

Prospectus Supplement
(To prospectus dated June 12, 2020)**13,089,002 Shares****Common stock**

We are offering 13,089,002 shares of our common stock, with a par value of \$0.001 per share for an issue price of \$1.91 per share in a registered direct offering directly to investors pursuant to this prospectus supplement and the accompanying prospectus and securities purchase agreements with such investors. Our common stock is listed on The Nasdaq Global Market under the symbol "AXLA." On March 15, 2022, the last reported sale price for our common stock on The Nasdaq Global Market was \$1.91 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company disclosure and reporting requirements.

This offering is being made without an underwriter or a placement agent and we will not be paying any underwriting discounts or commissions in connection with this offering. We will receive all of the proceeds from the common stock sold in this offering. We will receive net proceeds from the sale of these shares of approximately \$24.9 million.

In addition, certain of our officers and directors, each an affiliate of Axcella Health Inc. (d/b/a Axcella Therapeutics), will participate in this offering and will purchase an aggregate of 94,240 shares of common stock on the same terms as the other investors. See "Plan of Distribution" beginning on page [S-17](#) of this prospectus supplement for more information regarding these arrangements.

Investing in our common stock involves a high degree of risk. See "Risk factors" beginning on page [S-6](#) of this prospectus supplement (including without limitation, the risk factor entitled "The price of our stock may be volatile, and our stockholders could lose all or part of their investment"), as well as those risks described in our most recent [Quarterly Report on Form 10-Q for the quarter ended September 30, 2021](#) and in our other filings with the Securities and Exchange Commission that are incorporated by reference into this prospectus supplement.

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.

Delivery of the common stock at the closing of the offering is expected to be made on or about March 16, 2022.

The date of this prospectus supplement is March 16, 2022.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated June 12, 2020, including the documents incorporated by reference therein, provides more general information. 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 or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or the SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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 the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections titled “Where you can find more information” and “Incorporation of certain information by reference” in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement, the accompanying prospectus, or any free writing prospectus provided in connection with this offering, and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus supplement, the accompanying prospectus and the information incorporated by referenced herein or therein to “Axcella,” “the company,” “we,” “us,” “our” and similar terms refer to Axcella Health Inc. (d/b/a Axcella Therapeutics) and, where appropriate, our subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement. This summary does not contain all of the information you should consider before investing in our common stock. Before you decide to invest in our common stock, you should carefully read the prospectus supplement and the accompanying prospectus and any related free writing prospectus, including the section titled “Risk factors” contained in this prospectus supplement, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering. You should also carefully read the information incorporated by reference into this prospectus supplement and the accompanying prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part.

Company overview

We are a clinical-stage biotechnology company focused on pioneering a new approach to treat complex diseases using compositions of endogenous metabolic modulators, or EMMs. Our product candidates are comprised of multiple EMMs that are engineered in distinct combinations and ratios with the goal of simultaneously impacting multiple biological pathways. Our pipeline includes lead therapeutic candidates for the treatment of non-alcoholic steatohepatitis, or NASH, the treatment of Long COVID (also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19, or “PASC”) associated fatigue, and for the reduction in risk of recurrent overt hepatic encephalopathy, or OHE.

Using our discovery platform, we have efficiently designed product candidates that are comprised of amino acids and their derivatives, which have a general history of safe use. The orally administered EMM compositions that we have tested to date in our development model have shown the potential to generate multifactorial effects in our initial Clinical Studies.

An overview of our current therapeutic product candidates and their planned next development steps is illustrated below:

PRODUCT CANDIDATE	POTENTIAL INDICATION	INITIAL CLINICAL STUDIES ¹		THERAPEUTIC DEVELOPMENT
AXA1125	Adult NASH	AXA1125-002 N=32, 1 arm, 1 dose	AXA1125-003 N=102, 4 arms, 1 AXA1125 dose	EMMPACT SM Phase 2b Clinical Trial N=270, 3 arms, 2 doses
AXA1125	Pediatric NASH			Next Step: Regulatory Engagement
AXA1125	Long COVID			Phase 2a Clinical Trial N=40, 2 arms, 1 dose
AXA1665	Overt Hepatic Encephalopathy	AXA1665-001 N=16, 2 periods, 2 doses	AXA1665-002 N=60, 3 arms, 2 doses	EMMPOWER SM Phase 2 Clinical Trial N=150, 2 arms, 1 dose

■ Completed ■ Underway ■ Planned

¹ Initial Clinical Studies refers to Non-IND Clinical Studies initiated prior to a development path decision.

AXA1125 for the Treatment of NASH

We have conducted two prior Clinical Studies of AXA1125 in subjects with presumed NASH. AXA1125 was generally well tolerated in both of these studies with meaningful and sustained reductions shown in key measures of hepatic fat, insulin resistance, inflammation and fibrosis. In our most recent Clinical Study, AXA1125-003, reductions in these measures were even greater among subjects with type 2 diabetes. Notably, the forementioned results were seen without an impact on mean body weight or serum lipids. In August 2021, results from the AXA1125-003 Clinical Study were published in the *American Journal of Gastroenterology*.

In April 2021, we received U.S. Food and Drug Administration (FDA) clearance of an Investigational New Drug (IND) application for AXA1125, and we initiated our EMMPACT Phase 2b Clinical Trial for

this candidate in the second quarter of 2021. This randomized, double-blind, placebo-controlled, multi-center Clinical Trial is evaluating the efficacy, safety and tolerability of AXA1125 in adult patients with biopsy-confirmed F2/F3 NASH. Approximately 270 patients will be enrolled and randomized 1:1:1 to receive either 45.2 or 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 48 weeks, with a four-week safety follow-up period. Patients will be stratified based on the presence or absence of type 2 diabetes.

