

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered(1)	Maximum offering price per share	Maximum aggregate offering price	Amount of registration fee(2)
Common stock, par value \$0.0001 per share	2,300,000	\$87.00	\$200,100,000	\$25,972.98

- (1) Includes 300,000 shares of common stock issuable upon exercise of the underwriters' option to purchase additional shares of common stock.
 - (2) The filing fee is calculated and being paid pursuant to Rule 457(r) of the Securities Act of 1933, as amended, or the Securities Act, and relates to the registrant's Registration Statement on Form S-3ASR (File No. 333-235372), or the Registration Statement. In accordance with Rules 456(b) and 457(r) of the Securities Act, the registrant initially deferred payment of the registration fee for the Registration Statement.
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PROSPECTUS SUPPLEMENT
(To Prospectus dated December 5, 2019)

2,000,000 Shares

AXSOME
THERAPEUTICS

Axsome Therapeutics, Inc.

Common Stock

We are offering 2,000,000 shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol "AXSM." On December 18, 2019, the last reported sale price of our common stock was \$89.57 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 reporting requirements.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-4 of this prospectus and the risk factors in the documents incorporated by reference in 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.

	<u>Per Share</u>	<u>Total</u>
Public offering price	\$ 87.000	\$ 174,000,000
Underwriting discounts and commissions ⁽¹⁾	\$ 5.655	\$ 11,310,000
Proceeds, before expenses, to us	\$ 81.345	\$ 162,690,000

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters an option for 30 days from the date of this prospectus supplement to purchase up to 300,000 additional shares of our common stock. See "Underwriting" for more information.

The underwriters expect to deliver the shares to the investors on or about December 23, 2019.

Joint Bookrunning Managers

SVB Leerink

Morgan Stanley

Co-Lead Managers

Cantor

**Ladenburg
Thalman**

**SunTrust Robinson
Humphrey**

William Blair

Co-Managers

BTIG

H.C. Wainwright & Co.

The date of this prospectus supplement is December 18, 2019

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those 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 and the underwriters 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 together constitute an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The 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 is current only as of its date. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Information Incorporated by Reference.”

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of an automatic “shelf” registration statement on Form S-3ASR (File No. 333-235372) that we filed with the Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the “prospectus,” we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, and any related free writing prospectus that we have authorized for use in connection with this offering. You should rely only on the information that we have included or incorporated by reference in this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the underwriters have authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any related free writing prospectus that we have authorized for use in connection with this offering.

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 supplement or the accompanying 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.

This prospectus supplement, the accompanying prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus supplement, the accompanying prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference herein or therein is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement, the accompanying prospectus or any related free writing prospectus is delivered, or securities are sold, on a later date. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, 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.

This prospectus supplement contains or incorporates by reference summaries of certain provisions contained in some of the documents described herein, but all such summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed or have been or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement forms a part, and you may obtain copies of those documents as described in this prospectus supplement under the heading “Where You Can Find More Information.”

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain matters discussed in this prospectus supplement and the accompanying prospectus, including matters discussed under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations," incorporated by reference herein from our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, may constitute forward-looking statements for purposes of the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under the headings "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus supplement and the documents incorporated by reference herein, as well as other factors which may be identified from time to time in our other filings with the SEC, or in the documents in which such forward-looking statements appear. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

In particular, our statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation and completion of the trials, futility analyses and receipt of interim results; the timing of and our ability to obtain and maintain regulatory approval from the U.S. Food and Drug Administration, European Medicines Agency or other regulatory authority, or other anticipated regulatory action with respect to, our current or future product candidates; our ability to obtain additional capital necessary to fund our operations and our expectations relating to future capital requirements; our ability to generate revenues in the future; our ability to defend our intellectual property successfully or obtain the necessary licenses at a cost acceptable to us, if at all; the successful implementation of our research and development programs; the enforceability and success of our license agreements; the acceptance by the market of our product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within our control and discussed under the heading "Risk Factors," including those risk factors that are incorporated by reference in this prospectus supplement and the accompanying prospectus.

The forward-looking statements contained in this prospectus supplement and the accompanying prospectus reflect our views and assumptions only as of the date of this prospectus supplement. Except as required by law, we assume no responsibility for updating any forward-looking statements.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. You should read all such documents carefully and you should pay special attention to the information contained under the caption entitled "Risk Factors" in this prospectus, in our Annual Reports on Form 10-K, in any subsequent Quarterly Reports on Form 10-Q and in our other reports filed from time to time with the SEC, which are incorporated by reference into this prospectus, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus supplement and the accompanying prospectus to "Axsome," "we," "us" and "our" refer to Axsome Therapeutics, Inc. and our subsidiaries.

Company Overview

We are a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system, or CNS, disorders for which there are limited treatment options. By focusing on this therapeutic area, we are addressing significant and growing markets where current treatment options are limited or inadequate. Our core CNS portfolio includes four CNS product candidates, AXS-05, AXS-07, AXS-09, and AXS-12, which are being developed for multiple indications. AXS-05 is currently in a Phase 3 trial in treatment resistant depression, or TRD, which we refer to as the STRIDE-1 study, a Phase 3 open-label safety trial in patients with TRD and major depressive disorder, or MDD; and a Phase 2/3 trial in agitation associated with Alzheimer's disease, or AD, which we refer to as the ADVANCE-1 study. We have completed a Phase 2 trial in MDD, which we refer to as the ASCEND study, a Phase 3 trial which we refer to as the GEMINI study, and a Phase 2 trial in smoking cessation. AXS-07 is currently in two Phase 3 trials for the acute treatment of migraine, which we refer to as the MOMENTUM and the INTERCEPT studies, and a Phase 3 open-label safety trial in patients with migraine. AXS-12 is being developed for the treatment of narcolepsy. We have completed a Phase 2 trial, which we refer to as the CONCERT study. The Axsome Pain and Primary Care business unit, or Axsome PPC, houses our pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by us and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of nonsteroidal anti-inflammatory drug, or NSAID, associated gastrointestinal ulcers. Additionally, we are currently evaluating other product candidates, which we intend to develop for CNS disorders. We aim to become a fully integrated biopharmaceutical company that develops and commercializes differentiated therapies that expand the treatment options available to caregivers and improve the lives of patients living with CNS disorders.

AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of CNS disorders. AXS-05 consists of bupropion and dextromethorphan, or DM, and utilizes our metabolic inhibition technology. We are developing AXS-05 initially for the following four indications: TRD, agitation associated with AD, MDD, and as an aid to smoking cessation. The DM component of AXS-05 is a non-competitive N-methyl-D-aspartate, or NMDA, receptor antagonist, also known as a glutamate receptor modulator. The DM component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. We intend to seek U.S. Food and Drug Administration, or FDA, approval for AXS-05 utilizing the 505(b)(2) regulatory development pathway.

AXS-07 is a novel, oral, investigational medicine with distinct dual mechanisms of action consisting of MoSEIC™, or Molecular Solubility Enhanced Inclusion Complex, meloxicam and rizatriptan. We are developing AXS-07 initially for the acute treatment of migraine. Meloxicam is a long-acting nonsteroidal anti-inflammatory drug, or NSAID, with COX-2, an enzyme involved in inflammation and pain pathways, preferential inhibition and potent pain-relieving effects. However, standard meloxicam has an extended time to maximum plasma concentration, or T_{max} , which delays its onset of action. AXS-07 utilizes our proprietary MoSEIC™ technology to substantially increase the solubility and speed the absorption of meloxicam while potentially maintaining durability of action. Meloxicam is a new molecular entity for migraine enabled by our MoSEIC™ technology. Rizatriptan is a 5-HT_{1B/D} agonist that inhibits calcitonin gene-related peptide, or CGRP-mediated vasodilation, has been shown to have central trigeminal antinociceptive activity, and may reduce the release of inflammatory mediators from trigeminal nerves. Rizatriptan is approved as a single agent for the acute treatment of migraine. We intend to seek FDA approval for AXS-07 utilizing the 505(b)(2) regulatory development pathway.

AXS-09 is a novel, oral, investigational medicine consisting of esbupropion and DM, which is being developed for the treatment of CNS disorders. AXS-09 contains esbupropion, the chirally pure *S*-enantiomer of bupropion, as compared to the company's first generation product candidate AXS-05 which contains racemic bupropion, equal amounts of the *S*- and *R*-enantiomers. We have demonstrated in a Phase 1 trial that DM plasma levels are substantially increased into a potentially therapeutic range with repeated administration of AXS-09. Results of this Phase 1 trial coupled with preclinical data also indicate the potential for enhanced absorption and therapeutic effect of the *S*-enantiomer as compared to the *R*-enantiomer.

AXS-12, reboxetine, is a novel, oral, investigational medicine in development for treatment of narcolepsy. AXS-12 is a highly selective and potent norepinephrine reuptake inhibitor. The potential utility of AXS-12 in narcolepsy is supported by positive pre-clinical and clinical results in narcolepsy, and an extensive positive clinical safety record. Reboxetine, the active agent in AXS-12, significantly and dose-dependently reduced narcoleptic episodes in hypocretin, or orexin-deficient mice, a well-established genetic animal model of narcolepsy.

The Axsome PPC unit houses Axsome's pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs, and chronic low back pain, or CLBP, associated with Modic changes, or MCs. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastrointestinal ulcers.

AXS-02, disodium zoledronate tetrahydrate, is a potentially first-in-class, oral, targeted, non-opioid therapeutic for chronic pain. AXS-02 is a potent inhibitor of osteoclasts, which are bone remodeling cells that break down bone tissue. We are developing AXS-02 for the treatment of pain in the following two conditions: knee OA associated with BMLs and CLBP associated with type 1 or mixed type 1 and type 2 MCs. These conditions exhibit target lesions or specific pathology that we believe may be addressed by the mechanisms of action of AXS-02, such as inhibition of osteoclast activity. These mechanisms may result in a reduction of pain in these conditions. We intend to seek FDA approval for AXS-02 utilizing the 505(b)(2) regulatory development pathway.

AXS-06 is a novel, oral, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole. We are developing AXS-06 initially for the treatment of osteoarthritis and rheumatoid arthritis. Esomeprazole is a proton pump inhibitor which lowers stomach acidity and which has been shown to reduce the occurrence of NSAID-associated gastrointestinal ulcers. AXS-06 is designed to provide rapid, effective pain relief, and to reduce the risk of NSAID-associated gastrointestinal ulcers, with convenient once-daily dosing. We have successfully completed a Phase 1 trial of AXS-06 to characterize the pharmacokinetics of meloxicam and esomeprazole after oral administration of AXS-06. The results of our Phase 1 trial demonstrated that the median T_{max} for meloxicam, the trial's primary endpoint, was nine times faster for AXS-06 as compared to standard meloxicam. We intend to seek FDA approval for AXS-06 utilizing the 505(b)(2) regulatory development pathway.

