

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED AUGUST 11, 2020

**Preliminary prospectus supplement
(To prospectus dated August 8, 2019)**

\$200,000,000



Common stock

We are offering \$200,000,000 of our common stock.

The common stock is quoted on The Nasdaq Global Market under the symbol "ADVM." The last reported sale price of the common stock on August 10, 2020 was \$18.70 per share.

See "[Risk Factors](#)" beginning on page S-9 of this prospectus supplement and page 6 of the accompanying prospectus to read about factors you should consider before buying shares of the common stock.

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

	Per Share	Total
Initial price to public	\$	\$
Underwriting discounts and commissions (1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) See "Underwriting" for additional information regarding underwriting compensation.

To the extent that the underwriters sell more than _____ shares of common stock, the underwriters have the option to purchase up to an additional \$30,000,000 of our common stock at the initial price to public less the underwriting discount.

Our CEO has indicated an interest in purchasing in the aggregate approximately \$100,000 of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, our CEO may determine to purchase a lesser amount than he indicated an interest in purchasing or not to purchase any shares in this offering.

The underwriters expect to deliver the shares against payment in New York, New York on August _____, 2020.

Joint Book-Running Managers

Goldman Sachs & Co. LLC

Cowen

SVB Leerink

Piper Sandler

Prospectus Supplement dated August _____, 2020

[Table of Contents](#)

TABLE OF CONTENTS
PROSPECTUS SUPPLEMENT

	<u>Page</u>
About this Prospectus Supplement	S-ii
Prospectus Supplement Summary	S-1
Risk Factors	S-9
Special Note Regarding Forward-Looking Statements	S-10
Use of Proceeds	S-12
Dilution	S-13
Capitalization	S-15
Material U.S. Federal Income Tax Considerations For Non-U.S. Holders	S-16
Underwriting	S-20
Legal Matters	S-26
Experts	S-26
Where You Can Find Additional Information	S-26
Incorporation of Certain Information By Reference	S-27

PROSPECTUS

About this Prospectus	i
Prospectus Summary	1
Risk Factors	6
Special Note Regarding Forward-Looking Statements	7
Use of Proceeds	8
Description of Capital Stock	8
Description of Debt Securities	13
Description of Warrants	20
Legal Ownership of Securities	22
Plan of Distribution	25
Legal Matters	27
Experts	27
Where You Can Find Additional Information	28
Incorporation of Certain Information By Reference	28

We have not 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 prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of the respective dates of such documents.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated August 8, 2019 form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (“SEC”), utilizing a “shelf” registration process. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

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

We have not, and the underwriters have not, authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. We 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 do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein or therein, is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections titled “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement and the accompanying prospectus.

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

[Table of Contents](#)

supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus supplement to “Adverum,” “the company,” “we,” “us,” “our” and similar references refer to Adverum Biotechnologies, Inc., a corporation under the laws of the State of Delaware, and its wholly owned subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, you should read and consider carefully the more detailed information included or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the factors described in the section titled "Risk Factors" in this prospectus supplement beginning on page S-9 and in our Quarterly Report on Form 10-Q filed with the SEC on August 10, 2020, as well as in any free writing prospectus we have authorized for use in connection with this offering. You also should carefully read the other information incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements, other information and the exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part.

Company Overview

Adverum is a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases. We develop gene therapy product candidates intended to provide durable efficacy by inducing sustained expression of a therapeutic protein. Our core capabilities include novel vector discovery, preclinical and clinical development and in-house manufacturing expertise, specifically in scalable process development, assay development, and current Good Manufacturing Practices ("cGMP") quality control.

Our lead product candidate ADVM-022 is a single intravitreal ("IVT") injection gene therapy designed to deliver long-term durability with robust treatment response, reduce the treatment burden of frequent anti-vascular endothelial growth factor ("anti-VEGF") injections, and improve real-world vision outcomes for patients. ADVM-022 is targeting the treatment of patients with chronic retinal diseases that respond to standard-of-care anti-VEGF therapy, including wet age-related macular degeneration ("wet AMD") and diabetic macular edema ("DME"). ADVM-022 utilizes a proprietary vector capsid, AAV.7m8, carrying an aflibercept coding sequence under the control of a proprietary expression cassette.

Wet AMD is a leading cause of vision loss in patients over 60 years of age, with a prevalence of approximately 1.2 million individuals in the U.S. and 3 million worldwide. In recognition of the need for new treatment options for wet AMD, the U.S. Food and Drug Administration ("FDA") granted Fast Track designation for ADVM-022 for the treatment of wet AMD.