The Clinical Trial's primary endpoint will assess the proportion of patients with a biopsy-confirmed ≥ 2 point improvement in their non-alcoholic fatty liver disease, or NAFLD, Activity Score (NAS) after the 48-week treatment period. Secondary endpoints will include the proportion of patients achieving biopsy-confirmed resolution of NASH without worsening of fibrosis and the proportion of patients achieving a ≥ 1 stage improvement in fibrosis without worsening of NASH.

AXA1125 for the Treatment of Long COVID

In October, 2021, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) accepted a Phase 2a clinical trial authorization (CTA) to investigate AXA1125 as a potential treatment for patients with Long COVID. We are conducting this trial at Oxford Centre for Clinical Magnetic Resonance Research, University of Oxford, and patient screening in the Phase 2a trial began in December 2021.

The Phase 2a trial is a randomized, double-blind, placebo-controlled investigation to evaluate the efficacy and safety of AXA1125 in patients with exertional fatigue related to Long COVID. Approximately 40 patients will be enrolled and randomized evenly to receive either 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 28 days, with a one-week safety follow-up period. This same daily dose of AXA1125 already been investigated in a 12-week Clinical Study in subjects with presumed NASH and was safe and generally well tolerated.

The trial's primary endpoint will assess the improvement of mitochondrial function within the skeletal muscle as measured by changes in phosphocreatine (PCr) recovery time, as measured by 31-phosphorus magnetic resonance spectroscopy (MRS), from baseline to Day 28. PCr recovery time is a well-established and highly sensitive measure that has been strongly correlated with a registrational endpoint (i.e., 6-minute walk test) in a number of other diseases in which fatigue and muscle weakness play a central role, including amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy, and chronic kidney disease. Key secondary endpoints include lactate levels, a 6-minute walk test, fatigue scores, and safety and tolerability.

AXA1665 for the Reduction in Risk of Recurrent OHE

We have conducted two prior Clinical Studies of AXA1665 in subjects with mild (Child Pugh A) and moderate (Child Pugh B) hepatic insufficiency. AXA1665 was generally well tolerated in both of these studies, with multifactorial effects seen in subjects. The findings from our most recent Clinical Study, AXA1665-002, which were presented at the Digestive Disease Week 2021 Annual Meeting, replicated those seen on amino acid metabolism from our previous short-term Clinical Study. We also noted dose dependent, directionally consistent improvement across all three psychometric tests that were utilized in AXA1665-002.

In January 2021, we received U.S. Food and Drug Administration (FDA) clearance of an Investigational New Drug (IND) application for AXA1665, and we initiated our EMMPOWER Phase 2 Clinical Trial for this candidate in the second quarter of 2021. This global randomized, double-blind, placebo-controlled, multi-center investigation is evaluating the efficacy and safety of AXA1665 in patients who have experienced at least one prior OHE event and have neurocognitive dysfunction at screening. Approximately 150 patients on lactulose \pm rifaximin (stratified by rifaximin use) will be randomized 1:1 to receive either 53.8 grams per day of AXA1665 or a matched placebo in three divided doses for 24 weeks, with a four-week safety follow-up period.

The Clinical Trial's primary endpoint will assess the proportion of patients with a ≥ 2 point increase in the psychometric hepatic encephalopathy score (PHES) after the 24-week treatment period. Key secondary endpoints will focus on the proportion of patients experiencing an OHE breakthrough event and time to first

OHE breakthrough event, including time to hospitalization. Other secondary endpoints include changes in physical function and patient-reported outcomes.

Effects of COVID-19 Pandemic

The extent to which COVID-19 impacts our business, operations or financial results will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, new information that may emerge concerning the severity of COVID-19 or the nature or effectiveness of actions to contain COVID-19 or treat its impact, among others. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. However, if we or any of the third parties with whom we engage 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, results of operations and financial condition.

Corporate information

We were incorporated in August 2008 under the laws of the state of Delaware under the name Newco LS16, Inc. Our legal name was changed to Axcella Health Inc. in June 2016 and our operating name was changed to Axcella Therapeutics in October 2021. Our principal executive offices are located at 840 Memorial Drive, Cambridge, MA 02139, and our phone number is (857) 320-2200. Our website address is <https://www.axcellatx.com>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name and our logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of being an emerging growth company and smaller reporting company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm under Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these exemptions until December 31, 2024 or until we are no longer an “emerging growth company,” whichever is earlier. We will cease to be an emerging growth company prior to the end of such period if certain earlier events occur, including if we become a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, our annual gross revenues exceed \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of accounting standards that have different effective dates for public and private companies until those standards would otherwise apply to private companies. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take

advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common stock offered by us	\$25.0 million of shares of our common stock.
Common stock to be outstanding immediately after this offering	51,777,957 shares.
Use of proceeds	<p>We estimate that our net proceeds from this offering will be approximately \$24.9 million, after deducting estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds we receive from this offering, together with our existing cash, cash equivalents and investments, to complete our Long COVID Phase 2a clinical trial and, assuming positive data, our regulatory dialogue regarding next steps for this program; advance and complete enrollment of our EMMPOWER Phase 2b clinical trial in non-alcoholic steatohepatitis (NASH); advance our EMMPOWER Phase 2 clinical trial in OHE; and for working capital and other general corporate purposes. See “Use of proceeds” for additional information.</p>
Insider Participation	Certain of our officers and directors, each an affiliate of Axcella, will participate in this offering and will purchase an aggregate of 94,240 shares of common stock on the same terms as the other investors. See “Plan of Distribution” beginning on page S-17 of this prospectus supplement for more information regarding these arrangements.
Risk factors	See “Risk factors” beginning on page S-6 of this prospectus supplement and other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should carefully consider before deciding to invest in our common stock.
Nasdaq Global Market symbol	“AXLA”