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Our current CNS product candidate pipeline is summarized in the table below:

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Designation			Ongoing
	Major Depressive Disorder: Breakthrough Therapy Designation			
	Agitation in Alzheimer's Disease: Fast Track Designation			Ongoing
	Smoking Cessation			
AXS-07 (MoSEIC™ Mx + Riz)	Migraine: Special Protocol Assessment			
AXS-12 (Reboxetine)	Narcolepsy; U.S. Orphan Designation			
AXS-09 (DM + S-BUP)	CNS Disorders			

Abbreviations: BUP = Bupropion; CNS = Central Nervous System; DM = Dextromethorphan; Mx = Meloxicam; Riz = Rizatriptan; S-BUP = Esbupropion.

Additionally, our PPC product candidate pipeline is summarized in the table below:

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-02 (DZT)	Knee OA with BMLs: SPA Received; Fast Track Designation			
	CLBP with MCs			
AXS-06 (MoSEIC™ Mx + Eso)	OA and RA			

Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

Corporate Information

We were incorporated under the laws of the State of Delaware in January 2012. Our principal executive offices are located at 200 Broadway, 3rd Floor, New York, New York 10038, and our telephone number is (212) 332-3241.

Information concerning our business and our prospects is included in the documents that we file with the SEC as a reporting company under the Exchange Act, which are accessible at www.sec.gov, and on our website at www.axsome.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. Investors should not rely on any such information in deciding whether to purchase our common stock. We have included our website address in this prospectus supplement solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise generally applicable to public companies. These provisions include:

- requirement for only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- exemption from the auditor attestation requirement on the effectiveness of our internal controls over financial reporting;
- reduced disclosure about our executive compensation arrangements; and
- no requirements for non-binding advisory votes on executive compensation or golden parachute arrangements.

We may take advantage of these provisions until December 31, 2020 or such earlier time that we no longer qualify as an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in total annual gross revenue, have more than \$700 million in market value of our capital stock held by non-affiliates or issue more than \$1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some but not all of these reduced reporting requirements and other burdens. We have taken advantage of some reduced reporting burdens in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. Accordingly, the information that we provide stockholders may be different than what you might obtain from other public companies in which you hold equity interests.

THE OFFERING

Common stock offered by us	2,000,000 shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to 300,000 additional shares of our common stock.
Common stock to be outstanding after this offering	36,496,846 shares (or 36,796,846 shares, if the underwriters exercise in full their option to purchase additional shares).
Use of proceeds	We intend to use the net proceeds from this offering to continue to fund the ongoing clinical development of our late stage product candidates and for other general corporate purposes, including funding existing and potential new clinical programs and product candidates. See “Use of Proceeds.”
Risk factors	Investing in our common stock involves a high degree of risk. You should read the “Risk Factors” section of this prospectus supplement beginning on page S-6 as well as those risk factors that are incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Market ticker symbol	“AXSM”

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 34,496,846 shares of our common stock outstanding as of September 30, 2019, and excludes:

- 3,184,842 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2019, at a weighted average exercise price of \$9.01 per share;
- 110,603 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2019, consisting of 11,780 warrants with an exercise price of \$5.94 per share, 32,614 warrants with an exercise price of \$7.41 per share, 7,875 warrants with an exercise price of \$3.06, 58,334 warrants with an exercise price of \$8.10 per share, and 11,500 warrants with an exercise price of \$25.71, which are not yet outstanding, but which will become outstanding if and when the additional \$4.0 million tranche available to us under our term loan with Silicon Valley Bank and WestRiver Innovation Lending Fund VIII, L.P. is funded; and
- 3,668,590 shares of common stock available for future grant under our 2015 Omnibus Incentive Compensation Plan as of September 30, 2019.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering, does not assume or give effect to the exercise of the underwriters’ option to purchase 300,000 additional shares in this offering.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks described below and those discussed under the caption entitled “Risk Factors” in our Annual Reports on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus supplement and the accompanying prospectus, together with other information in this prospectus supplement and the accompanying prospectus, the information and documents incorporated by reference herein, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to this Offering

We have incurred significant losses since our inception, anticipate that we will incur substantial and increasing losses for the foreseeable future, and may never achieve or maintain profitability, which would depress the market price of our common stock, and could cause you to lose all or a part of your investment.

We are a clinical stage biopharmaceutical company with a limited operating history. For the last several years, we have focused our efforts primarily on developing CNS product candidates, AXS-05, AXS-07, AXS-09 and AXS-12, as well as our Axsome PPC product candidates, AXS-02 and AXS-06, which we refer to herein as our product candidates, with the goal of achieving regulatory approval. Since inception, we have incurred significant operating losses. Our net losses were \$43.5 million and \$31.0 million for nine months ended September 30, 2019 and the year ended December 31, 2018, respectively. As of September 30, 2019, we had an accumulated deficit of \$151.1 million. To date, we have not received regulatory approvals for any of our product candidates or generated any revenue from the sale of products, and we do not expect to generate any revenue in the foreseeable future. We expect to continue to incur substantial and increasing expenses and operating losses over the next several years, as we continue to develop our current and future product candidates. In addition, we expect to incur significant sales, marketing, and manufacturing expenses related to the commercialization of our current and future product candidates, if they are approved by the U.S. Food and Drug Administration, or FDA. As a result, we expect to continue to incur significant losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- conduct our Phase 3 clinical trial with AXS-05 for the treatment of depression;
- conduct our open-label safety extension trial for AXS-05;
- conduct our Phase 2/3 clinical trials with AXS-05 for the treatment of agitation associated with Alzheimer’s disease, or AD agitation;
- conduct our two Phase 3 clinical trials with AXS-07 for the acute treatment of migraine;
- conduct our open-label safety extension trial for AXS-07;
- conduct our planned Phase 3 clinical trial with AXS-12 in narcolepsy;
- continue to evaluate, plan for, and conduct, clinical trials for AXS-05 for smoking cessation treatment and AXS-09 for the treatment of CNS disorders;
- continue to evaluate, plan for, and conduct, clinical trials for our Axsome PPC product candidates, including AXS-02 for the treatment of pain associated with knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs and AXS-06 for the treatment of osteoarthritis and rheumatoid arthritis;
- develop, in-license, or acquire additional product candidates;
- conduct late-stage clinical trials for any product candidates that successfully complete early-stage clinical trials;
- seek regulatory approval for any product candidates that successfully complete late-stage clinical trials;
- conduct additional non-clinical studies with any product candidates;
- conduct clinical studies with any additional product candidates;
- increase manufacturing batch sizes of our product candidates to satisfy FDA requirements for a marketing application submission;
- establish a sales, marketing, and distribution infrastructure, and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval and that we choose not to license to a third party;
- require larger quantities of product;

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- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical, quality control, and scientific personnel; and
- add operational, financial, and management information systems and personnel, including personnel to support our product candidate development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for and successfully commercialize one or more of our product candidates. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, potentially entering into collaboration and license agreements, obtaining regulatory approval for product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval, achieving market acceptance of our products, satisfying any post-marketing requirements, maintaining appropriate distribution, setting prices, and obtaining reimbursement for our products from private insurance or government payors. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, may never achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we may incur or when, or if, we will be able to achieve profitability. If we are required by the FDA or comparable foreign regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings, or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need additional funding to conduct our future clinical trials and to complete development and commercialization of our product candidates. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our product development programs or commercialization efforts.

Conducting clinical trials, pursuing regulatory approvals, establishing outsourced manufacturing relationships, and successfully manufacturing and commercializing our product candidates is, and will be, a very time-consuming, expensive, and uncertain process that takes years to complete. We will need to raise additional capital to:

- fund our future clinical trials for our current product candidates, especially if we encounter any unforeseen delays or difficulties in our planned development activities;
- fund our operations and continue our efforts to hire additional personnel and build a commercial infrastructure to prepare for the commercialization of our current and future product candidates, if approved by the FDA or other comparable foreign regulatory authorities;
- qualify and outsource the commercial-scale manufacturing of our products under current good manufacturing practices;
- develop additional product candidates; and
- in-license other product candidates.

We may not have sufficient financial resources to meet all of our objectives if any of our product candidates is approved by regulatory authorities, which could require us to postpone, scale back or eliminate some or all of these objectives, including our potential launch activities relating to our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and costs related to the development of our product candidates;
- the costs associated with conducting additional non-clinical studies with any of our product candidates;
- the potential for delays in our efforts to seek regulatory approval for our product candidates, and any costs associated with such delays;
- the costs of establishing a commercial organization to sell, market and distribute our product candidates;

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- the rate of progress and costs of our efforts to prepare for the submission of a new drug application for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical or preclinical trials to support applications for regulatory approval;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates;
- the cost and timing of manufacturing sufficient supplies of our product candidates in preparation for commercialization;
- the effect of competing technological and market developments;
- revenue, if any, received from commercial sales of our product candidates, subject to the receipt of regulatory approval;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish; and
- the success of the commercialization of any of our current or future product candidates.

Future capital requirements will also depend on the extent to which we acquire or invest in additional businesses, products, and technologies. Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings, royalties, and corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our development programs or our commercialization efforts.

Management will have broad discretion as to the use of any proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion with respect to the use of any proceeds of this offering, including for any of the purposes described in “Use of Proceeds.” You will be relying on the judgment of our management regarding the application of any proceeds of this offering. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

If you purchase our common stock in this offering, you may incur immediate and substantial dilution in the book value of your shares.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$87.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and based on a net tangible book value of our common stock of \$0.20 per share as of September 30, 2019, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$82.35 per share in the net tangible book value of common stock.

To the extent outstanding options or warrants are exercised, you will experience further dilution. See the section titled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering. Because the sales of the shares offered hereby will be made directly into the market, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing shareholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

Future sales and issuances of our common stock or rights to purchase common stock pursuant to our equity compensation plans could result in additional dilution of the percentage ownership of our stockholders and could cause the price of our common stock to decline.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, or if we issue common stock pursuant to our equity compensation plans, investors may be materially diluted by subsequent sales or issuances. These sales or issuances may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 2,000,000 million shares of common stock in this offering will be approximately \$162.2 million, or approximately \$186.6 million if the underwriters exercise their option to purchase additional shares in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to continue to fund the ongoing clinical development of our late stage product candidates and for other general corporate purposes, including funding existing and potential new clinical programs and product candidates.

