Filed Pursuant to Rule 424(b)(5)
Registration No. 333-238983

PROSPECTUS

Up to $35,000,000

Common Stock

We have entered into a sales agreement, or the Sales Agreement, with SVB Leerink LLC, or SVB Leerink, relating to shares of our common stock offered by this prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $35,000,000 from time to time through SVB Leerink, acting as our agent.

Our common stock is listed on the Nasdaq Global Market under the symbol "AXLA." On June 4, 2020, the last reported sale price of our common stock on the Nasdaq Global Market was $5.50 per share.

Sales of our common stock, if any, under this prospectus will be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. SVB Leerink is not required to sell any specific number or dollar amount of shares of our common stock, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between SVB Leerink and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

SVB Leerink will be entitled to compensation at a fixed commission rate of up to 3.0% of the gross proceeds of any shares of common stock sold through it pursuant to the Sales Agreement. See "Plan of Distribution" beginning on page S-13 for additional information regarding the compensation to be paid to SVB Leerink. In connection with the sale of our common stock on our behalf, SVB Leerink may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of SVB Leerink may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to SVB Leerink with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

We are an "emerging growth company" as defined under U.S. federal securities laws and will be subject to reduced public company reporting requirements. See "Prospectus Summary — Implications of being an emerging growth company."

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 S-6 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.

SVB Leerink

The date of this prospectus is June 12, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission ("SEC"). Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to $35,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of the offering.

If the information contained in this prospectus differs or varies from the information contained in any document incorporated by reference herein that was filed with the SEC before the date of this prospectus, you should rely on the information set forth in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date (for example, a subsequently filed document deemed incorporated by reference in this prospectus), the statement in the document having the later date modifies or supersedes the earlier statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the sales agent has not, authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus or contained in any permitted free writing prospectuses we have authorized for use in connection with this offering. We and the sales agent take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide.

The information contained in this prospectus and the documents incorporated by reference herein is accurate only as of their respective dates, regardless of the time of delivery of any such document or the time of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained or incorporated by reference in this prospectus in making your investment decision. You should read this prospectus, as well as the documents incorporated by reference herein, the additional information described under the section titled "Where You Can Find More Information" and "Incorporation by Reference" in this prospectus and any free writing prospectus that we have authorized for use in connection with this offering, before investing in our common stock.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The distribution of this prospectus and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. Before investing in our common stock, 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.

Our Company

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.

THE OFFERING

Common stock offered by us:	Shares of our common stock having an aggregate offering price of up to $35,000,000.
Common stock to be outstanding after this offering:	Up to 42,202,452 shares (as more fully described in the notes following this table), assuming sales of 6,363,636 shares of our common stock in this offering at an assumed offering price of $5.50 per share, which was the last reported sale price of our common stock on the Nasdaq Global Market on June 4, 2020. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
Manner of offering:	"At the market offering" that may be made from time to time through our sales agent, SVB Leerink LLC, or SVB Leerink. See "Plan of Distribution" on page S-13 of this prospectus.
Use of proceeds:	Our management will retain broad discretion regarding the allocation and use of the net proceeds. We intend to use the net proceeds from this offering to fund research and development of current or additional pipeline programs, working capital and general corporate purposes. See "Use of Proceeds."
Risk factors:	You should carefully read the "Risk Factors" section of this prospectus and under similar headings in documents incorporated by reference into this prospectus for a discussion of factors that you should 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 is based on 23,188,816 shares of our common stock outstanding as of March 31, 2020, gives effect to our subsequent issuance and sale of an aggregate of 12,650,000 shares of common stock in an underwritten public offering that closed on May 18, 2020, and excludes:

- 5,443,078 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2020 under our 2010 Stock Incentive Plan, or our 2010 Plan, and our 2019 Stock Option and Incentive Plan, or our 2019 Plan, with a weighted-average exercise price of $7.09 per share;
- 162,967 shares of common stock reserved for vesting of restricted stock units outstanding as of March 31, 2020 under our 2019 Plan;
- 601,721 shares of common stock available for future issuance as of March 31, 2020 under our 2019 Plan; and
- 469,069 shares of our common stock available for future issuance as of March 31, 2020 under our 2019 Employee Stock Purchase Plan, or our 2019 ESPP.