We are conducting the OPTIC trial, designed as a multi-center, open-label, Phase 1, dose-ranging safety trial of ADVM-022 in patients with wet AMD who have demonstrated responsiveness to anti-VEGF treatment. Patients in OPTIC are treatment experienced, and previously required frequent anti-VEGF injections to control their wet AMD and to maintain functional vision. Patients received a high dose (6×10^{11} vg/eye) of ADVM-022 in Cohort 1 (n=6) and Cohort 4 (n=9), and patients received a low dose (2×10^{11} vg/eye) of ADVM-022 in Cohort 2 (n=6) and Cohort 3 (n=9).

In OPTIC, ADVM-022 continues to show robust treatment response from both high and low doses. We have observed long-term durability beyond 15 months from a single IVT injection of ADVM-022 with zero anti-VEGF rescue injections in Cohort 1 (high dose). ADVM-022 continues to be well-tolerated across all four cohorts. In addition, we have seen encouraging early safety data with prophylactic steroid eye drops from Cohort 4 (high dose) consistent with Cohort 3 (low dose).

Interim data from all four cohorts of the OPTIC trial (July 23, 2020 cutoff date) demonstrate the transformative potential of ADVM-022 to greatly reduce the treatment burden for patients with wet AMD:

- ADVM-022 continues to show a robust treatment response
 - Mean BCVA¹ maintained
 - Mean CRT² maintained to improved
- Long-term durability beyond 15 months from single IVT injection with zero anti-VEGF rescue injections in Cohort 1 (high dose)
- Further evidence of a dose response:
 - High dose: 6/63 patients rescue injection free
 - Low dose: 10/154 patients rescue injection free
- Substantial reduction in annualized anti-VEGF injection rate following administration of ADVM-022⁵:
 - High dose: 100%
 - Low dose: 87%
- ADVM-022 continues to be well tolerated with a favorable safety profile in all 4 cohorts (n=30)
 - All ADVM-022-related ocular adverse events (AE) were mild (78%) to moderate (22%)
 - One AE of special interest of moderate recurrent uveitis deemed to be related to ADVM-022 was responsive to steroid eye drops (Cohort 1)
 - Ocular inflammation, when observed, has been responsive to steroid eye drops
 - No clinical or fluorescein⁶ evidence of posterior inflammation
 - No vasculitis, retinitis, choroiditis, vascular occlusions, or endophthalmitis
- Early evidence from Cohort 4, consistent with Cohort 3, suggests that a prophylactic regimen of steroid eye drops results in fewer adverse events and less inflammation, when compared to a prophylactic regimen of oral steroids as used in Cohorts 1 and 2. In Cohorts 3 or 4, no patients have required more than steroid eye drops.

¹ Best corrected visual acuity (BCVA)

² Central retinal thickness (CRT)

³ All patients from Cohort 1 (n=6)

⁴ All patients from Cohort 2 (n=6) and Cohort 3 (n=9)

⁵ Annualized rate (Before) = (number of IVTs in 12 months prior to ADVM-022) / (days from the first IVT in the past 12 months to ADVM-022 / 365.25)

Annualized rate (After) = (number of aflibercept IVTs since ADVM-022) / (days from ADVM-022 to the last study follow-up / 365.25).

⁶ Fluorescein angiography of posterior pole

The following table summarized the OPTIC Phase 1 clinical trial data:

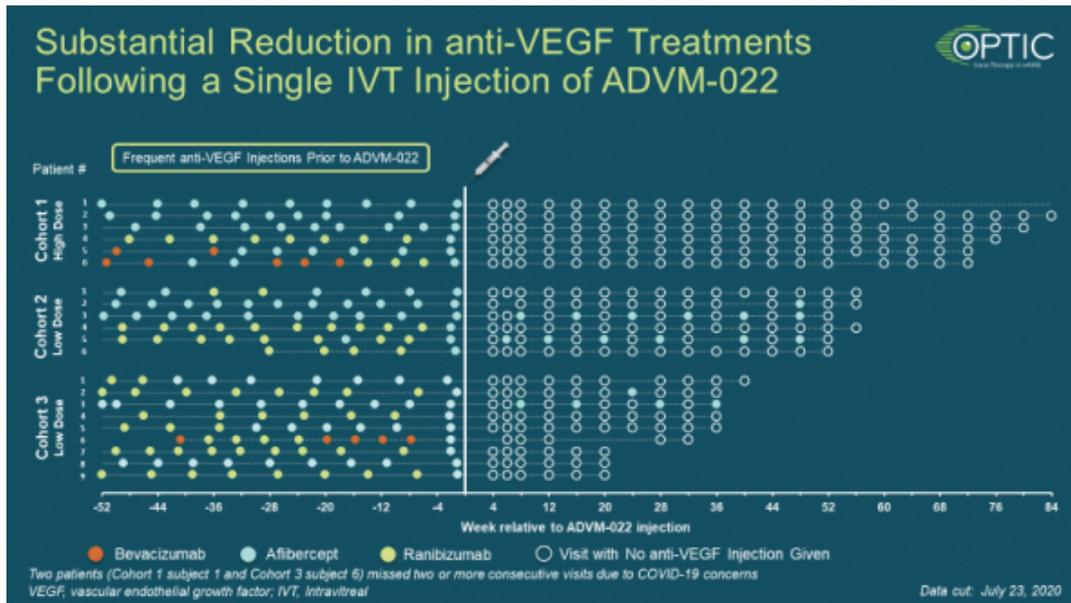
Results Following a Single ADVM-022 Dose:	Cohort 1	Cohort 2	Cohort 3	Cohort 4		
Patients	n=6	n=6	n=9	n=9		
Median follow-up visit (weeks)	72	52	36	4		
ADVM-022 Dose	High dose 6 x 10 ¹¹ vg/eye	Low dose 2 x 10 ¹¹ vg/eye	Low dose 2 x 10 ¹¹ vg/eye	High dose 6 x 10 ¹¹ vg/eye		
Prophylactic steroid regimen	13-day oral	13-day oral	6-week eye drops	6-week eye drops		
Rescue Injections:						
Number of patients requiring anti-VEGF rescue injections	0/6 patients	3/6 patients	2/9 patients	0/9 patients		
Total anti-VEGF rescue injections	0 injections	13 injections	5 injections	0 injections		
Mean annualized anti-VEGF injection frequency before and after ADVM-0223	Before: 9.6 After: 0	Before: 10.0 After: 1.3		N/A		
Reduction in mean annualized anti-VEGF injection frequency after ADVM-0223	100%	87%		N/A		
Follow-up BCVA1 and CRT2:						
	All Patients	All Patients	Rescue Free Patients 50% (3/6)	All Patients	Rescue Free Patients 78% (7/9)	N/A
BCVA mean change from baseline (letters)	-3.2	-2.0	0	+4.0	+6.4	N/A
CRT mean change from baseline (µm)	-21.0 µm	-24.8 µm	-8.3 µm	-118.6 µm	-152.7 µm	N/A

¹ Best corrected visual acuity (BCVA)

² Central retinal thickness (CRT)

³ Annualized rate (Before) = (number of IVTs in 12 months prior to ADVM-022) / (days from the first IVT in the past 12 months to ADVM-022 / 365.25)
Annualized rate (After) = (number of aflibercept IVTs since ADVM-022) / (days from ADVM-022 to the last study follow-up / 365.25).

The following table shows the substantial reduction in anti-VEGF Treatments following a single IVT injection of ADVM-022.



With OPTIC enrollment complete, we plan to present clinical data from all four cohorts by the end of 2020 and initiate a pivotal trial for ADVM-022 in wet AMD in mid-2021. As we advance ADVM-022 for two large ocular disease indications, we are initiating process scale-up from 200L to 1000L scale to support the expected future commercial product launch of ADVM-022, if approved. In addition, we are beginning to plan for in-house manufacturing capabilities with the initiation of site selection.

Diabetes impacts over 30 million people in the United States, over 400 million people globally and is increasing in prevalence. Approximately 5% of adults with diabetes are impacted by DME, a vision-threatening complication of diabetic retinopathy (“DR”) and the leading cause of vision loss in patients with DR. Based on the promising safety and efficacy data from the OPTIC trial for ADVM-022 in patients with wet AMD, we are advancing our novel gene therapy for patients with DME. We recently initiated the INFINITY Phase 2 trial, a multi-center, randomized, double-masked, active comparator-controlled study evaluating a single IVT injection of ADVM-022 in patients with DME.