Our expected use of the net proceeds to us from this offering represents our current intentions based upon our present plans and business condition. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our research and development efforts, the status of and results from our current or future clinical trials, the timing of regulatory submissions and any unforeseen cash needs. Accordingly, our management will have broad discretion in the application of any net proceeds from this offering.

Until we use the net proceeds of this offering for the purposes described above, we intend to invest any funds we receive in short-term, investment-grade, interest-bearing instruments and U.S. government securities. We cannot predict whether these investments will yield a favorable return.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted immediately to the extent of the difference between the price per share you pay in this offering and the as adjusted net tangible book value per share of our common stock after giving effect to this offering. Net tangible book value per share represents our total assets, less total liabilities, divided by the number of shares of our common stock outstanding.

At September 30, 2019, our net tangible book value was approximately \$6.8 million or \$0.20 per share of common stock, based on 34,496,846 shares of common stock then outstanding. After giving effect to the sale by us of an aggregate of 2,000,000 shares of our common stock at the public offering price of \$87.00 per share, and after deducting underwriting discounts and commissions, and estimated offering expenses payable by us, our net tangible book value at September 30, 2019 would have been approximately \$169.0 million or \$4.63 per share of common stock. This represents an immediate increase in net tangible book value to existing stockholders of \$4.43 per share and an immediate dilution of \$82.37 per share to new investors purchasing common stock at the public offering price of \$87.00 per share in this offering.

The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering:

Public offering price per share		\$	87.00
Net tangible book value per share at September 30, 2019		\$	0.20
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering			<u>4.43</u>
As adjusted net tangible book value per share at September 30, 2019, after giving effect to this offering			4.63
Dilution per share to new investors in this offering		\$	<u>82.37</u>

If the underwriters exercise in full their option to purchase 300,000 additional shares of common stock at the public offering price of \$87.00 per share, the as adjusted net tangible book value after this offering would be \$5.26 per share, representing an increase in net tangible book value of \$5.06 per share to existing stockholders and immediate dilution in net tangible book value of \$81.74 per share to investors in this offering at the public offering price.

The foregoing table and calculations are based on 34,496,846 shares of our common stock outstanding as of September 30, 2019, and excludes:

- 3,184,842 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2019, at a weighted average exercise price of \$9.01 per share;
- 110,603 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2019, consisting of 11,780 warrants with an exercise price of \$5.94 per share, 32,614 warrants with an exercise price of \$7.41 per share, 7,875 warrants with an exercise price of \$3.06, 58,334 warrants with an exercise price of \$8.10 per share, and 11,500 warrants with an exercise price of \$25.71, which are not yet outstanding, but which will become outstanding if and when the additional \$4.0 million tranche available to us under our term loan with Silicon Valley Bank and WestRiver Innovation Lending Fund VIII, L.P. is funded; and
- 3,668,590 shares of common stock available for future grant under our 2015 Omnibus Incentive Compensation Plan as of September 30, 2019.

The above table does not assume or give effect to the exercise of the underwriters' option to purchase 300,000 additional shares in this offering. Furthermore, to the extent outstanding options or warrants are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe 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, you will experience further dilution.

UNDERWRITING

SVB Leerink LLC and Morgan Stanley & Co. LLC are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Shares</u>
SVB Leerink LLC	800,000
Morgan Stanley & Co. LLC	440,000
Cantor Fitzgerald & Co.	140,000
Ladenburg Thalmann & Co. Inc.	140,000
SunTrust Robinson Humphrey, Inc.	140,000
William Blair & Company, L.L.C.	140,000
BTIG, LLC	100,000
H.C. Wainwright & Co., LLC	100,000
Total	<u>2,000,000</u>

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$3.393 per share. After the offering of the shares, the public offering price, concession or any other term of this offering may be changed by the representatives.

The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	<u>Per Share</u>	<u>Total</u>	
		<u>Without Option</u>	<u>With Option</u>
Public offering price	\$ 87.000	\$ 174,000,000	\$ 200,100,000
Underwriting discounts and commissions	\$ 5.655	\$ 11,310,000	\$ 13,006,500
Proceeds, before expenses, to us	\$ 81.345	\$ 162,690,000	\$ 187,093,500

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$500,000. We have also agreed to reimburse the underwriters for up to \$15,000 for their FINRA counsel fee, and we have paid an aggregate total of \$675,000 in fees for advisory services to certain of the underwriters named herein. In accordance with FINRA Rule 5110, this reimbursed FINRA counsel fee and the advisory fees paid to certain of the underwriters named herein are deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 300,000 additional shares at the public offering price, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to the conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We and our executive officers and directors have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus supplement without first obtaining the written consent of SVB Leerink LLC on behalf of the underwriters. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

The lock-up provisions apply to common stock and to securities convertible into or exchangeable or exercisable for common stock. They also apply to common stock owned now or acquired later by the person executing the lock-up agreement or for which the person executing the lock-up agreement later acquires the power of disposition.

Nasdaq Global Market Listing

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

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares granted to them under the underwriting agreement described above. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is

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more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of this offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses. For example, Silicon Valley Bank, one of the lenders under our growth capital term loan facility is an affiliate of SVB Leerink LLC.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a “qualified investor” within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the representatives and each of our and the representatives’ affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither we nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression “an offer to the public” in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

MiFID II Product Governance

Any person offering, selling or recommending the shares (a “distributor”) should take into consideration the manufacturers’ target market assessment; however, a distributor subject to MiFID II is responsible for undertaking its own target market assessment in respect of the shares (by either adopting or refining the manufacturers’ target market assessment) and determining appropriate distribution channels.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the common stock being offered by this prospectus supplement has been passed upon for us by DLA Piper LLP (US), Short Hills, New Jersey. Covington & Burling LLP, New York, New York, is acting as counsel to the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our [Annual Report on Form 10-K for the year ended December 31, 2018](#) as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement of which this prospectus forms a part. Our financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated by reference in reliance on Ernst & Young LLP's reports pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission), given on the authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus form part of the automatic “shelf” registration statement on Form S-3ASR (File No. 333-235372) that we filed with the SEC as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act. This prospectus supplement and the accompanying prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement or the documents incorporated by reference herein and therein. For further information with respect to us and the securities that we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement and the documents incorporated by reference herein and therein. You should rely only on the information contained in this prospectus supplement or the accompanying prospectus or incorporated by reference herein. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered hereby.

We file annual, quarterly and other reports, proxy and information statements and other information with the Securities and Exchange Commission. The SEC maintains a website that contains reports, proxy statements and other information regarding us. The address of the SEC website is www.sec.gov. We maintain a website at www.axsome.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. Investors should not rely on any such information in deciding whether to purchase our common stock. We have included our website address in this prospectus supplement solely as an inactive textual reference.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement and the accompanying prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus and information that we file later with the SEC will automatically update and supersede information contained in this prospectus supplement and the accompanying prospectus.

The following documents are incorporated by reference into this document (other than the portions of these documents deemed to be “furnished” or not deemed to be “filed,” including the portions of these documents that are furnished under Item 2.02 or Item 7.01 of a Current Report on Form 8-K, including any exhibits included with such Items):

- [our annual report on Form 10-K for the fiscal year ended December 31, 2018 filed with the SEC on March 15, 2019](#)
- [the information contained in our definitive proxy statement on Schedule 14A for our 2019 Annual Meeting of Stockholders, filed with the SEC on April 26, 2019, to the extent incorporated by reference in Part III of the Form 10-K for the fiscal year ended December 31, 2018;](#)
- [our quarterly report on Form 10-Q for the three months ended March 31, 2019 filed with the SEC on May 9, 2019](#)
- [our quarterly report on Form 10-Q for the three months ended June 30, 2019 filed with the SEC on August 8, 2019](#)
- [our quarterly report on Form 10-Q for the three months ended September 30, 2019 filed with the SEC on November 7, 2019;](#)
- [our current reports on Form 8-K filed with the SEC on January 7, 2019 \(two filings\); January 8, 2019; January 30, 2019; February 6, 2019; March 4, 2019; March 6, 2019; March 14, 2019; March 27, 2019; April 15, 2019; May 6, 2019; May 9, 2019 \(two filings\); June 7, 2019; June 24, 2019; July 11, 2019; July 29, 2019; August 8, 2019; August 20, 2019; September 5, 2019; October 2, 2019; October 16, 2019; October 21, 2019; October 28, 2019 \(two filings\); November 7, 2019 \(two filings\); December 3, 2019; December 5, 2019 and December 16, 2019; and](#)
- [the description of our common stock contained in our registration statement on Form 8-A12B, filed with the SEC on November 16, 2015 \(File No. 001-37635\), and all amendments or reports filed for the purpose of updating such description.](#)

We also incorporate by reference into this prospectus supplement and the accompanying prospectus all documents (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and until the completion or termination of the offering contemplated hereby. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K.

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.

We make available, free of charge, through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. You may also obtain, free of charge, a copy of any of these documents (other than exhibits to these documents, unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus supplement or the accompanying prospectus) by writing or calling us at the following address and telephone number:

Axsome Therapeutics, Inc.
200 Broadway
3rd Floor
New York, New York 10038
(212) 332-3241

PROSPECTUS

AXSOME

THERAPEUTICS

AXSOME THERAPEUTICS, INC.
Common Stock
Preferred Stock
Warrants
Debt Securities
**Rights to Purchase Common Stock, Preferred Stock,
Debt Securities or Units
Units**

We may offer and sell from time to time our shares of common stock, shares of preferred stock, warrants, debt securities and rights to purchase common stock, preferred stock, debt securities or units, as well as units that include any of these securities.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities pursuant to this prospectus, we will provide a prospectus supplement containing specific terms of the particular offering together with this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. The prospectus supplement also may add, update or change information contained in this prospectus. This prospectus may not be used to offer and sell securities unless accompanied by the applicable prospectus supplement.

Our common stock is listed on the Nasdaq Global Market under the symbol "AXSM." On December 3, 2019, the last reported sale price of our common stock on the Nasdaq Global Market was \$45.61.

Investing in our securities involves significant risks. We strongly recommend that you read carefully the risks we describe in this prospectus and in any accompanying prospectus supplement, as well as the risk factors that are incorporated by reference into this prospectus from our filings made with the Securities and Exchange Commission. See "Risk Factors" on page 3 of this prospectus.