The number of shares of our common stock to be outstanding after this offering set forth above is based on 38,269,974 shares of our common stock outstanding as of September 30, 2021, and excludes:

- 6,030,046 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2021, at a weighted-average exercise price of \$5.97 per share;
- 1,143,830 shares of our common stock reserved for future issuance under our 2019 Stock Option and Incentive Plan, or 2019 Plan, as of September 30, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 Plan;
- 635,742 shares of our common stock reserved for issuance under our 2019 Employee Stock Purchase Plan, or ESPP, as of September 30, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our ESPP; and
- 345,409 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2021.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding options described above after September 30, 2021.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our most recent [Quarterly Report on Form 10-Q for the quarter ended September 30, 2021](#) as updated or superseded by the risks and uncertainties described in our subsequent filings under the Exchange Act, each of which is incorporated by reference into this prospectus supplement and the accompanying prospectus, and all of the other information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks is realized, our business, financial condition, results of operations and prospects could be harmed. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Related to this Offering

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of our existing cash, cash equivalents and the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the right or opportunity as part of your investment decision to assess whether such proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of our existing cash, cash equivalents and the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our existing cash, cash equivalents and the net proceeds from this offering in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

If you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of your investment.

The offering price will be substantially higher than the as adjusted net tangible book value per share of our common stock after this offering. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the as adjusted net tangible book value per share after this offering. As a result, investors purchasing common stock in this offering will incur immediate substantial dilution of \$[•] per share, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering and the offering price. To the extent outstanding stock options are exercised, new stock options are issued or we issue additional shares of common stock in the future, including through the sale of equity or convertible debt securities, there will be further dilution to new investors. As a result of the dilution to investors purchasing common stock in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. For a further description of the dilution that you will experience immediately after this offering, see “Dilution.”

COVID-19 may materially and adversely affect our business and our financial results.

The COVID-19 pandemic has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions, supply chain disruptions, business shutdowns and clinical site closures to non-essential care and clinical trials. For example, our AXA1957-002 Clinical Study was temporarily suspended in March 2020 due to COVID-19’s impact on our Clinical Study sites. Subsequently, based on positive data in our AXA1125-003 Clinical Study announced on May 6, 2020, we decided against reinitiating our AXA1957-002 Clinical Study and to move forward with AXA1125 as our NASH product candidate for both adult and pediatric patients. Although we cannot presently predict the full scope and severity of COVID-19, these developments and measures could materially and adversely affect our business, our results of operation and financial condition. Furthermore, the COVID-19 pandemic

may adversely impact our ability to complete our Clinical Trial for AXA1665 and our ongoing and planned Clinical Trials for AXA1125 in a timely manner or at all due to patient or principal investigator recruitment or availability challenges, Clinical Trial site shutdowns or other interruptions. Additionally, we may also experience potential limitations on the quality, completeness and interpretability of data we are able to collect. For instance, on May 7, 2020, a subject death was reported as a result of COVID-19 by one of our principal investigators in our recently completed AXA1665-002 Clinical Study. This serious adverse event and any others that may result from COVID-19 may impact the quality, completeness and interpretability of the data that we were able to collect. The supply chain disruptions that resulted from COVID-19-related manufacturing shutdowns, global transportation changes, and loss of workers in key industries could affect access to raw materials and operations for manufacturing our product candidates, and distribution of product candidates to clinical sites or for commercialization. In addition, as a result of the COVID-19 pandemic, we or our key third-party service providers may be not able to complete key program and product development milestones on time or at all; quarantines, shelter-in-place and similar government orders may impact personnel at third-party manufacturing facilities that negatively impact the availability or cost of materials used in our product candidates; market volatility and conditions may limit our ability to raise additional capital to finance our business plans on attractive terms or at all; our business continuity plans may not be effective at limiting operational disruptions or delays; we may suffer negative impacts to operations that may be vulnerable as a result of government or company measures taken to control the spread of COVID-19; potential shutdowns of government agencies such as the SEC or FDA may limit our ability to raise capital and negatively impact our product development timelines; the passage of new legislation may increase our operating costs or limit our operations, such as the Families First Coronavirus Response Act; we may suffer negative consequences due to vulnerabilities that emerge as a result of our limited operations, such as a cybersecurity incident; or one of our key executives, scientists or other personnel may become incapacitated by COVID-19. Additionally, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

The extent to which COVID-19 impacts our business, operations or financial results will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, new information that may emerge concerning the severity of COVID-19 or the nature or effectiveness of actions to contain COVID-19 or treat its impact, among others. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. However, if we or any of the third parties with whom we engage 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, results of operation and financial condition.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

In this prospectus supplement, we use the following defined terms:

“product candidate” to refer to one of our investigational product candidates.

“development platform” to refer to our proprietary human-focused development platform.

“dose” to refer to the exposure amount of a product candidate in Clinical Studies or Clinical Trials.

“non-drug” to refer to a non-therapeutic use of a product candidate. Such use may be as a medical food, food product or dietary supplement.

