority in aggregate principal amount of the outstanding debt securities of each series affected by the amendment or modification. However, no modification or amendment may, without the consent of the holder of each outstanding debt security affected:

- change the maturity date or the stated payment date of any payment of premium or interest payable on the debt securities;
- reduce the principal amount, or extend the fixed maturity, of the debt securities;

- change the method of computing the amount of principal or any interest of any debt security;
- change or waive the redemption or repayment provisions of the debt securities;
- change the currency in which principal, any premium or interest is paid or the place of payment;
- reduce the percentage in principal amount outstanding of debt securities of any series which must consent to an amendment, supplement or waiver or consent to take any action;
- impair the right to institute suit for the enforcement of any payment on the debt securities;
- waive a payment default with respect to the debt securities;
- reduce the interest rate or extend the time for payment of interest on the debt securities;
- adversely affect the ranking or priority of the debt securities of any series; or
- release any guarantor or co-obligor from any of its obligations under its guarantee or the indenture, except in compliance with the terms of the indenture.

Satisfaction, Discharge and Covenant Defeasance

We may terminate our obligations under the indenture with respect to the outstanding debt securities of any series, when:

- either:
 - all debt securities of any series issued that have been authenticated and delivered have been delivered to the trustee for cancellation; or
 - all the debt securities of any series issued that have not been delivered to the trustee for cancellation have become due and payable, will become due and payable within one year, or are to be called for redemption within one year and we have made arrangements satisfactory to the trustee for the giving of notice of redemption by such trustee in our name and at our expense, and in each case, we have irrevocably deposited or caused to be deposited with the trustee sufficient funds to pay and discharge the entire indebtedness on the series of debt securities; and
- we have paid or caused to be paid all other sums then due and payable under the indenture; and
- we have delivered to the trustee an officers' certificate and an opinion of counsel, each stating that all conditions precedent under the indenture relating to the satisfaction and discharge of the indenture have been complied with.

We may elect to have our obligations under the indenture discharged with respect to the outstanding debt securities of any series ("legal defeasance"). Legal defeasance means that we will be deemed to have paid and discharged the entire indebtedness represented by the outstanding debt securities of such series under the indenture, except for:

- the rights of holders of the debt securities to receive principal, interest and any premium when due;
- our obligations with respect to the debt securities concerning issuing temporary debt securities, registration of transfer of debt securities, mutilated, destroyed, lost or stolen debt securities and the maintenance of an office or agency for payment for security payments held in trust;
- the rights, powers, trusts, duties and immunities of the trustee; and
- the defeasance provisions of the indenture.

In addition, we may elect to have our obligations released with respect to certain covenants in the indenture (“covenant defeasance”). If we so elect, any failure to comply with these obligations will not constitute a default or an event of default with respect to the debt securities of any series. In the event covenant defeasance occurs, certain events, not including non-payment, bankruptcy and insolvency events, described under “Events of Default and Remedies,” will no longer constitute an event of default for that series.

In order to exercise either legal defeasance or covenant defeasance with respect to outstanding debt securities of any series:

- we must irrevocably have deposited or caused to be deposited with the trustee as trust funds for the purpose of making the following payments, specifically pledged as security for, and dedicated solely to the benefits of the holders of the debt securities of a series:
 - money in an amount; or
 - U.S. government obligations (or equivalent government obligations in the case of debt securities denominated in other than U.S. dollars or a specified currency) that will provide, not later than one day before the due date of any payment, money in an amount; or
 - a combination of money and U.S. government obligations (or equivalent government obligations, as applicable),

in each case sufficient, in the written opinion (with respect to U.S. or equivalent government obligations or a combination of money and U.S. or equivalent government obligations, as applicable) of a nationally recognized firm of independent public accountants to pay and discharge, and which shall be applied by the trustee to pay and discharge, all of the principal (including mandatory sinking fund payments), interest and any premium at due date or maturity;