We may sell the securities directly to investors, or to or through underwriters or dealers, and also to other purchasers or through agents. The names of any underwriters or agents that are included in a sale of securities to you, and any applicable commissions or discounts, will be stated in an accompanying prospectus supplement. In addition, the underwriters, if any, may over-allot a portion of the securities.

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

The date of this prospectus is December 5, 2019

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic “shelf” registration statement on Form S-3ASR that we filed with the Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, we may offer and sell from time to time any combination of the securities described in this prospectus in one or more offerings in amounts, at prices and on terms that we determine at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this registration statement we will provide a prospectus supplement that describes the terms of the relevant offering. The prospectus supplement also may add, update or change information contained in this prospectus. Before making an investment decision, you should read carefully both this prospectus and any prospectus supplement together with the documents incorporated by reference into this prospectus as described below under the heading “Information Incorporated by Reference.”

The registration statement that contains this prospectus, including the exhibits to the registration statement and the information incorporated by reference, provides additional information about us and our securities. That registration statement can be read at the SEC website (www.sec.gov), as discussed below under the heading “Where You Can Find More Information.”

You should rely only on the information provided in the registration statement, this prospectus and in any prospectus supplement, including the information incorporated by reference. We have not authorized anyone to provide you with different information. You should not assume that the information in this prospectus or any supplement to this prospectus is accurate at any date other than the date indicated on the cover page of these documents or the filing date of any document incorporated by reference, regardless of its time of delivery. We are not making an offer to sell the securities in any jurisdiction where the offer or sale is not permitted.

We may sell our securities to or through underwriters, initial purchasers, dealers or agents, directly to purchasers or through a combination of any of these methods of sale, as designated from time to time. We and our agents reserve the sole right to accept or reject in whole or in part any proposed purchase of our securities. An applicable prospectus supplement, which we will provide each time we offer the securities, will set forth the names of any underwriters, initial purchasers, dealers or agents involved in the sale of our securities, and any related fee, commission or discount arrangements. See “Plan of Distribution.”

The terms “Axsome,” the “Company,” “our,” “us” and “we,” as used in this prospectus, refer to Axsome Therapeutics, Inc., unless we state otherwise or the context indicates otherwise.

AXSOME THERAPEUTICS, INC.

We are a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system, or CNS, disorders for which there are limited treatment options. By focusing on this therapeutic area, we are addressing significant and growing markets where current treatment options are limited or inadequate. Our core CNS portfolio includes four CNS product candidates, AXS-05, AXS-07, AXS-09, and AXS-12, which are being developed for multiple indications. AXS-05 is currently in a Phase 3 trial in treatment resistant depression, or TRD, which we refer to as the STRIDE-1 study, a Phase 3 trial in major depressive disorder, or MDD, which we refer to as the GEMINI study, a Phase 3 open-label safety trial in patients with TRD and MDD; and a Phase 2/3 trial in agitation associated with Alzheimer's disease, or AD, which we refer to as the ADVANCE-1 study. We have completed a Phase 2 trial in MDD, which we refer to as the ASCEND study and a Phase 2 trial in smoking cessation. AXS-07 is currently in two Phase 3 trials for the acute treatment of migraine, which we refer to as the MOMENTUM and the INTERCEPT studies, and a Phase 3 open-label safety trial in patients with migraine. AXS-12 is being developed for the treatment of narcolepsy. We have completed a Phase 2 trial, which we refer to as the CONCERT study. The Axsome Pain and Primary Care business unit, or Axsome PPC, houses our pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by us and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of nonsteroidal anti-inflammatory drug, or NSAID, associated gastrointestinal ulcers. Additionally, we are currently evaluating other product candidates, which we intend to develop for CNS disorders. We aim to become a fully integrated biopharmaceutical company that develops and commercializes differentiated therapies that expand the treatment options available to caregivers and improve the lives of patients living with CNS disorders.

AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of CNS disorders. AXS-05 consists of bupropion and dextromethorphan, or DM, and utilizes our metabolic inhibition technology. We are developing AXS-05 initially for the following four indications: TRD, agitation associated with AD, MDD, and as an aid to smoking cessation. The DM component of AXS-05 is a non-competitive N-methyl-D-aspartate, or NMDA, receptor antagonist, also known as a glutamate receptor modulator. The DM component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. We intend to seek U.S. Food and Drug Administration, or FDA, approval for AXS-05 utilizing the 505(b)(2) regulatory development pathway.

AXS-07 is a novel, oral, investigational medicine with distinct dual mechanisms of action consisting of MoSEIC™, or Molecular Solubility Enhanced Inclusion Complex, meloxicam and rizatriptan. We are developing AXS-07 initially for the acute treatment of migraine. Meloxicam is a long-acting nonsteroidal anti-inflammatory drug, or NSAID, with COX-2, an enzyme involved in inflammation and pain pathways, preferential inhibition and potent pain-relieving effects. However, standard meloxicam has an extended time to maximum plasma concentration, or T_{max}, which delays its onset of action. AXS-07 utilizes our proprietary MoSEIC™ technology to substantially increase the solubility and speed the absorption of meloxicam while potentially maintaining durability of action. Meloxicam is a new molecular entity for migraine enabled by our MoSEIC™ technology. Rizatriptan is a 5-HT_{1B/D} agonist that inhibits calcitonin gene-related peptide, or CGRP-mediated vasodilation, has been shown to have central trigeminal antinociceptive activity, and may reduce the release of inflammatory mediators from trigeminal nerves. Rizatriptan is approved as a single agent for the acute treatment of migraine. We intend to seek FDA approval for AXS-07 utilizing the 505(b)(2) regulatory development pathway.

AXS-09 is a novel, oral, investigational medicine consisting of esbupropion and DM, which is being developed for the treatment of CNS disorders. AXS-09 contains esbupropion, the chirally pure *S*-enantiomer of bupropion, as compared to the company's first generation product candidate AXS-05 which contains racemic bupropion, equal amounts of the *S*- and *R*-enantiomers. We have demonstrated in a Phase 1 trial that DM plasma levels are substantially increased into a potentially therapeutic range with repeated administration of AXS-09. Results of this Phase 1 trial coupled with preclinical data also indicate the potential for enhanced absorption and therapeutic effect of the *S*-enantiomer as compared to the *R*-enantiomer.

AXS-12, reboxetine, is a novel, oral, investigational medicine in development for treatment of narcolepsy. AXS-12 is a highly selective and potent norepinephrine reuptake inhibitor. The potential utility of AXS-12 in narcolepsy is supported by positive pre-clinical and clinical results in narcolepsy, and an extensive positive clinical safety record. Reboxetine, the active agent in AXS-12, significantly and dose-dependently reduced narcoleptic episodes in hypocretin, or orexin-deficient mice, a well-established genetic animal model of narcolepsy.

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The Axsome PPC unit houses Axsome’s pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs, and chronic low back pain, or CLBP, associated with Modic changes, or MCs. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastrointestinal ulcers.

AXS-02, disodium zoledronate tetrahydrate, is a potentially first-in-class, oral, targeted, non-opioid therapeutic for chronic pain. AXS-02 is a potent inhibitor of osteoclasts, which are bone remodeling cells that break down bone tissue. We are developing AXS-02 for the treatment of pain in the following two conditions: knee OA associated with BMLs and CLBP associated with type 1 or mixed type 1 and type 2 MCs. These conditions exhibit target lesions or specific pathology that we believe may be addressed by the mechanisms of action of AXS-02, such as inhibition of osteoclast activity. These mechanisms may result in a reduction of pain in these conditions. We intend to seek FDA approval for AXS-02 utilizing the 505(b)(2) regulatory development pathway.

AXS-06 is a novel, oral, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole. We are developing AXS-06 initially for the treatment of osteoarthritis and rheumatoid arthritis. Esomeprazole is a proton pump inhibitor which lowers stomach acidity and which has been shown to reduce the occurrence of NSAID-associated gastrointestinal ulcers. AXS-06 is designed to provide rapid, effective pain relief, and to reduce the risk of NSAID-associated gastrointestinal ulcers, with convenient once-daily dosing. We have successfully completed a Phase 1 trial of AXS-06 to characterize the pharmacokinetics of meloxicam and esomeprazole after oral administration of AXS-06. The results of our Phase 1 trial demonstrated that the median T_{max} for meloxicam, the trial’s primary endpoint, was nine times faster for AXS-06 as compared to standard meloxicam. We intend to seek FDA approval for AXS-06 utilizing the 505(b)(2) regulatory development pathway.

Our current CNS product candidate pipeline is summarized in the table below:

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-05 (DM + BUP)	Treatment Resistant Depression: Fast Track Designation			Ongoing
	Major Depressive Disorder: Breakthrough Therapy Designation			Ongoing
	Agitation in Alzheimer’s Disease: Fast Track Designation			Ongoing
	Smoking Cessation			
AXS-07 (MoSEIC™ Mx + Riz)	Migraine: Special Protocol Assessment			Ongoing
AXS-12 (Reboxetine)	Narcolepsy; U.S. Orphan Designation			
AXS-09 (DM + S-BUP)	CNS Disorders			

Abbreviations: BUP = Bupropion; CNS = Central Nervous System; DM = Dextromethorphan; Mx = Meloxicam; Riz = Rizatriptan; S-BUP = Esbupropion; SPA = Special Protocol Assessment.

Additionally, our PPC product candidate pipeline is summarized in the table below:

Product Candidate	Preclinical	Phase 1	Phase 2	Phase 3
AXS-02 (DZT)	Knee OA with BMLs: SPA Received; Fast Track Designation			
	CLBP with MCs			
AXS-06 (MoSEIC™ Mx + Eso)	OA and RA			

Abbreviations: BML = Bone Marrow Lesions; CLBP = Chronic Low Back Pain; DZT = Disodium Zoledronate Tetrahydrate; Eso = Esomeprazole; MC = Modic Changes; Mx = Meloxicam; OA = Osteoarthritis; RA = Rheumatoid Arthritis; SPA = Special Protocol Assessment

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Our principal executive offices are located at 200 Broadway, 3rd Floor, New York, New York 10038, and our telephone number is (212) 332-3241. Our website address is www.axsome.com. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our securities.

Our filings with the SEC are posted on our website at www.axsome.com. The information found on our website is not part of this or any other report we file with or furnish to the SEC.