“Clinical Trial” to refer to a human clinical study of a drug product candidate subject to the requirements for an effective Investigational New Drug application, or an IND.

“Clinical Study” to refer to Institutional Review Board-Approved, or IRB-Approved, clinical studies conducted in humans with our product candidates under U.S. Food and Drug Administration, or the FDA, regulations and guidance supporting research with food outside of an IND (prior to any decision to develop a product candidate as a drug product candidate under an IND or a non-drug product candidate). In these food studies, based on our understanding of FDA regulations and guidance, we evaluate in humans, including individuals with disease, a product candidate for safety, tolerability and effects on the normal structures and functions of the body. These studies are not designed or intended to evaluate a product candidate’s ability to diagnose, cure, mitigate, treat or prevent a disease as these would be evaluated in Clinical Trials if we decide to develop a product candidate as a drug or therapeutic.

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we may authorize for use contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act, and the Private Securities Litigation Reform Act of 1995. These statements are based on our management’s current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. All statements other than statements of historical facts contained in this prospectus supplement and the accompanying prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plan, objectives of management, results of preclinical studies, clinical studies or clinical trials and expected market growth are forward-looking statements.

You can identify forward-looking statements by the use of words such as “outlook,” “believes,” “expects,” “potential,” “continues,” “may,” “will,” “should,” “seeks,” “approximately,” “predicts,” “intends,” “plans,” “estimates,” “anticipates” or the negative version of these words or other comparable words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under “Risk Factors” including, among other things:

- the benefits of our product candidates to health and/or disease and their commercial potential;
- the success, cost and timing of our product development activities, including statements regarding the timing of initiation and completion of preclinical studies, Clinical Studies or Clinical Trials and related preparatory work, and the timing of the availability of the results of these preclinical studies, Clinical Studies and Clinical Trials, including our ongoing and planned Clinical Trials for AXA1125 and AXA1665;
- our ability to use our research platform to design new product candidates with desirable biological activity;
- our ability to obtain and maintain regulatory approval or find alternate regulatory commercialization pathways from the FDA, the European Medicines Agency, or the EMA, and other comparable regulatory authorities for our product candidates, and any related restrictions, limitations or warnings in the label of an approved product candidate;

- our financing needs and the sufficiency of our funds to support company operations and business plans through certain periods of time, including funding necessary to complete further development of our product candidates, and, if successful, commercialization of these candidates as drug or non-drug products;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates, development platform and the type of such protection;
- our ability to successfully manufacture our product candidates for preclinical studies, Clinical Studies and Clinical Trials and for commercial use, if approved;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets, either alone or in combination with others;
- the rate and degree of market acceptance of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to enter into a collaboration, partnership, or other agreement with a third party on reasonable terms or at all to develop one or more product candidates or commercialize any of our product candidates, if approved;
- our ability to secure sufficient manufacturing and supply chain capacity;
- the success of competing products or therapies that are or may become available;
- our ability to attract and retain key scientific, management or other necessary personnel;
- our estimates regarding expenses for both product development and as a public company, future revenue, capital requirements and needs for additional financing;
- the potential for faults in our internal controls;
- the effect of the COVID-19 pandemic on any of the foregoing; and
- other risks and uncertainties, including those discussed in “Risk Factors” in our [Quarterly Report on Form 10-Q for the quarter ended September 30, 2021](#), which is incorporated by reference into this prospectus supplement.

All of our forward-looking statements are as of the date of this prospectus supplement only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this prospectus supplement or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this prospectus supplement, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this prospectus supplement that modify or impact any of the forward-looking statements contained herein will be deemed to modify or supersede such statements in this prospectus supplement.

USE OF PROCEEDS

We expect that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately \$24.9 million, after deducting estimated offering expenses payable by us.

We intend to use the net proceeds we receive from this offering, together with our existing cash, cash equivalents and investments, to complete our Long COVID Phase 2a clinical trial and, assuming positive data, our regulatory dialogue regarding next steps for this program; advance and complete enrollment of our EMMPOWER Phase 2b clinical trial in non-alcoholic steatohepatitis (NASH); advance our EMMPOWER Phase 2 clinical trial in OHE; and for working capital and other general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the time and cost necessary to conduct our planned clinical trials, the results of our planned clinical trials and other factors described in the section titled “Risk factors” in this prospectus supplement and the accompanying prospectus, as well as the amount of cash used in our operations and any unforeseen cash needs. Therefore, our actual expenditures may differ materially from the estimates described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds.

We will have broad discretion over how to use the net proceeds to us from this offering. We intend to invest the net proceeds to us from the offering that are not used as described above in short-term, investment-grade, interest-bearing instruments.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. In addition, our ability to pay cash dividends is currently restricted by the terms of our Loan and Security Agreement with SLR Investment Corp., formerly known as Solar Capital Ltd., dated September 2, 2021 and future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited in the foreseeable future to the appreciation of their stock.

Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

DILUTION

As of September 30, 2021, we had a historical net tangible book value of \$35.6 million, or \$0.93 per share of common stock, based on 38,269,974 shares of common stock outstanding. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding.