- in the case of legal defeasance, we have delivered to the trustee an opinion of counsel stating that, under then applicable federal income tax law, the holders of the debt securities of that series will not recognize income, gain or loss for federal income tax purposes as a result of the deposit, defeasance and discharge to be effected and will be subject to the same federal income tax as would be the case if the deposit, defeasance and discharge did not occur;
- in the case of covenant defeasance, we have delivered to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for federal income tax purposes as a result of the deposit and covenant defeasance to be effected and will be subject to the same federal income tax as would be the case if the deposit and covenant defeasance did not occur;
- no event of default or default with respect to the outstanding debt securities of that series has occurred and is continuing at the time of such deposit after giving effect to the deposit or, in the case of legal defeasance, no default relating to bankruptcy or insolvency has occurred and is continuing at any time on or before the 91st day after the date of such deposit, it being understood that this condition is not deemed satisfied until after the 91st day;
- the legal defeasance or covenant defeasance will not cause the trustee to have a conflicting interest within the meaning of the Trust Indenture Act, assuming all debt securities of a series were in default within the meaning of such Act;
- the legal defeasance or covenant defeasance will not result in a breach or violation of, or constitute a default under, any other agreement or instrument to which we are a party;
- if prior to the stated maturity date, notice shall have been given in accordance with the provisions of the indenture;
- the legal defeasance or covenant defeasance will not result in the trust arising from such deposit constituting an investment company within the meaning of the Investment Company Act of 1940, as amended, unless the trust is registered under such Act or exempt from registration; and

- we have delivered to the trustee an officers' certificate and an opinion of counsel stating that all conditions precedent with respect to the legal defeasance or covenant defeasance have been complied with.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

Paying Agent and Registrar

The trustee will initially act as paying agent and registrar for all debt securities. We may change the paying agent or registrar for any series of debt securities without prior notice, and we or any of our subsidiaries may act as paying agent or registrar.

Form of Securities

Each debt security will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of the series of debt securities. Certificated securities will be issued in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depository or its nominee as the owner of the debt securities represented by these global securities. The depository maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the registered debt securities in the form of one or more fully registered global securities that will be deposited with a depository or its custodian identified in the applicable prospectus supplement and registered in the name of that depository or its nominee. In those cases, one or more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depository for the registered global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depository arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a registered global security, the depository will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depository, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depository, or its nominee, is the registered owner of a registered global security, that depository or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the indenture. Except as described below, owners of beneficial interests in a registered global security will not be entitled to have the securities represented by the registered global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the indenture. Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for that registered global security and, if that person is not a participant,

on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the indenture. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the indenture, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities represented by a registered global security registered in the name of a depository or its nominee will be made to the depository or its nominee, as the case may be, as the registered owner of the registered global security. Neither we nor the trustee or any other agent of ours or the trustee will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depository for any of the securities represented by a registered global security, upon receipt of any payment of principal, premium, interest or other distribution of underlying securities or other property to holders on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depository. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name," and will be the responsibility of those participants.

If the depository for any of these securities represented by a registered global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act, and a successor depository registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depository. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depository gives to the trustee or other relevant agent of ours or theirs. It is expected that the depository's instructions will be based upon directions received by the depository from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depository.

Unless we state otherwise in a prospectus supplement, the Depository Trust Company ("DTC") will act as depository for each series of debt securities issued as global securities. DTC has advised us that DTC is a limited-purpose trust company created to hold securities for its participating organizations (collectively, the "Participants") and to facilitate the clearance and settlement of transactions in those securities between Participants through electronic book-entry changes in accounts of its Participants. The Participants include securities brokers and dealers, banks, trust companies, clearing corporations and certain other organizations. Access to DTC's system is also available to other entities such as banks, brokers, dealers and trust companies that clear through or maintain a custodial relationship with a Participant, either directly or indirectly (collectively, the "Indirect Participants"). Persons who are not Participants may beneficially own securities held by or on behalf of DTC only through the Participants or the Indirect Participants. The ownership interests in, and transfers of ownership interests in, each security held by or on behalf of DTC are recorded on the records of the Participants and the Indirect Participants.