RISK FACTORS

Investing in our securities involves risk. You should carefully consider the specific risks discussed or incorporated by reference into the applicable prospectus supplement, together with all the other information contained in the prospectus supplement or incorporated by reference into this prospectus and the applicable prospectus supplement. You should also consider the risks, uncertainties and assumptions discussed under the caption “Risk Factors” included in our [Annual Report on Form 10-K for the year ended December 31, 2018](#) and in subsequent filings, which are incorporated by reference into this prospectus. These risk factors may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future or by a prospectus supplement relating to a particular offering of our securities. These risks and uncertainties are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us, or that we currently view as immaterial, may also impair our business. If any of the risks or uncertainties described in our SEC filings or any prospectus supplement or any additional risks and uncertainties actually occur, our business, financial condition and results of operations could be materially and adversely affected. In that case, the trading price of our securities could decline and you might lose all or part of your investment.

FORWARD-LOOKING STATEMENTS

From time to time, in reports filed with the Securities and Exchange Commission (including this registration statement), in press releases and in other communications to stockholders or the investment community, we may provide forward-looking statements concerning possible or anticipated future results of operations or business developments. These statements are based on our management’s current expectations or predictions of future conditions, events or results based on various assumptions and our management’s estimates of trends and economic factors in the markets in which we are active, as well as our business plans. Words such as “expects,” “anticipates,” “intends,” “plans,” “believes,” “seeks,” “estimates,” “projects,” “forecasts,” “may,” “should,” and variations of such words and similar expressions are intended to identify such forward-looking statements. The forward-looking statements may include, without limitation, statements regarding product candidate development, product candidate potential, regulatory environment, sales and marketing strategies, capital resources or operating performance. The forward-looking statements are subject to risks and uncertainties, which may cause results to differ materially from those set forth in the statements. Forward-looking statements in this registration statement should be evaluated together with the many uncertainties that affect our business and our market, particularly those discussed in the “Risk Factors” section of our [Annual Report on Form 10-K for the year ended December 31, 2018](#) and our subsequent filings, which are incorporated by reference into this prospectus, to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are representative only as of the date of this prospectus and except as required by law, we assume no responsibility to update any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read this prospectus and the documents that we reference in this prospectus and have been filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any issuance or sale of our common shares. Except as required by law, we do not assume any obligation to update any forward-looking statements.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we will use the net proceeds from the sale of the securities offered hereby for general corporate purposes, which may include, but are not limited to working capital, capital expenditures, funding the ongoing clinical development of our product candidates, general and administrative expenses or other corporate obligations. We may use a portion of the net proceeds to pay off outstanding indebtedness, if any, or acquire or invest in businesses, products and technologies.

DESCRIPTION OF CAPITAL STOCK

The following description is a general summary of the terms of the shares of common stock or shares of preferred stock that we may issue. The description below and in any prospectus supplement does not include all of the terms of the shares of common stock or shares of preferred stock and should be read together with our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, copies of which have been filed previously with the SEC. For more information on how you can obtain copies of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, see “Where You Can Find More Information.”

Common Stock

General

Our Amended and Restated Certificate of Incorporation provides the authority to issue 150,000,000 shares of common stock, par value \$0.0001 per share. As of November 1, 2019, there were 34,508,626 shares of common stock outstanding. Each share of our common stock has the same relative rights and is identical in all respects to each other share of our common stock. The rights, preferences and privileges of holders of our common stock are subject to the rights, preferences and privileges of the holders of shares of any series of preferred stock that we have issued or may issue in the future.

Voting Rights

The holders of our common stock are entitled to one vote per share on any matter to be voted upon by our stockholders. Our Amended and Restated Certificate of Incorporation does not permit cumulative voting in connection with the election of directors.

Dividends

The holders of our common stock are entitled to dividends, if any, as our board of directors may declare from time to time from funds legally available for that purpose, subject to the holders of other classes of stock, if any, at the time outstanding having prior rights as to dividends, if any.

Liquidation Rights

Upon any voluntary or involuntary liquidation, dissolution, or winding up of our affairs, the holders of our common stock are entitled to share ratably in all assets remaining after the payment of creditors, subject to any prior liquidation distribution rights of holders of other classes of stock, if any, at the time outstanding.

Miscellaneous

Holders of our common stock have no preemptive, conversion, redemption or sinking fund rights. The outstanding shares of our common stock are, and the shares of common stock to be offered hereby when issued will be, validly issued, fully paid and non-assessable.

Nasdaq Listing

Our common stock is listed on the Nasdaq Global Market under the symbol “AXSM.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Preferred Stock

General

Our Amended and Restated Certificate of Incorporation authorizes the issuance of up to 10,000,000 shares of preferred stock, par value \$0.0001 per share, none of which are issued and outstanding as of the date of this prospectus. We may issue, from time to time in one or more series, the terms of which may be determined at the time of issuance by our board of directors, without further action by our stockholders, shares of preferred stock and such shares may include voting rights, preferences as to dividends and liquidation, conversion rights, redemption rights and sinking fund provisions. The shares of each series of preferred stock shall have preferences, limitations and relative rights, including voting rights, identical with those of other shares of the same series and, except to the extent provided in the description of such series, of those of other series of preferred stock.

The issuance of any preferred stock could adversely affect the rights of the holders of common stock and, therefore, reduce the value of the common stock. The ability of our board of directors to issue preferred stock could discourage, delay or prevent a takeover or change in control.

The description of the terms of a particular series of preferred stock in the applicable prospectus supplement will not be complete. You should refer to the applicable certificate of designation for complete information regarding a series of preferred stock. The prospectus supplement will also contain a description of U.S. federal income tax consequences relating to the preferred stock, if material.

The terms of any particular series of preferred stock will be described in the prospectus supplement relating to that particular series of preferred stock, including, where applicable:

- the series designation, stated value and liquidation preference of such preferred stock and the number of shares offered;
- the offering price;
- the dividend rate or rates (or method of calculation), the date or dates from which dividends shall accrue, and whether such dividends shall be cumulative or noncumulative and, if cumulative, the dates from which dividends shall commence to cumulate;
- any redemption or sinking fund provisions;
- the amount that shares of such series shall be entitled to receive in the event of our liquidation, dissolution or winding-up;
- the terms and conditions, if any, on which shares of such series shall be convertible or exchangeable for shares of our stock of any other class or classes, or other series of the same class;
- the voting rights, if any, of shares of such series in addition to those set forth under the caption entitled, "Voting Rights" below;
- the status as to reissuance or sale of shares of such series redeemed, purchased or otherwise reacquired, or surrendered to us on conversion or exchange;
- the conditions and restrictions, if any, on the payment of dividends or on the making of other distributions on, or the purchase, redemption or other acquisition by us, of our common stock or of any other class of our stock ranking junior to the shares of such series as to dividends or upon liquidation (including, but not limited to, at such times as there are arrearages in the payment of dividends or sinking fund installments);

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- the conditions and restrictions, if any, on the creation of Company indebtedness, or on the issue of any additional stock ranking on a parity with or prior to the shares of such series as to dividends or upon liquidation; and
- any additional dividend, liquidation, redemption, sinking or retirement fund and other rights, preferences, privileges, limitations and restrictions of such preferred stock.

If we issue shares of preferred stock under this prospectus and any related prospectus supplement, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

Voting Rights

The General Corporation Law of Delaware, or the DGCL provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Transfer Agent and Registrar

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

Other

Our issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of common stock or could adversely affect the rights and powers, including voting rights, of the holders of common stock. The issuance of preferred stock could have the effect of decreasing the market price of our common stock.

Delaware Law and Certain Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws Provisions

Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions:

- Authorize the issuance of preferred stock which can be created and issued by the board of directors without prior stockholder approval, with rights senior to those of our common stock;
- Provide for a classified board of directors, with each director serving a staggered three-year term;
- Prohibit our stockholders from filling board vacancies, calling special stockholder meetings or taking action by written consent;
- Provide for the removal of a director only with cause and by the affirmative vote of the holders of 66 2/3 % or more of the shares then entitled to vote at an election of our directors;
- Require advance written notice of stockholder proposals and director nominations; and
- Require any action instituted against our officers or directors in connection with their service to us to be brought in the state of Delaware.

In addition, we are subject to the provisions of Section 203 of the DGCL, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our Amended and Restated Certificate of Incorporation, Amended and Restated Bylaws and the DGCL could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including a merger, tender offer or proxy contest involving our company. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

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Further, our Amended and Restated Certificate of Incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL, or (4) any action asserting a claim governed by the internal affairs doctrine, in each such case subject to such Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein.

Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Amended and Restated Certificate of Incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents. Further, this choice of forum provision does not preclude or contract the scope of exclusive federal or concurrent jurisdiction for any actions brought under the Securities Act or the Exchange Act. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. In addition, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Securities Act or any other claim for which the federal and state courts have concurrent jurisdiction. Accordingly, our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

Indemnification

Our Amended and Restated Certificate of Incorporation contains provisions permitted under the DGCL relating to the liability of directors. The provisions eliminate, to the extent legally permissible, a director's liability for monetary damages for a breach of fiduciary duty, except in circumstances involving wrongful acts, such as the breach of a director's duty of loyalty or acts or omissions that involve intentional misconduct or a knowing violation of law. The limitation of liability described above does not alter the liability of our directors and officers under federal securities laws. Furthermore, our certificate of incorporation contains provisions to indemnify our directors and officers to the fullest extent permitted by the DGCL. These provisions do not limit or eliminate our right or the right of any stockholder of ours to seek non-monetary relief, such as an injunction or rescission in the event of a breach by a director or an officer of his duty of care to us. We believe that these provisions assist us in attracting and retaining qualified individuals to serve as directors.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock, shares of our preferred stock or debt securities. The following description sets forth certain general terms and provisions of the warrants that we may offer pursuant to this prospectus. The particular terms of the warrants and the extent, if any, to which the general terms and provisions may apply to the warrants so offered will be described in the applicable prospectus supplement.

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

A copy of the forms of the warrant agreement and the warrant certificate relating to any particular issue of warrants will be filed with the SEC each time we issue warrants, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the warrant agreement and the related warrant certificate, see "Where You Can Find More Information."

Stock Warrants

The prospectus supplement relating to a particular issue of warrants to issue shares of our common stock or shares of our preferred stock will describe the terms of the common share warrants and preferred share warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the shares of common stock or shares of preferred stock that may be purchased upon exercise of the warrants;
- the terms for changes or adjustments to the exercise price of the warrants;
- if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or shares of preferred stock that may be purchased upon exercise of a warrant and the price at which the shares may be purchased upon exercise;
- the dates on which the right to exercise the warrants commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material United States federal income tax considerations;
- anti-dilution provisions of the warrants, if any;
- redemption or call provisions, if any, applicable to the warrants;
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants; and
- any other information we think is important about the warrants.