After giving effect to the sale by us of 13,089,002 shares of common stock in this offering at the price of \$1.91 per share, and after deducting estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2021 would have been \$60.4 million, or \$1.18 per share. This amount represents an immediate increase in our net tangible book value of \$0.25 per share to our existing stockholders and an immediate dilution in our net tangible book value of \$0.73 per share to investors purchasing common stock in this offering. We determine dilution by subtracting our as adjusted net tangible book value per share after this offering from the amount of cash paid by an investor for a share of common stock in this offering. The following table illustrates this dilution on a per share basis:

Offering price per share	<u>\$1.91</u>
Historical net tangible book value per share as of September 30, 2021	\$0.93
Increase in net tangible book value per share attributable to investors purchasing shares in this offering	<u>\$0.25</u>
As adjusted net tangible book value per share after this offering	<u>\$1.18</u>
Dilution in net tangible book value per share to investors purchasing shares in this offering	<u>\$0.73</u>

The number of shares of our common stock to be outstanding after this offering set forth above is based on 38,269,974 shares of our common stock outstanding as of September 30, 2021, and excludes:

- 6,030,046 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2021, at a weighted-average exercise price of \$5.97 per share;
- 1,143,830 shares of our common stock reserved for future issuance under our 2019 Plan, as of September 30, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 Plan;
- 635,742 shares of our common stock reserved for issuance under our ESPP, as of September 30, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our ESPP; and
- 345,409 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2021.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding options described above after September 30, 2021.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax considerations for non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, U.S. Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. There can be no assurance that the U.S. Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address U.S. state, local or non-U.S. taxes, U.S. federal estate or gift tax laws, the alternative minimum tax, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, the Medicare tax on net investment income or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds" as defined in Section 897(I)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;

- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

As described in the “Dividend Policy” section above, we do not anticipate paying any cash dividends to our stockholders in the foreseeable future. Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to such holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “Gain on Sale or Other Taxable Disposition of Our Common Stock.” Any such distributions will also be subject to the discussions below in the sections titled “Backup Withholding and Information Reporting” and “FATCA.”

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence. Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is generally taxed at the same regular U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gains on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under “Backup Withholding and Information Reporting” and “FATCA,” a non-U.S. holder generally will not be subject to any U.S. federal income or withholding tax on any gain realized upon such holder’s sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder’s conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in “Distributions on Our Common Stock” also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case

the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a U.S. real property holding corporation, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are or were a U.S. real property holding corporation during the relevant period and the foregoing exception does not apply, the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the regular U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity either certifies it does not

have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner and such entity meets certain other specified requirements, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to gross proceeds from the sale or other disposition of our common stock, although under proposed U.S. Treasury Regulations, no withholding would apply to such gross proceeds. The preamble to the proposed regulations specifies that taxpayers (including withholding agents) are permitted to rely on the proposed regulations pending finalization. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

PLAN OF DISTRIBUTION

We have arranged for the sale of the common stock we are offering pursuant to this prospectus supplement and the accompanying prospectus to the investors pursuant to a securities purchase agreement directly between the investors and us. The shares were offered on a best efforts basis directly to the investors without a placement agent, underwriter, broker or dealer. All of the common stock sold in this offering will be sold at the same price and we expect a single closing. It is possible that not all of the shares we are offering pursuant to this prospectus supplement will be sold at the closing, in which case our net proceeds would be reduced. The closing of this offering is subject to customary closing conditions. We expect that the sale of the shares will be completed on or around the date indicated on the cover page of this prospectus supplement.

In addition, certain of our officers and directors, each an affiliate of Axcella will participate in this offering and will purchase an aggregate of 94,240 shares of common stock on the same terms as the other investors.

Our common stock is traded on the Nasdaq Global Market under the symbol "AXLA." The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

We have entered into a securities purchase agreement with investors covering the sale of the shares offered under this prospectus supplement. We have agreed with the investors in this offering, for a period of [6] months from the date of the securities purchase agreement, the investors have a right to participate in up to an amount of any subsequent financing as at least equals the aggregate purchase price paid for the shares of common stock purchased in this offering, subject to certain customary exceptions set forth in the securities purchase agreement, which exceptions include any firm commitment public offerings and sales pursuant to an "at-the-market" facility. In addition, from the date until 60 days after the date of the securities purchase agreement, we may not issue, enter into any agreement to issue, or announce the issuance or proposed issuance of any shares of common stock or common stock equivalents, subject to certain exceptions set forth in the securities purchase agreement.

For the complete terms of the securities purchase agreement, you should refer to the form of securities purchase agreement which will be filed as an exhibit to the Current Report on Form 8-K to be filed with the SEC in connection with this offering and which is incorporated by reference into the registration statement of which this prospectus supplement is part. We currently anticipate that closing of the sale of all 13,089,002 shares of our common stock offered hereby will take place on or about March 16, 2022.

LEGAL MATTERS

Goodwin Procter LLP, Boston, Massachusetts, which has acted as our counsel in connection with this offering, will pass upon the validity of the shares of common stock offered hereby.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference to the [Annual Report on Form 10-K for the year ended December 31, 2020](#) have been so incorporated in reliance on the report of Deloitte and Touche LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all of the information set forth in the registration statement and the exhibits thereto. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference therein. For further information with respect to us and the common stock we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at www.axcellatx.com. Information contained in or accessible through our website does not constitute a part of this prospectus supplement or the accompanying prospectus and is not incorporated by reference into this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement or the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made by us with the SEC (other than Current Reports or portions thereof 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 and other portions of documents that are furnished, but not filed, pursuant to applicable rules promulgated by the SEC) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the filing and concurrent effectiveness of the registration statement but prior to the termination of all offerings covered by this prospectus supplement:

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on March 17, 2021;](#)
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021, June 30, 2021 and September 30, 2021 filed with the SEC on [May 6, 2021](#), [July 29, 2021](#) and [November 10, 2021](#), respectively;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [March 3, 2021](#), [May 6, 2021](#), [May 21, 2021](#), [September 7, 2021](#), [November 10, 2021](#), [December 7, 2021](#), [January 10, 2022](#) and [February 7, 2022](#); and
- [the description of our Common Stock in our registration statement on Form 8-A filed with the SEC on May 7, 2019, including any amendments or reports filed for the purpose of updating such description.](#)

We will provide to each person, including any beneficial owner, to whom a prospectus supplement or the underlying prospectus is delivered, without charge upon the written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus supplement but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at AxcellaTherapeutics, 840 Memorial Drive, Cambridge, Massachusetts 02139, (857) 320-2200.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

PROSPECTUS

\$125,000,000



Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may from time to time issue, in one or more series or classes, up to \$125,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units, in any combination, together or separately, in one or more offerings in amounts, at prices and on the terms that we will determine at the time of the offering and which will be set forth in a prospectus supplement and any related free writing prospectus. We may offer these securities separately or together in units. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on the Nasdaq Global Market under the symbol "AXLA." On June 4, 2020, the closing price for our common stock, as reported on the Nasdaq Global Market, was \$5.50 per share. Our principal executive offices are located at 840 Memorial Drive, Cambridge, Massachusetts 02139.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in this prospectus beginning on page 2 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

The date of this prospectus is June 12, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$125,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the headings “Where You Can Find More Information” and “Incorporation by Reference.”

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “Axcella”, “we”, “our”, “us” and “the Company” refer, collectively, to Axcella Health Inc. and its subsidiaries.

We own various U.S. federal trademark applications and unregistered trademarks, including “Axcella” and our corporate logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

In this prospectus, we use the following defined terms:

“product candidate” to refer to one of our investigational product candidates.

“development platform” to refer to our proprietary human focused development platform.

“non drug” to refer to a non therapeutic use of a product candidate. Such use may be as a food product or dietary supplement.

“Clinical Trial” to refer to a human clinical study of a drug product candidate subject to the requirements for an effective Investigational New Drug application, or an IND.

“Clinical Study” to refer to Institutional Review Board Approved, or IRB Approved, clinical studies conducted in humans with our product candidates under U.S. Food and Drug Administration, or the FDA, regulations and guidance supporting research with food outside of an IND (prior to any decision to develop a product candidate as a drug product candidate under an IND or a non drug product candidate). In these food studies, based on our understanding of FDA regulations and guidance, we evaluate in humans, including individuals with disease, a product candidate for safety, tolerability and effects on the normal structures and functions of the body. These studies are not designed or intended to evaluate a product candidate’s ability to diagnose, cure, mitigate, treat or prevent a disease as these would be evaluated in Clinical Trials if we decide to develop a product candidate as a drug or therapeutic.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including (i) [our annual report on Form 10-K for the fiscal year ended December 31, 2019](#), which is on file with the SEC and is incorporated herein by reference, (ii) [our quarterly report on Form 10-Q for the fiscal quarter ended March 31, 2020](#), which is on file with the SEC and are incorporated herein by reference and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this prospectus contain forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference into this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, success, cost and timing of our product development activities, preclinical studies, Clinical Studies and Clinical Trials, including statements regarding the timing of initiation and completion of preclinical studies, Clinical Studies or Clinical Trials and related preparatory work, the timing of the availability of the results of these preclinical studies, Clinical Studies and Clinical Trials and the subject and timing of planned interactions with the FDA or other regulatory agencies, including the timing of IND application submissions;
- our ability to obtain funding for our operations, including funding necessary to complete further development of our initial product candidates, and if successful, commercialization of these candidates as drug or non-drug products;
- the potential for our identified research priorities to advance our development platform, development programs or product candidates;
- our ability to obtain and maintain regulatory approval or find alternate regulatory commercialization pathways from the FDA, the European Medicines Agency, or the EMA, and other comparable regulatory authorities for our product candidates, and any related restrictions, limitations or warnings in the label of an approved product candidate;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates, development platform and the type of such protection;
- our ability and the potential to successfully manufacture our product candidates for preclinical studies, Clinical Studies and Clinical Trials and for commercial use, if approved;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets, either alone or in combination with others;
- the rate and degree of market acceptance of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to enter into a collaboration, partnership, or other agreement with a third party on reasonable terms or at all to develop one or more product candidates or commercialize any of our product candidates, if approved;
- our ability to secure sufficient manufacturing and supply chain capacity;
- the success of competing products or therapies that are or may become available;
- our ability to attract and retain key scientific, management or other necessary personnel;
- our estimates regarding expenses for both product development and as a public company, future revenue, capital requirements and needs for additional financing;
- the potential for faults in our internal controls;
- the effect of the COVID-19 outbreak on any of the foregoing; and
- other risks and uncertainties, including those discussed in “Risk Factors” and “Item 1A. Risk Factors” in our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2020](#), which is incorporated by reference into this prospectus.

Any forward-looking statements in this prospectus and the documents incorporated by reference into this prospectus reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under “Risk Factors” and “Item 1A. Risk Factors” in our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2020](#), which is incorporated by reference into this prospectus, and elsewhere in this prospectus and the documents incorporated by reference into this prospectus. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this prospectus and the documents incorporated by reference into this prospectus. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

THE COMPANY

This summary highlights information contained elsewhere in this prospectus. Before investing in our securities, you should carefully read this entire prospectus, including our consolidated financial statements and the related footnotes and the other documents incorporated by reference herein. As used in this prospectus, unless the context otherwise requires, references to the “company,” “we,” “us” and “our” refer to Axcella Health Inc. together with its consolidated subsidiaries.