Governing Law

The indenture and each series of debt securities are governed by, and construed in accordance with, the laws of the State of New York.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate agreement. We may enter into a warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Additional Information

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- a discussion on any material or special United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and

- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5 p.m., Eastern time, on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other 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 unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units;
- the terms of the unit agreement governing the units;
- United States federal income tax considerations relevant to the units; and
- whether the units will be issued in fully registered global form.

This summary of certain general terms of units and any summary description of units in the applicable prospectus supplement do not purport to be complete and are qualified in their entirety by reference to all provisions of the applicable unit agreement and, if applicable, collateral arrangements and depositary arrangements relating to such units. The forms of the unit

agreements and other documents relating to a particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus from time to time in one or more transactions, including without limitation:

- directly to one or more purchasers;
- through agents;
- in "at the market offerings" to or through a market maker or into an existing trading market, or a securities exchange or otherwise;
- to or through underwriters, brokers or dealers; or
- through a combination of any of these methods.

A distribution of the securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants, subscriptions, exchangeable securities, forward delivery contracts and the writing of options.

In addition, the manner in which we may sell some or all of the securities covered by this prospectus includes, without limitation, through:

- a block trade in which a broker-dealer will attempt to sell as agent, but may position or resell a portion of the block, as principal, in order to facilitate the transaction;
- purchases by a broker-dealer, as principal, and resale by the broker-dealer for its account;
- ordinary brokerage transactions and transactions in which a broker solicits purchasers; or
- privately negotiated transactions.

We may also enter into hedging transactions. For example, we may:

- enter into transactions with a broker-dealer or affiliate thereof in connection with which such broker-dealer or affiliate will engage in short sales of the Common Stock pursuant to this prospectus, in which case such broker-dealer or affiliate may use shares of Common Stock received from us to close out its short positions;
- sell securities short and redeliver such shares to close out our short positions;
- enter into option or other types of transactions that require us to deliver Common Stock to a broker-dealer or an affiliate thereof, who will then resell or transfer the Common Stock under this prospectus; or
- loan or pledge the Common Stock to a broker-dealer or an affiliate thereof, who may sell the loaned shares or, in an event of default in the case of a pledge, sell the pledged shares pursuant to this prospectus.

In addition, we may enter into derivative or hedging transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with such a transaction, the third parties may sell securities covered by and pursuant to this prospectus and an applicable prospectus supplement or other offering materials, as the case may be. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and an applicable prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and the applicable prospectus supplement or other offering materials, as the case may be.

A prospectus supplement with respect to each offering of securities will state the terms of the offering of the securities, including:

- the terms of the offering;
- the name or names of any underwriters or agents and the amounts of securities underwritten or purchased by each of them, if any;
- the public offering price or purchase price of the securities and the net proceeds to be received by us from the sale;
- any delayed delivery arrangements;
- any underwriting discounts or agency fees and other items constituting underwriters' or agents' compensation;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or markets on which the securities may be listed.

The offer and sale of the securities described in this prospectus by us, the underwriters or the third parties described above may be effected from time to time in one or more transactions, including privately negotiated transactions, either:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale, including in "at the market offerings";
- at prices related to the prevailing market prices; or
- at negotiated prices.

General

Any public offering price and any discounts, commissions, concessions or other items constituting compensation allowed or reallocated or paid to underwriters, dealers, agents or remarketing firms may be changed from time to time. Underwriters, dealers, agents and remarketing firms that participate in the distribution of the offered securities may be "underwriters" as defined in the Securities Act. Any discounts or commissions they receive from us and any profits they receive on the resale of the offered securities may be treated as underwriting discounts and commissions under the Securities Act. We will identify any underwriters, agents or dealers and describe their commissions, fees or discounts in the applicable prospectus supplement or other offering materials, as the case may be.