Debt Warrants

The prospectus supplement relating to a particular issue of warrants to issue debt securities will describe the terms of those warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;

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- the designation and terms of the debt securities purchasable upon exercise of the warrants;
- the terms for changes or adjustments to the exercise price of the warrants;
- if applicable, the designation and terms of the debt securities that the warrants are issued with and the number of warrants issued with each debt security;
- if applicable, the date from and after which the warrants and any debt securities issued with them will be separately transferable;
- the principal amount of debt securities that may be purchased upon exercise of a warrant and the price at which the debt securities may be purchased upon exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- whether the warrants represented by the warrant certificates or debt securities that may be issued upon exercise of the warrants will be issued in registered or bearer form;
- information relating to book-entry procedures, if any;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material United States federal income tax considerations;
- anti-dilution provisions of the warrants, if any;
- redemption or call provisions, if any, applicable to the warrants;
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants; and
- any other information we think is important about the warrants.

Exercise of Warrants

Each warrant will entitle the holder of the warrant to purchase at the exercise price set forth in the applicable prospectus supplement the number of shares of common stock, shares of preferred stock or the principal amount of debt securities being offered. Holders may exercise warrants at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants are void. Holders may exercise warrants as set forth in the prospectus supplement relating to the warrants being offered.

Until a holder exercises the warrants to purchase our shares of common stock, shares of preferred stock or debt securities, the holder will not have any rights as a holder of our shares of common stock, shares of preferred stock or debt securities, as the case may be, by virtue of ownership of warrants.

DESCRIPTION OF DEBT SECURITIES

The following is a general description of the terms of debt securities we may issue from time to time unless we provide otherwise in the applicable prospectus supplement. Particular terms of any debt securities we offer will be described in the prospectus supplement relating to such debt securities.

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As required by Federal law for all bonds and notes of companies that are publicly offered, any debt securities we issue will be governed by a document called an “indenture,” the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part. We have summarized the general features of the debt securities to be governed by the indenture. The summary is not complete. An indenture is a contract between us and a financial institution acting as trustee on behalf of the holders of the debt securities, and is subject to and governed by the Trust Indenture Act of 1939, as amended. The trustee has two main roles. First, the trustee can enforce holders’ rights against us if we default. There are some limitations on the extent to which the trustee acts on holders’ behalf, described in the second paragraph under “Description of Debt Securities—Events of Default.” Second, the trustee performs certain administrative duties, such as sending interest and principal payments to holders.

Because this section is a summary, it does not describe every aspect of any debt securities we may issue or the indenture governing any such debt securities. Particular terms of any debt securities we offer will be described in the prospectus supplement relating to such debt securities, and we urge you to read the applicable executed indenture, which will be filed with the SEC at the time of any offering of debt securities, because it, and not this description, will define the rights of holders of such debt securities.

A prospectus supplement will describe the particular terms of any series of debt securities we may issue, including some or all of the following:

- the designation or title of the series of debt securities;
- the total principal amount of the series of debt securities, the denominations in which the offered debt securities will be issued and whether the offering may be reopened for additional securities of that series and on what terms;
- the percentage of the principal amount at which the series of debt securities will be offered;
- the date or dates on which principal will be payable;
- the rate or rates (which may be either fixed or variable) and/or the method of determining such rate or rates of interest, if any;
- the date or dates from which any interest will accrue, or the method of determining such date or dates, and the date or dates on which any interest will be payable;
- the terms for redemption, extension or early repayment, if any;
- the currencies in which the series of debt securities are issued and payable;
- whether the amount of payments of principal, interest or premium, if any, on a series of debt securities will be determined with reference to an index, formula or other method and how these amounts will be determined;
- the place or places of payment, transfer, conversion and/or exchange of the debt securities;
- the provision for any sinking fund;
- any restrictive covenants;
- events of default;
- whether the series of debt securities are issuable in certificated form;
- any provisions for legal defeasance or covenant defeasance;

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- whether and under what circumstances we will pay additional amounts in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem the debt securities rather than pay the additional amounts (and the terms of this option);
- any provisions for convertibility or exchangeability of the debt securities into or for any other securities;
- whether the debt securities are subject to subordination and the terms of such subordination;
- any listing of the debt securities on any securities exchange;
- if applicable, a discussion of certain U.S. Federal income tax considerations, including those related to original issue discount, if applicable; and
- any other material terms.

The debt securities may be secured or unsecured obligations. Unless the prospectus supplement states otherwise, principal, interest and premium, if any, will be paid by us in immediately available funds.

General

The indenture may provide that any debt securities proposed to be sold under this prospectus and the applicable prospectus supplement relating to such debt securities (“offered debt securities”) and any debt securities issuable upon conversion or exchange of other offered securities (“underlying debt securities”) may be issued under the indenture in one or more series.

For purposes of this prospectus, any reference to the payment of principal of, or interest or premium, if any, on, debt securities will include additional amounts if required by the terms of the debt securities.

Debt securities issued under an indenture, when a single trustee is acting for all debt securities issued under the indenture, are called the “indenture securities.” The indenture may also provide that there may be more than one trustee thereunder, each with respect to one or more different series of securities issued thereunder. See “Description of Debt Securities—Resignation of Trustee” below. At a time when two or more trustees are acting under an indenture, each with respect to only certain series, the term “indenture securities” means the one or more series of debt securities with respect to which each respective trustee is acting. In the event that there is more than one trustee under an indenture, the powers and trust obligations of each trustee described in this prospectus will extend only to the one or more series of indenture securities for which it is trustee. If two or more trustees are acting under an indenture, then the indenture securities for which each trustee is acting would be treated as if issued under separate indentures.

We refer you to the applicable prospectus supplement relating to any debt securities we may issue from time to time for information with respect to any deletions from, modifications of 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, that will be applicable with respect to such debt securities.

We have the ability to issue indenture securities with terms different from those of indenture securities previously issued and, without the consent of the holders thereof, to reopen a previous issue of a series of indenture securities and issue additional indenture securities of that series unless the reopening was restricted when that series was created.

Conversion and Exchange

If any debt securities are convertible into or exchangeable for other securities, the related prospectus supplement will explain the terms and conditions of the conversion or exchange, including the conversion price or exchange ratio (or the calculation method), the conversion or exchange period (or how the period will be determined), if conversion or exchange will be mandatory or at the option of the holder or us, provisions for adjusting the conversion price or the exchange ratio and provisions affecting conversion or exchange in the event of the redemption of the underlying debt securities. These terms may also include provisions under which the number or amount of other securities to be received by the holders of the debt securities upon conversion or exchange would be calculated according to the market price of the other securities as of a time stated in the prospectus supplement.

Payment and Paying Agents

We will pay interest to the person listed in the applicable trustee's records as the owner of the debt security at the close of business on a particular day in advance of each due date for interest, even if that person no longer owns the debt security on the interest due date. That day, often approximately two weeks in advance of the interest due date, is called the "record date." Because we will pay all the interest for an interest period to the holders on the record date, holders buying and selling debt securities must work out between themselves the appropriate purchase price. The most common manner is to adjust the sales price of the debt securities to prorate interest fairly between buyer and seller based on their respective ownership periods within the particular interest period. This prorated interest amount is called "accrued interest."

Events of Default

Holders of debt securities of any series will have rights if an Event of Default occurs in respect of the debt securities of such series and is not cured, as described later in this subsection. The term "Event of Default" in respect of the debt securities of any series means any of the following:

- we do not pay the principal of, or any premium on, a debt security of the series on its due date;
- we do not pay interest on a debt security of the series within 30 days of its due date;
- we do not deposit any sinking fund payment in respect of debt securities of the series on its due date and we do not cure this default within five days;
- we remain in breach of a covenant in respect of debt securities of the series for 90 days after we receive a written notice of default stating we are in breach. The notice must be sent by either the trustee or holders of at least 25% of the principal amount of debt securities of the series;
- we file for bankruptcy or certain other events of bankruptcy, insolvency or reorganization occur; and
- any other Event of Default occurs in respect of debt securities of the series described in the prospectus supplement.

An Event of Default for a particular series of debt securities does not necessarily constitute an Event of Default for any other series of debt securities issued under the same or any other indenture. The trustee may withhold notice to the holders of debt securities of any default, except in the payment of principal, premium or interest, if it considers the withholding of notice to be in the best interests of the holders.

Remedies if an Event of Default Occurs

If an Event of Default has occurred and has not been cured or waived, the trustee or the holders of not less than 25% in principal amount of the debt securities of the affected series may declare the entire principal amount of all the debt securities of that series to be due and immediately payable. This is called a declaration of acceleration of maturity. A declaration of acceleration of maturity may be canceled by the holders of a majority in principal amount of the debt securities of the affected series if the default is cured or waived and certain other conditions are satisfied.

Except in cases of default, where the trustee has some special duties, the trustee typically is not required to take any action under an indenture at the request of any holders unless the holders offer the trustee reasonable protection from expenses and liability (called an "indemnity"). If reasonable indemnity is provided, the holders of a majority in principal amount of the outstanding debt securities of the relevant series may direct the time, method and place of conducting any lawsuit or other formal legal action seeking any remedy available to the trustee. The trustee may refuse to follow those directions in certain circumstances.

Before a holder is allowed to bypass the trustee and bring its own lawsuit or other formal legal action or take other steps to enforce its rights or protect its interests relating to any debt securities, the following must occur:

- the holder must give the trustee written notice that an Event of Default has occurred and remains uncured;

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- the holders of at least 25% in principal amount of all outstanding debt securities of the relevant series must make a written request that the trustee take action because of the default and must offer reasonable indemnity to the trustee against the cost and other liabilities of taking that action;
- the trustee must not have taken action for 60 days after receipt of the above notice and offer of indemnity; and
- the holders of a majority in principal amount of the debt securities must not have given the trustee a direction inconsistent with the above notice during that 60-day period.

However, a holder is entitled at any time to bring a lawsuit for the payment of money due on its debt securities on or after the due date. Each year, we will furnish to each trustee a written statement of certain of our officers certifying that to their knowledge we are in compliance with the indenture and the debt securities, or else specifying any default.

Waiver of Default

The holders of a majority in principal amount of the relevant series of debt securities may waive a default for all such series of debt securities. If this happens, the default will be treated as if it had not occurred. No one can waive a payment default on a holder's debt security, however, without the holder's approval.