We are a clinical-stage biotechnology company focused on leveraging endogenous metabolic modulators, or EMMs, to pioneer a new approach for treating complex diseases and improving health. Our product candidates are comprised of multiple EMMs that are engineered in distinct combinations and ratios with the goal of simultaneously impacting multiple biological pathways. Our pipeline includes lead therapeutic candidates for non-alcoholic steatohepatitis, or NASH, and the reduction in risk of overt hepatic encephalopathy, or OHE, recurrence. Additional muscle- and blood-related programs are in earlier-stage development.

Using our development platform, we have efficiently designed a pipeline of product candidates that are comprised of amino acids and their derivatives, which have a general history of safe use. These orally administered compositions are designed to have multifactorial effects.

Once we design a product candidate, we decide whether to initially evaluate it in (i) a non-investigational new drug application, or non-IND, Institutional Review Board, or IRB, approved Clinical Study under U.S. Food and Drug Administration, or the FDA, regulations and guidance supporting research with food (as noted herein, the term food also includes dietary supplements) or (ii) in a Clinical Trial under an IND. A Clinical Study allows us to evaluate a product candidate’s safety, tolerability and permissible secondary endpoints (e.g. impact on normal structures and functions of the body, including metabolic pathways), before we determine the next steps in its development. Our Clinical Studies are conducted at reputable medical centers following Good Clinical Practices, including IRB approval and monitoring, by qualified investigators, including key opinion leaders in their fields. Subsequent development options for a product candidate we initially investigate in a Clinical Study include, but are not limited to, conducting future research in a Clinical Trial for an identified therapeutic indication, continuing research in another Clinical Study, out-licensing the product candidate, or terminating development.

Corporate history

We were incorporated in August 2008 under the laws of the state of Delaware under the name Newco LS16, Inc. Our name was changed to Axcella Health Inc. in June 2016. Our principal executive offices are located at 840 Memorial Drive, Cambridge, MA 02139, and our phone number is (857) 320-2200. Our website address is <https://www.axcellahealth.com>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name and our logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of being an emerging growth company

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. For so long as we remain an emerging growth company, we are permitted and intend to rely on certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related

information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

We will remain an emerging growth company until the earlier to occur of (1) December 31, 2024, (2) the last day of the fiscal year in which we have total annual gross revenues of at least \$1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a “large accelerated filer,” under the rules of the U.S. Securities and Exchange Commission, or SEC, which means the market value of our equity securities that is held by non-affiliates exceeds \$700 million as of the prior June 30th and (4) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have elected not to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, including the conduct of Clinical Studies or Clinical Trials and advancement of our development platform and discovery efforts, expansion of our infrastructure and capabilities, support of organizational growth and for working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered.

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

DESCRIPTION OF CAPITAL STOCK

The description of our common stock and preferred stock set forth below, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description does not purport to be complete. It is subject to and qualified in its entirety by reference to our Restated Certificate of Incorporation, or our Certificate of Incorporation, and our Amended and Restated Bylaws, or our Bylaws, each of which are incorporated by reference as an exhibit to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common stock and preferred stock may also be affected by Delaware law. We encourage you to read our Certificate of Incorporation, our Bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

Authorized Capital Stock

Our authorized capital stock consists of 150,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share, all of which are undesignated preferred stock.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights, or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. All outstanding shares are fully paid and nonassessable.

Listing

Our common stock is listed and traded on the Nasdaq Global Market under the symbol "AXLA."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. Our board of directors may also designate the rights, preferences and privileges of the holders of each such series of preferred stock, any or all of which may be greater than or senior to those granted to the holders of common stock. While, the issuance of preferred stock provides flexibility in connection with possible future financings and acquisitions and other corporate purposes, the rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Though the actual effect of any such issuance on the rights of the holders of common stock will not be known until such time as our board of directors determines the specific rights of the holders of preferred 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, deferring or preventing a change in control of our company, which might harm the market price of our common stock.

No shares of preferred stock are outstanding as of the date hereof.

Anti-Takeover Effects of Delaware Law and Provisions of our Charter Documents

Certain provisions of the Delaware General Corporation Law and of our Charter Documents could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might 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 might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested 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 voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Charter Documents

Our Charter Documents include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies. In accordance with our Certificate of Incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our Certificate of Incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds ($\frac{2}{3}$) or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No Written Consent of Stockholders. Our Certificate of Incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders. Our by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements. Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to By-laws and Certificate of Incorporation. As required by the Delaware General Corporation Law, any amendment of our Certificate of Incorporation must first be approved by a majority of our board of directors and, if required by law or our Certificate of Incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our by-laws and Certificate of Incorporation must be approved by not less than two-thirds ($\frac{2}{3}$) of the outstanding shares entitled to vote on the amendment, and not less than two-thirds ($\frac{2}{3}$) of the outstanding shares of each class entitled to vote thereon as a class. Our by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the by-laws; and may also be amended by the affirmative vote of at least two-thirds ($\frac{2}{3}$) of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank Check Preferred Stock. Our Certificate of Incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or

other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our Certificate of Incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum. Our Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our Certificate of Incorporation or Bylaws; (4) any action to interpret, apply, enforce or determine the validity of our Certificate of Incorporation or Bylaws or (5) any action asserting a claim governed by the internal affairs doctrine, which we refer to as the Delaware Forum Provision. The Delaware Forum Provision does not apply to any actions arising under the Securities Act or the Exchange Act.