Underwriters and Agents

If underwriters are used in a sale, they will acquire the offered securities for their own account. The underwriters may resell the offered securities in one or more transactions, including negotiated transactions. These sales may be made at a fixed public offering price or prices, which may be changed, at market prices prevailing at the time of the sale, at prices related to such prevailing market price or at negotiated prices. We may offer the securities to the public through an underwriting syndicate or through a single underwriter. The underwriters in any particular offering will be mentioned in the applicable prospectus supplement or other offering materials, as the case may be.

Unless otherwise specified in connection with any particular offering of securities, the obligations of the underwriters to purchase the offered securities will be subject to certain conditions contained in an underwriting agreement that we will enter into with the underwriters at the time of the sale to them. The underwriters will be obligated to purchase all of the securities of the series offered if any of the securities are purchased, unless otherwise specified in connection with any particular offering of securities. Any initial offering price and any discounts or concessions allowed, reallocated or paid to dealers may be changed from time to time.

We may designate agents to sell the offered securities. Unless otherwise specified in connection with any particular offering of securities, the agents will agree to use their best efforts to solicit purchases for the period of their appointment. We may also sell the offered securities to one or more remarketing firms, acting as principals for their own accounts or as agents for us. These firms will remarket the offered securities upon purchasing them in accordance with a redemption or repayment

pursuant to the terms of the offered securities. A prospectus supplement or other offering materials, as the case may be, will identify any remarketing firm and will describe the terms of its agreement, if any, with us and its compensation.

In connection with offerings made through underwriters or agents, we may enter into agreements with such underwriters or agents pursuant to which we receive our outstanding securities in consideration for the securities being offered to the public for cash. In connection with these arrangements, the underwriters or agents may also sell securities covered by this prospectus to hedge their positions in these outstanding securities, including in short sale transactions. If so, the underwriters or agents may use the securities received from us under these arrangements to close out any related open borrowings of securities.

Dealers

We may sell the offered securities to dealers as principals. We may negotiate and pay dealers' commissions, discounts or concessions for their services. The dealer may then resell such securities to the public either at varying prices to be determined by the dealer or at a fixed offering price agreed to with us at the time of resale. Dealers engaged by us may allow other dealers to participate in resales.

Direct Sales

We may choose to sell the offered securities directly to multiple purchasers or a single purchaser. In this case, no underwriters or agents would be involved.

Institutional Purchasers

We may authorize agents, dealers or underwriters to solicit certain institutional investors to purchase offered securities on a delayed delivery basis pursuant to delayed delivery contracts providing for payment and delivery on a specified future date. The applicable prospectus supplement or other offering materials, as the case may be, will provide the details of any such arrangement, including the offering price and commissions payable on the solicitations.

We will enter into such delayed contracts only with institutional purchasers that we approve. These institutions may include commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions.

Indemnification; Other Relationships

We may have agreements with agents, underwriters, dealers and remarketing firms to indemnify them against certain civil liabilities, including liabilities under the Securities Act. Agents, underwriters, dealers and remarketing firms, and their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business. This includes commercial banking and investment banking transactions.

Market-Making, Stabilization and Other Transactions

There is currently no market for any of the offered securities, other than our Common Stock which is listed on The Nasdaq Capital Market. If the offered securities are traded after their initial issuance, they may trade at a discount from their initial offering price, depending upon prevailing interest rates, the market for similar securities and other factors. While it is possible that an underwriter could inform us that it intends to make a market in the offered securities, such underwriter would not be obligated to do so, and any such market-making could be discontinued at any time without notice. Therefore, no assurance can be given as to whether an active trading market will develop for the offered securities. We have no current plans for listing of the debt securities or preferred stock on any securities exchange or quotation system; any such listing with respect to any particular debt securities or preferred stock will be described in the applicable prospectus supplement or other offering materials, as the case may be.