Merger or Consolidation

Under the terms of an indenture, we may be permitted to consolidate or merge with another entity. We may also be permitted to sell all or substantially all of our assets to another entity. However, typically we may not take any of these actions unless all the following conditions are met:

- if we do not survive such transaction or we convey, transfer or lease our properties and assets substantially as an entirety, the acquiring company must be a corporation, limited liability company, partnership or trust, or other corporate form, organized under the laws of any state of the United States or the District of Columbia, and such company must agree to be legally responsible for our debt securities, and, if not already subject to the jurisdiction of any state of the United States or the District of Columbia, the new company must submit to such jurisdiction for all purposes with respect to the debt securities and appoint an agent for service of process;
- alternatively, we must be the surviving company;
- immediately after the transaction no Event of Default will exist;
- we must deliver certain certificates and documents to the trustee; and
- we must satisfy any other requirements specified in the prospectus supplement relating to a particular series of debt securities.

Modification or Waiver

There are three types of changes we may make to an indenture and the debt securities issued thereunder.

Changes Requiring Approval

First, there are changes that we cannot make to debt securities without specific approval of all of the holders. The following is a list of the types of changes that may require specific approval:

- change the stated maturity of the principal of or rate of interest on a debt security;
- reduce any amounts due on a debt security;
- reduce the amount of principal payable upon acceleration of the maturity of a security following a default;

- at any time after a change of control has occurred, reduce any premium payable upon a change of control;
- change the place or currency of payment on a debt security (except as otherwise described in the prospectus or prospectus supplement);
- impair the right of holders to sue for payment;
- adversely affect any right to convert or exchange a debt security in accordance with its terms;
- reduce the percentage of holders of debt securities whose consent is needed to modify or amend the indenture;
- reduce the percentage of holders of debt securities whose consent is needed to waive compliance with certain provisions of the indenture or to waive certain defaults;
- modify any other aspect of the provisions of the indenture dealing with supplemental indentures, modification and waiver of past defaults, changes to the quorum or voting requirements or the waiver of certain covenants; and
- change any obligation we have to pay additional amounts.

Changes Not Requiring Approval

The second type of change does not require any vote by the holders of the debt securities. This type is limited to clarifications and certain other changes that would not adversely affect holders of the outstanding debt securities in any material respect, including the addition of covenants and guarantees. We also do not need any approval to make any change that affects only debt securities to be issued under the indenture after the change takes effect.

Changes Requiring Majority Approval

Any other change to the indenture and the debt securities may require the following approval:

- if the change affects only one series of debt securities, it must be approved by the holders of a majority in principal amount of that series; and
- if the change affects more than one series of debt securities issued under the same indenture, it must be approved by the holders of a majority in principal amount of all of the series affected by the change, with all affected series voting together as one class for this purpose.

The holders of a majority in principal amount of all of the series of debt securities issued under an indenture, voting together as one class for this purpose, may waive our compliance obligations with respect to some of our covenants in that indenture. However, we cannot obtain a waiver of a payment default or of any of the matters covered by the bullet points included above under “Description of Debt Securities—Modification or Waiver—Changes Requiring Approval.”

Further Details Concerning Voting

When taking a vote on proposed changes to the indenture and the debt securities, we expect to use the following rules to decide how much principal to attribute to a debt security:

- for original issue discount securities, we will use the principal amount that would be due and payable on the voting date if the maturity of these debt securities were accelerated to that date because of a default;
- for debt securities whose principal amount is not known (for example, because it is based on an index), we will use a special rule for that debt security described in the related prospectus supplement; and
- for debt securities denominated in one or more foreign currencies, we will use the U.S. dollar equivalent.

Debt securities will not be considered outstanding, and therefore not eligible to vote, if we have deposited or set aside in trust money for their payment or redemption. Debt securities will also not be eligible to vote if they have been fully defeased as described later under “Description of Debt Securities—Defeasance—Legal Defeasance.”

We generally will be entitled to set any day as a record date for the purpose of determining the holders of outstanding indenture securities that are entitled to vote or take other action under the indenture. If we set a record date for a vote or other action to be taken by holders of one or more series, that vote or action may be taken only by persons who are holders of outstanding indenture securities of those series on the record date and must be taken within 11 months following the record date.

Book-entry and other indirect holders will need to consult their banks or brokers for information on how approval may be granted or denied if we seek to change the indenture or the debt securities or request a waiver.

Defeasance

The following provisions will be applicable to each series of debt securities unless we state in the applicable prospectus supplement that the provisions of covenant defeasance and legal defeasance will not be applicable to that series.

Covenant Defeasance

We can make the deposit described below and be released from some of the restrictive covenants in the indenture under which the particular series was issued. This is called “covenant defeasance.” In that event, the holders would lose the protection of those restrictive covenants but would gain the protection of having money and government securities set aside in trust to repay holders’ debt securities. If applicable, a holder also would be released from the subordination provisions described under “Description of Debt Securities—Indenture Provisions—Subordination” below. In order to achieve covenant defeasance, we must do the following:

- If the debt securities of the particular series are denominated in U.S. dollars, we must deposit in trust for the benefit of all holders of such debt securities a combination of money and U.S. government or U.S. government agency notes or bonds that will generate enough cash to make interest, principal and any other payments on the debt securities on their various due dates;
- We may be required to deliver to the trustee a legal opinion of our counsel confirming that, under current U.S. Federal income tax law, we may make the above deposit without causing the holders to be taxed on the debt securities any differently than if we did not make the deposit and just repaid the debt securities ourselves at maturity; and
- We must deliver to the trustee certain documentation stating that all conditions precedent to covenant defeasance have been complied with.

If we accomplish covenant defeasance, holders can still look to us for repayment of the debt securities if there were a shortfall in the trust deposit or the trustee is prevented from making payment. In fact, if one of the remaining Events of Default occurred (such as our bankruptcy) and the debt securities became immediately due and payable, there might be a shortfall. Depending on the event causing the default, holders may not be able to obtain payment of the shortfall.

Legal Defeasance

As described below, we can legally release ourselves from all payment and other obligations on the debt securities of a particular series (called “legal defeasance”), (1) if there is a change in U.S. Federal tax law that allows us to effect the release without causing the holders to be taxed any differently than if the release had not occurred, and (2) if we put in place the following other arrangements for holders to be repaid:

- If the debt securities of the particular series are denominated in U.S. dollars, we must deposit in trust for the benefit of all holders of such debt securities a combination of money and U.S. government or U.S. government agency notes or bonds that will generate enough cash to make interest, principal and any other payments on the debt securities on their various due dates;

- We may be required to deliver to the trustee a legal opinion confirming that there has been a change in current U.S. Federal tax law or an Internal Revenue Service ruling that allows us to make the above deposit without causing the holders to be taxed on the debt securities any differently than if we did not make the deposit and just repaid the debt securities ourselves at maturity. Under current U.S. Federal tax law, the deposit and our legal release from the debt securities would be treated as though we paid each holder its share of the cash and notes or bonds at the time the cash and notes or bonds were deposited in trust in exchange for its debt securities and holders would recognize gain or loss on the debt securities at the time of the deposit; and
- We must deliver to the trustee a legal opinion and officers' certificate stating that all conditions precedent to legal defeasance have been complied with.

If we ever did accomplish legal defeasance, as described above, holders would have to rely solely on the trust deposit for repayment of the debt securities. Holders could not look to us for repayment in the unlikely event of any shortfall. Conversely, the trust deposit would most likely be protected from claims of our lenders and other creditors if we ever became bankrupt or insolvent. If applicable, holders would also be released from the subordination provisions described later under "Description of Debt Securities—Indenture Provisions—Subordination."

Resignation of Trustee

Each trustee may resign or be removed with respect to one or more series of indenture securities provided that a successor trustee is appointed to act with respect to such series. In the event that two or more persons are acting as trustee with respect to different series of indenture securities under the indenture, each of the trustees will be a trustee of a trust separate and apart from the trust administered by any other trustee.

Indenture Provisions—Subordination

Upon any distribution of our assets upon our dissolution, winding up, liquidation or reorganization, the payment of the principal of (and premium, if any) and interest on any indenture securities denominated as subordinated debt securities is to be subordinated to the extent provided in the indenture in right of payment to the prior payment in full of all Senior Indebtedness (defined below), but our obligation to holders to make payment of the principal of (and premium, if any) and interest on such subordinated debt securities will not otherwise be affected. In addition, no payment on account of principal (or premium, if any), interest or sinking fund, if any, may be made on such subordinated debt securities at any time unless full payment of all amounts due in respect of the principal (and premium, if any), interest and sinking fund, if any, on Senior Indebtedness has been made or duly provided for in money or money's worth.

In the event that, notwithstanding the foregoing, any payment from us is received by the trustee in respect of subordinated debt securities or by the holders of any of such subordinated debt securities before all Senior Indebtedness is paid in full, the payment or distribution must be paid over to the holders of the Senior Indebtedness or on their behalf for application to the payment of all the Senior Indebtedness remaining unpaid until all the Senior Indebtedness has been paid in full, after giving effect to any concurrent payment or distribution to the holders of the Senior Indebtedness. Subject to the payment in full of all Senior Indebtedness, the holders of such subordinated debt securities will be subrogated to the rights of the holders of the Senior Indebtedness to the extent of payments made to the holders of the Senior Indebtedness out of the distributive share of such subordinated debt securities.

By reason of this subordination, in the event of a distribution of our assets upon our insolvency, certain of our senior creditors may recover more, ratably, than holders of any subordinated debt securities. The related indenture will provide that these subordination provisions will not apply to money and securities held in trust under the defeasance provisions of the indenture.

“Senior Indebtedness” will be defined in an applicable indenture as the principal of (and premium, if any) and unpaid interest on:

- our indebtedness (including indebtedness of others guaranteed by us), whenever created, incurred, assumed or guaranteed, for money borrowed (other than indenture securities issued under the indenture and denominated as subordinated debt securities), unless in the instrument creating or evidencing the same or under which the same is outstanding it is provided that this indebtedness is not senior or prior in right of payment to the subordinated debt securities; and
- renewals, extensions, modifications and refinancings of any of such indebtedness.

The prospectus supplement accompanying any series of indenture securities denominated as subordinated debt securities will set forth the approximate amount of our Senior Indebtedness outstanding as of a recent date.

Trustee

We intend to name the indenture trustee for each series of indenture securities in the related prospectus supplement.

Certain Considerations Relating to Foreign Currencies

Debt securities denominated or payable in foreign currencies may entail significant risks. These risks include the possibility of significant fluctuations in the foreign currency markets, the imposition or modification of foreign exchange controls and potential illiquidity in the secondary market. These risks will vary depending upon the currency or currencies involved and will be more fully described in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

The following is a general description of the terms of the rights we may issue from time to time unless we provide otherwise in the applicable prospectus supplement. Particular terms of any rights we offer will be described in the prospectus supplement relating to such rights.