Unless otherwise stated, all information contained in this prospectus assumes no exercise of stock options after March 31, 2020.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus and the documents incorporated by reference into this prospectus, including the risks identified under "Item 1A. Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described therein and below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks related to our common stock and this offering

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional securities in the future, which may result in additional dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior at the time of sale. Assuming that an aggregate of 6,363,636 shares of our common stock are sold at an assumed offering price of $5.50 per share, the last reported sale price of our common stock on the Nasdaq Global Market on June 4, 2020, for aggregate gross proceeds of approximately $35.0 million, after deducting commissions and estimated aggregate offering expenses payable by us, investors in this offering would experience immediate dilution of $2.27 per share, representing the difference between our as-adjusted net tangible book value per share, after giving effect to this offering, and the assumed 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."

We have broad discretion in the use of our existing cash, cash equivalents and 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.

It is not possible to predict the aggregate proceeds resulting from sales made under the Sales Agreement.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to SVB Leerink at any time throughout the term of the Sales Agreement. The number of shares that are sold through SVB Leerink after delivering a placement notice will fluctuate based on a number of factors, including the market price of our common stock during the sales period, any limits we may set with SVB Leerink in any applicable placement notice and the demand for our common stock. Because the price per share of each share sold pursuant to the Sales Agreement will fluctuate over time, it is not currently possible to predict the aggregate proceeds to be raised in connection with sales under the Sales Agreement.

The common stock offered hereby will be sold in "at-the-market offerings" and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and number of shares sold in this offering. In addition, subject to the final determination by our board of directors or any restrictions we may place in any applicable placement notice, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

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.

USE OF PROCEEDS

We may issue and sell shares of our common stock having an aggregate offering price of up to $35.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions to SVB Leerink and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under the Sales Agreement as a source of financing.

We intend to use the net proceeds from this offering to fund research and development of current or additional pipeline programs, working capital and general corporate purposes.

We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering. Due to uncertainties inherent in the development process, it is difficult to estimate the exact amounts of the net proceeds that will be used for any particular purpose. We may use our existing cash, cash equivalents and the future payments, if any, generated from any future collaboration agreements to fund our operations, either of which may alter the amount of net proceeds used for a particular purpose. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of our Clinical Studies and Clinical Trials and the timing of regulatory submissions. Accordingly, we will have broad discretion in using these proceeds.

Pending their uses, we plan to invest the net proceeds of this offering in short-term, interest-bearing, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of March 31, 2020 was $46.8 million, or $2.02 per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities. Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the 23,188,816 shares of our common stock outstanding as March 31, 2020. After giving effect to our issuance and sale of an aggregate of 12,650,000 shares of our common stock for net proceeds of approximately $55.9 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, in an underwritten public offering that closed on May 18, 2020 (the "Underwritten Offering"), our pro forma net tangible book value as of March 31, 2020 would have been $102.7 million, or $2.87 per share.

After giving further effect to our issuance and sale of an aggregate of 6,363,636 shares of our common stock in this offering at the assumed public offering price of $5.50 per share, the last reported trading price of our common stock on the Nasdaq Global Market on June 4, 2020, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2020 would have been $136.5 million, or $3.23 per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $0.36 to existing stockholders and immediate dilution of $2.27 in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		$5.50
Historical net tangible book value (deficit) per share as of March 31, 2020	$2.02	
Pro forma net tangible book value per share after giving effect to the Underwritten Offering	2.87	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing common stock in this offering	0.36	
Pro forma as adjusted net tangible book value per share after this offering		3.23
Dilution per share to new investors purchasing common stock in this offering		$2.27

An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $5.50 per share, the last reported trading price of our common stock on the Nasdaq Global Market on June 4, 2020, assuming all of our common stock in the aggregate amount of approximately $35,000,000 during the term of the Sales Agreement is sold at that price, would increase our pro forma as adjusted net tangible book value per share to $3.31 per share and would increase the dilution in net tangible book value per share to new investors in this offering to $3.19 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold from the assumed offering price of $5.50 per share, the last reported trading price of our common stock on the Nasdaq Global Market on June 4, 2020, assuming all of our common stock in the aggregate amount of approximately $35,000,000 during the term of the Sales Agreement is sold at that price, would decrease our pro forma as adjusted net tangible book value per share to $3.13 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to $1.37 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The table and discussion above are based on the number of shares of our common stock outstanding as of March 31, 2020 give effect to our issuance and sale of an aggregate of 12,650,000 shares of common stock in the Underwritten Offering, and exclude:

- 5,443,078 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2020 under our 2010 Plan and our 2019 Plan, with a weighted-average exercise price of $7.09 per share;
- 162,967 shares of common stock reserved for vesting of restricted stock units outstanding as of March 31, 2020 under our 2019 Plan;
- 601,721 shares of common stock available for future issuance as of March 31, 2020 under our 2019 Plan; and
- 469,069 shares of our common stock available for future issuance as of March 31, 2020 under our 2019 ESPP.

The information discussed above is illustrative only and the shares subject to our Sales Agreement are being sold from time to time at various prices. To the extent that outstanding stock options are exercised, new stock options are issued or we issue additional shares of common stock in the future, there will be further dilution to new investors. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into a Sales Agreement with SVB Leerink under which we may issue and sell up to $35,000,000 of shares of our common stock from time to time through SVB Leerink as our sales agent. Sales of our common stock, if any, will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415 under the Securities Act, including sales made directly on or through the Nasdaq Global Market, on or through any other existing trading market for the common stock or to or through a market maker.

SVB Leerink will offer our common stock subject to the terms and conditions of the Sales Agreement on a daily basis or as otherwise agreed upon by us and SVB Leerink. We will designate the maximum number or amount of common stock to be sold through SVB Leerink on a daily basis or otherwise determine such maximum number or amount together with SVB Leerink. Subject to the terms and conditions of the Sales Agreement, SVB Leerink will use commercially reasonable efforts consistent with its normal trading and sales practices to sell on our behalf all of the common stock requested to be sold by us. We may instruct SVB Leerink not to sell common stock if the sales cannot be effected at or above a minimum price designated by us in any such instruction. SVB Leerink or we may suspend the offering of our common stock being made through SVB Leerink under the Sales Agreement upon proper notice to the other party. SVB Leerink and we each have the right, by giving written notice as specified in the Sales Agreement, to terminate the Sales Agreement in each party's sole discretion at any time. The offering of our common stock pursuant to the Sales Agreement will otherwise terminate upon the termination of the Sales Agreement as provided therein.

The compensation payable to SVB Leerink as sales agent will be an amount up to 3.0% of the gross proceeds of any shares of common stock sold through it pursuant to the Sales Agreement. We have also agreed to reimburse SVB Leerink for certain actual outside legal expenses incurred by SVB Leerink in connection with this offering, including SVB Leerink's counsel fees in an amount up to $35,000, plus an additional amount of up to $10,000 in connection with each diligence bring-down thereafter. In accordance with FINRA Rule 5110 these reimbursed fees and expenses are deemed sales compensation to SVB Leerink in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to SVB Leerink under the Sales Agreement, will be approximately $250,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory or self-regulatory organization in connection with the sales of our common stock, will equal our net proceeds for the sale of such common stock.

SVB Leerink will provide written confirmation to us no later than the next succeeding trading day on the Nasdaq Global Market after each day on which common stock is sold through it as sales agent under the Sales Agreement. Each confirmation will include the number or amount of shares sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us from such sales.

We will report at least quarterly the number of shares of common stock sold through SVB Leerink under the Sales Agreement, the net proceeds to us and the compensation paid by us to SVB Leerink in connection with the sales of common stock during the relevant period.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf pursuant to the Sales Agreement, SVB Leerink may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation paid to SVB Leerink may be deemed to be underwriting commissions or discounts. We have agreed in the Sales Agreement to provide indemnification and contribution to SVB Leerink with respect to certain liabilities, including liabilities under the Securities Act or the Exchange Act. As sales agent, SVB Leerink will not engage in any transactions that stabilize our common stock.

Our common stock is listed and 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.

SVB Leerink and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received, and may in the future receive, customary fees.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Latham & Watkins LLP is counsel to SVB Leerink in connection with this offering.

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.

Up to $35,000,000

Common Stock

PROSPECTUS

SVB Leerink

June 12, 2020