In connection with any offering of Common Stock, the underwriters may purchase and sell shares of Common Stock in the open market. These transactions may include short sales, syndicate covering transactions and stabilizing transactions. Short sales involve syndicate sales of Common Stock in excess of the number of shares to be purchased by the underwriters in the offering, which creates a syndicate short position. "Covered" short sales are sales of shares made in an amount up to the number of shares represented by the underwriters' over-allotment option. In determining the source of shares to close out the covered syndicate short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Transactions to close out the covered syndicate short involve either purchases of the Common Stock in the open market after the distribution

has been completed or the exercise of the over-allotment option. The underwriters may also make "naked" short sales of shares in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares of Common Stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of bids for or purchases of shares in the open market while the offering is in progress for the purpose of pegging, fixing or maintaining the price of the securities.

In connection with any offering, the underwriters may also engage in penalty bids. 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 these transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

LEGAL MATTERS

Unless otherwise specified in the applicable prospectus supplement, the validity of the securities offered hereby will be passed upon for us by Mintz Levin Cohn Ferris Glovsky and Popeo, P.C. ("Mintz Levin"). Certain other legal matters will also be passed upon for us by Mintz Levin. If legal matters in connection with offerings made by this prospectus are passed on by counsel for the underwriters, dealers or agents, if any, that counsel will be named in the applicable prospectus supplement.

EXPERTS

The audited financial statements incorporated by reference in this prospectus and elsewhere in the registration statement have been incorporated by reference in reliance upon the report of Grant Thornton LLP, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

We incorporate by reference into this prospectus the documents listed below (excluding any portions of such documents that have been "furnished" but not "filed" for purposes of the Exchange Act):

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 22, 2018;
- Our Amended Annual Report on Form 10-K/A for the fiscal year ended December 31, 2017, filed with the SEC on April 2, 2018;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, filed with the SEC on May 10, 2018;
- Our Current Reports on Form 8-K filed with the SEC on June 20, 2018; May 10, 2018; March 22, 2018; March 14, 2018 and February 8, 2018; and
- The description of our common stock set forth in our Registration Statement on Form 8-A, filed with the SEC on August 2, 2013 (including any amendment or report filed with the SEC for the purpose of updating such description).

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, and (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. Any such filings shall be deemed to be incorporated by reference and to be a part of this prospectus from the respective dates of filing of those documents. The SEC file number for each document incorporated by reference is 1-33650.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, copies of these filings, excluding all exhibits unless an exhibit has been specifically incorporated by reference in such filings, at no cost, upon written or oral request made to:

Caladrius Biosciences, Inc.
800 Westchester Ave.
Ste. N341
Rye Brook, NY 10573
(212) 584-4178
Attention: Todd C. Girolamo, SVP, General Counsel and Corporate Secretary

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 of which this prospectus is a part with the SEC under the Securities Act of 1933. This prospectus omits some information and exhibits included in the registration statement, copies of which may be obtained upon payment of a fee prescribed by the Commission or may be examined free of charge at the principal office of the SEC in Washington, DC. You may also access our Form S-3 registration statement on the SEC's website as discussed below.

We are subject to the informational requirements of the Securities Exchange Act of 1934 and in accordance therewith file reports, proxy statements and other information with the SEC. The reports, proxy statements and other information filed by us with the SEC can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. Copies of filings can be obtained from the Public Reference Room maintained by the SEC by calling the SEC at 1-800-SEC-0330. In addition, the Commission maintains a website that contains reports, proxy and informational statements and other information filed electronically with the SEC at <http://www.sec.gov>.

You may request, orally or in writing, a copy of these documents, which will be provided to you at no cost, by contacting Todd C. Girolamo, Esq., SVP, General Counsel and Corporate Secretary, Caladrius Biosciences, Inc., 800 Westchester Ave., Suite N341, Rye Brook, New York 10573, telephone (212) 584-4178.

You should rely only on the information contained in this prospectus, including information incorporated by reference as described above, or any prospectus supplement that we have specifically referred you to. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

**1,632,652 Shares of Common Stock
Warrants to Purchase 816,326 Shares of Common Stock**



PROSPECTUS SUPPLEMENT

February 12, 2021