General

We may issue rights to purchase common stock, preferred stock, debt securities or units. Rights may be issued independently or together with other securities and may or may not be transferable by the person purchasing or receiving the rights. In connection with any rights offering to our stockholders, we may enter into a standby underwriting, backstop or other arrangement with one or more underwriters or other persons pursuant to which such underwriters or other persons would purchase any offered securities remaining unsubscribed for after such rights offering. In connection with a rights offering to our stockholders, we would distribute certificates evidencing the rights and a prospectus supplement to our stockholders on or about the record date that we set for receiving rights in such rights offering.

The applicable prospectus supplement will describe the following terms of any rights we may issue, including some or all of the following:

- the title and aggregate number of the rights;
- the subscription price or a formula for the determination of the subscription price for the rights and the currency or currencies in which the subscription price may be payable;
- if applicable, the designation and terms of the securities with which the rights are issued and the number of rights issued with each such security or each principal amount of such security;
- the number or a formula for the determination of the number of the rights issued to each stockholder;
- the extent to which the rights are transferable;
- in the case of rights to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one right;

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- in the case of rights to purchase common stock or preferred stock, the type of stock and number of shares of stock purchasable upon exercise of one right;
- the date on which the right to exercise the rights will commence, and the date on which the rights will expire (subject to any extension);
- if applicable, the minimum or maximum amount of the rights that may be exercised at any one time;
- the extent to which such rights include an over-subscription privilege with respect to unsubscribed securities;
- if applicable, the procedures for adjusting the subscription price and number of shares of common stock or preferred stock purchasable upon the exercise of each right upon the occurrence of certain events, including stock splits, reverse stock splits, combinations, subdivisions or reclassifications of common stock or preferred stock;
- the effect on the rights of any merger, consolidation, sale or other disposition of our business;
- the terms of any rights to redeem or call the rights;
- information with respect to book-entry procedures, if any;
- the terms of the securities issuable upon exercise of the rights;
- if applicable, the material terms of any standby underwriting, backstop or other purchase arrangement that we may enter into in connection with the rights offering;
- if applicable, a discussion of certain U.S. Federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the exchange and exercise of the rights.

Exercise of Rights

Each right will entitle the holder to purchase for cash or other consideration such shares of stock or principal amount of securities at the subscription price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the rights offered thereby. Rights may be exercised as set forth in the applicable prospectus supplement beginning on the date specified therein and continuing until the close of business on the expiration date set forth in the prospectus supplement relating to the rights offered thereby. After the close of business on the expiration date, unexercised rights will become void.

Upon receipt of payment and a subscription certificate properly completed and duly executed at the corporate trust office of the subscription agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the securities purchasable upon such exercise. If less than all of the rights represented by such subscription certificate are exercised, a new subscription certificate will be issued for the remaining rights. If we so indicate in the applicable prospectus supplement, holders of the rights may surrender securities as all or part of the exercise price for rights.

We may determine to offer any unsubscribed offered securities directly to stockholders, persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting, backstop or other arrangements, as set forth in the applicable prospectus supplement.

Prior to exercising their rights, holders of rights will not have any of the rights of holders of the securities purchasable upon subscription, including, in the case of rights to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise any voting rights or, in the case of rights to purchase debt securities, the right to receive principal, premium, if any, or interest payments, on the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

DESCRIPTION OF UNITS

We may issue units comprising one or more securities described in this prospectus in any combination. The following description sets forth certain general terms and provisions of the units that we may offer pursuant to this prospectus. The particular terms of the units and the extent, if any, to which the general terms and provisions may apply to the units so offered will be described in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit also is the holder of each security included in the unit. Thus, the unit will have the rights and obligations of a holder of each included security. Units will be issued pursuant to the terms of a unit agreement, which 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. A copy of the forms of the unit agreement and the unit certificate relating to any particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the unit agreement and the related unit certificate, see “Where You Can Find More Information.”

The prospectus supplement relating to any particular issuance of units will describe the terms of those units, including, to the extent applicable, the following:

- the designation and terms of the units and the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provision for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- whether the units will be issued in fully registered or global form.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus in any one or more of the following ways from time to time:

- to or through one or more underwriters, initial purchasers, brokers or dealers;
- through agents to investors or the public;
- in short or long transactions;
- through put or call option transactions relating to our common stock;
- directly to agents or other purchasers;
- in “at the market offerings” within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- through a combination of any such methods of sale; or
- through any other method described in the applicable prospectus supplement.

The applicable prospectus supplement will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, initial purchasers, dealers or agents in connection with the offering, including:

- the terms of the offering;
- the names of any underwriters, dealers or agents;
- the name or names of any managing underwriter or underwriters;

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- the purchase price of the securities and the proceeds to us from the sale;
- any over-allotment options under which the underwriters may purchase additional shares of common stock from us;
- any underwriting discounts, concessions, commissions or agency fees and other items constituting compensation to underwriters, dealers or agents;
- any delayed delivery arrangements;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid by underwriters or dealers to other dealers; or
- any securities exchange or market on which the common stock offered in the prospectus supplement may be listed.

If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account for resale to the public, either on a firm commitment basis or a best efforts basis. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer the securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. If an underwriter or underwriters are used in the sale of securities hereunder, an underwriting agreement will be executed with the underwriter or underwriters at the time an agreement for sale is reached. Unless we inform you otherwise in the applicable prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions. We may change from time to time any public offering price and any discounts or concessions the underwriters allow or pay to dealers.

During and after an offering through underwriters, the underwriters may purchase and sell the securities in the open market. These transactions may include overallotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, which means that selling concessions allowed to syndicate members or other broker-dealers for the offered securities sold for their account may be reclaimed by the syndicate if the offered securities are repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered securities, which may be higher than the price that might otherwise prevail in the open market. If commenced, the underwriters may discontinue these activities at any time.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell our securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities that we offer.

If dealers are used for the sale of securities, we, or an underwriter, will sell the securities to them as principals. The dealers may then resell those securities to the public at varying prices determined by the dealers at the time of resale. We will include in the applicable prospectus supplement the names of the dealers and the terms of the transaction.

We may also sell the securities through agents designated from time to time. In the applicable prospectus supplement, we will name any agent involved in the offer or sale of the offered securities, and we will describe any commissions payable to the agent. Unless we inform you otherwise in the applicable prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly in transactions not involving underwriters, dealers or agents.

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

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Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the applicable securities laws and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the applicable securities laws. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the applicable securities laws.

Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses for which they may receive customary fees and reimbursement of expenses.

We may use underwriters with whom we have a material relationship. We will describe the nature of such relationship in the applicable prospectus supplement.

Under the securities laws of some states, the securities offered by this prospectus may be sold in those states only through registered or licensed brokers or dealers.

We may enter into hedging transactions with broker-dealers and the broker-dealers may engage in short sales of the securities in the course of hedging the positions they assume with us, including, without limitation, in connection with distributions of the securities by those broker-dealers. We may enter into option or other transactions with broker-dealers that involve the delivery of the securities offered hereby to the broker-dealers, who may then resell or otherwise transfer those securities. We may also loan or pledge the securities offered hereby to a broker-dealer and the broker-dealer may sell the securities offered hereby so loaned or upon a default may sell or otherwise transfer the pledged securities offered hereby.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon for us by DLA Piper LLP (US), Short Hills, New Jersey.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our [Annual Report on Form 10-K for the year ended December 31, 2018](#) as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy and information statements and other information with the Securities and Exchange Commission. The SEC maintains a website that contains reports, proxy statements and other information regarding us. The address of the SEC website is www.sec.gov. We maintain a website at www.axsome.com. Information contained on our website is not incorporated into this prospectus and you should not consider information contained on our website to be part of this prospectus or any prospectus supplement.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus the information contained in documents that we file with them, 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 before the date of this prospectus, while information that we file later with the SEC will automatically update and supersede prior information. Any information so updated and superseded shall not be deemed, except as so updated and superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, prior to the termination of the offering. Notwithstanding the foregoing, unless specifically stated to the contrary, none of the information that is not deemed “filed” with the SEC, including information furnished under Items 2.02 or 7.01 of any Current Report on Form 8-K, will be incorporated by reference into, or otherwise included in, this prospectus:

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 filed with the SEC on March 15, 2019;](#)
- [the information contained in our definitive proxy statement on Schedule 14A for our 2019 annual meeting of stockholders filed with the SEC on April 26, 2019, to the extent incorporated by reference in Part III of the Form 10-K for the fiscal year ended December 31, 2018;](#)
- [our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed with the SEC on May 9, 2019;](#)
- [our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 filed with the SEC on August 8, 2019;](#)
- [our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 filed with the SEC on November 7, 2019;](#)
- our Current Reports on Form 8-K filed with the SEC on [January 7, 2019 \(two filings\); January 8, 2019; January 30, 2019; February 6, 2019; March 4, 2019; March 6, 2019; March 14, 2019; March 27, 2019; April 15, 2019; May 6, 2019; May 9, 2019 \(two filings\); June 7, 2019; June 24, 2019; July 11, 2019; July 29, 2019; August 8, 2019; August 20, 2019; September 5, 2019; October 2, 2019; October 16, 2019; October 21, 2019; October 28, 2019 \(two filings\); November 7, 2019 \(two filings\) and December 3, 2019;](#) and
- the description of our common stock contained in our registration statement on [Form 8 A12B, filed with the SEC on November 16, 2015 \(File No. 001-37635\)](#), and all amendments or reports filed for the purpose of updating such description.

We make available, free of charge, through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part. We will provide, upon written or oral request, to each person to whom a prospectus is delivered, including any beneficial owner, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus), free of charge, by writing or calling us at the following address and telephone number:

Axsome Therapeutics, Inc.
200 Broadway
3rd Floor
New York, New York 10038
(212) 332-3241

AXSOME

THERAPEUTICS

**Common Stock
Preferred Stock
Warrants
Debt Securities
Rights to Purchase Common Stock, Preferred Stock, Debt Securities or Units
Units**

PROSPECTUS

December 5, 2019

2,000,000 Shares

AXSOME

THERAPEUTICS

Axsome Therapeutics, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Joint Bookrunning Managers

SVB Leerink

Morgan Stanley

Co-Lead Managers

Cantor

**Ladenburg
Thalmann**

**SunTrust Robinson
Humphrey**

William Blair

Co-Managers

BTIG, LLC

H.C. Wainwright & Co.

December 18, 2019