Our Bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which we refer to as the Federal Forum Provision. We have chosen the United States District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. In addition, our Bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to senior debt securities and subordinated debt securities collectively as debt securities. Each series of debt securities may have different terms. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series, under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information. As used in this prospectus, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time; and
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

Unless otherwise provided in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “— Subordination” and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;

- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or other securities of ours or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of common stock or other securities of ours received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which such dates will be determined;
- the persons to whom interest will be payable;
- the place or places where the principal of, and any premium or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or repurchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or repurchase the debt securities as a result of such obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the debt securities will be in registered form, bearer form, or both, and (i) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (ii) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;
- any restrictions applicable to the offer, sale or delivery of securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for securities in registered form of the series and vice versa, if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without coupons and, if so, whether beneficial owners of interests in any such permanent global security may, or shall be required to, exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;
- the identity of the depository for securities in registered form, if such series are to be issuable as a global security;
- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;

- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge;
- whether and under what circumstances the debt securities being offered are convertible into common stock or other securities of ours, as the case may be, including the conversion price or rate and the manner or calculation thereof;
- the name of the applicable trustee and the nature of any material relationship with us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture.

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Except as described under “— Merger, Consolidation or Sale of Assets” or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (i) would limit our ability to incur indebtedness or (ii) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Our governing instruments do not define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless otherwise provided in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period during which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise provided in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of \$1,000 and integral multiples of \$1,000.

Interest on the debt securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

Subject to the limitations imposed upon debt securities that are evidenced by a computerized entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and
- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;
- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and
- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium or make-whole amount, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in the applicable indenture;
- after giving effect to the transaction, there is no event of default under the applicable indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to "events of default" as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 90 days unless such date has been extended or deferred;
- default in the payment of principal of, or any premium or make-whole amount on, any debt security of such series when due and payable unless such date has been extended or deferred;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 days after written notice described below;

- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
- any other event of default provided with respect to a particular series of debt securities.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium or make-whole amount, have been cured or waived.

The indentures require each trustee to give notice to the holders of debt securities within the later of 90 days after an event of default and 30 days after the event of default is actually known to a responsible officer of such trustee, unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 90 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

The indentures provide that modifications and amendments may be made only with the consent of the affected holders of a majority in principal amount of all outstanding debt securities issued under that indenture.

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of debt securities;
- to make any change that does not adversely affect the rights of any securityholder in any material respect;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee; or
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture.

Voting

The indentures provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities, the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof.

Subordination

Unless otherwise provided in the applicable prospectus supplement, subordinated debt securities will be subject to the following subordination provisions.

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated debt securities will be subordinated to the extent provided in the applicable indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated debt securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated debt securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated debt securities are paid in full, holders of subordinated debt securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated debt securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of ours. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated debt securities may recover less, ratably, than our general creditors.

No restrictions will be included in any indenture relating to subordinated debt securities upon the creation of additional senior debt.

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

Discharge, Defeasance and Covenant Defeasance

Unless otherwise provided in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable, an amount sufficient to pay the entire indebtedness on such debt securities
- in respect of principal and any premium or make-whole amount, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date;
- we have paid or caused to be paid all other sums payable; and
- an officers' certificate and an opinion of counsel stating the conditions to discharging the debt securities have been satisfied have been delivered to the trustee.

Unless otherwise provided in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company shall be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

Notwithstanding the above, we may not elect to defease and be discharged from the obligation to pay any additional amounts upon the occurrence of particular events of tax, assessment or governmental charge with respect to payments on such debt securities and the obligations to register the transfer or exchange of such debt securities, to replace temporary or mutilated, destroyed, lost or stolen debt securities, to maintain an office or agency in respect of such debt securities, or to hold monies for payment in trust.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

No Recourse

No recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the debt securities, waives and releases all such liability.

Governing Law

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

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, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or 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 warrant agreement. We will enter into the 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.

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 periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- 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;
- 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.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue 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 of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any applicable prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity, including modifying any provisions of the governing unit agreement that differ from those described below;

- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

Form, Exchange and Transfer

We will issue each unit in global — i.e., book-entry — form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.

Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.

If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an "underwriter" as that term

is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over allot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions.

If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such 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

This prospectus is part of a registration statement on Form S-3 that we have filed with the SEC. This prospectus, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC.

We are subject to the informational requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. We also maintain a website at <https://www.axcellahealth.com/>. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendment to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. We do not incorporate the information on our website into this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus).

INCORPORATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (File No. 001-38901):

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 23, 2020;](#)
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the year ended December 31, 2019](#) from our [definitive proxy statement on Schedule 14A \(other than information furnished rather than filed\)](#), which was filed with the SEC on April 3, 2020;
- [our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on May 11, 2020;](#)
- our Current Reports on Form 8-K, filed with the SEC on [May 6, 2020](#), [May 8, 2020](#), [May 18, 2020](#) and [May 20, 2020](#); and
- [the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on May 7, 2019, including any amendments or reports filed for the purposes of updating this description.](#)

We also incorporate by reference any future filings (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) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until the termination of the offering as to which this prospectus relates. Information in such future filings updates and supplements the information provided or incorporated by reference in this prospectus.

Any information in this prospectus or any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Axcella Health Inc., Attn: Corporate Secretary, 840 Memorial Drive, Cambridge, MA 02139.

You also may access these filings on our website at <https://www.axcellahealth.com/>. We do not incorporate the information on our website into this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

13,089,002 Shares



Common stock

Prospectus supplement

March 16, 2022