In the INFINITY trial, we have begun randomizing patients and plan to enroll approximately 33 patients. The INFINITY trial is designed to demonstrate superior control of disease activity following a single IVT injection of ADVM-022 compared to a single aflibercept injection, as measured by time to worsening of DME disease activity in the study eye. Additional objectives include assessments of treatment burden, visual acuity, retinal anatomy and safety outcomes. Participants in this double-masked trial are being randomized to one of three arms for their study eye treatment: Arm 1 will receive high dose (6×10^{11} vg/eye) of ADVM-022, Arm 2 will receive low dose (2×10^{11} vg/eye) of ADVM-022, and Arm 3 will receive aflibercept at a dose of 2 mg. As we advance the INFINITY trial, we plan to present clinical data from this trial in the second half of 2021.

We have licensed the right to use AAV.7m8 to GenSight Biologics S.A. (“GenSight”) to deliver certain therapeutic transgenes, including channel rhodopsin protein, which GenSight is using in their product candidate GS030 for retinitis pigmentosa, currently in clinical development.

In the first quarter of 2020, we moved into our new facility in Redwood City, California. This new 81,000 square foot facility serves as our corporate headquarters and includes expanded laboratory space as well as space for expanded manufacturing process capabilities.

Risks Associated with our Business

Our business is subject to numerous risks. You should read these risks before you invest in our common stock. In particular, our risks include, but are not limited to, the following:

- We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability;
- Our business will depend substantially on the success of one or more of our product candidates. If we are unable to develop, obtain regulatory approval for, or successfully commercialize, any or all of our product candidates, our business will be materially harmed;
- Our gene therapy platform is based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval;
- The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval;
- Preliminary and interim data from our clinical trials that we may announce or publish from time to time may change as each clinical trial progresses;
- Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates;
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected;
- The occurrence of serious complications or side effects in connection with use of our product candidates, either in preclinical studies or clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business prospects, financial condition and results of operations;
- We will rely on third parties to conduct some preclinical testing and all of our planned clinical trials. If these third parties do not meet our deadlines or otherwise fail to conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all;
- We have relied and expect to continue to rely, on third parties to conduct some or all aspects of our vector production, product manufacturing, product testing, protocol development, and research, and these third parties may not perform satisfactorily;

- Any suspension of, or delays in the commencement or completion of, clinical trials for our product candidates could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects;
- The coronavirus (“COVID-19”) pandemic has impacted our business practices and the effects of its continued impact on our business, results of operations, and financial condition will depend on future developments, which cannot be predicted; and
- Our management will have broad discretion over the use of the net proceeds from this offering, and you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Corporate Information

We were incorporated in Delaware in 2006 under the name “Avalanche Biotechnologies, Inc.” We completed the initial public offering of our common stock in August 2014. On May 11, 2016, upon the completion of our acquisition of Annapurna Therapeutics SAS, we changed our name to “Adverum Biotechnologies, Inc.” Our common stock is currently listed on The Nasdaq Global Market under the symbol “ADVM.”

Our principal executive offices are located at 800 Saginaw Drive, Redwood City, CA 94063, and our telephone number is (650) 656-9323. Our internet address is www.adverum.com. The information on our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our internet address is included in this prospectus as an inactive textual reference only.

All brand names or trademarks appearing in this prospectus supplement are the property of their respective holders. Use or display by us of other parties’ trademarks, trade dress, or products in this prospectus supplement and the accompanying prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

The Offering

Common stock offered by us	\$200,000,000 of common stock.
Common stock to be outstanding immediately after this offering	91,334,162 shares of common stock, which is based on an aggregate offering of \$200,000,000 of our common stock at an assumed public offering price of \$18.70 per share of common stock (the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020).
Option to purchase additional common stock	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to additional shares of common stock.
Use of proceeds	<p>We estimate that the net proceeds to us from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be \$187.6 million, or \$215.8 million if the underwriters exercise in full their option to purchase additional shares of common stock.</p> <p>We currently intend to use the net proceeds from this offering for general corporate purposes. General corporate purposes may include, without limitation, the research and development of our gene therapy pipeline and our AAV vector discovery platform, process development, expansion and improvement in manufacturing capabilities, clinical development, acquisitions or in-licenses of complementary companies or businesses, working capital and capital expenditures. See "Use of Proceeds" on page S-12 of this prospectus supplement.</p>
Indication of interest by insider	Our CEO has indicated an interest in purchasing in the aggregate approximately \$100,000 of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, our CEO may determine to purchase a lesser amount than he indicated an interest in purchasing or not to purchase any shares in this offering.
Risk factors	Investing in our common stock involves significant risks. See "Risk Factors" on page S-9 of this prospectus supplement.

The Nasdaq Global Market symbol

Our shares are listed on The Nasdaq Global Market under the symbol "ADVM."

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of June 30, 2020. As of that date, we had 80,638,975 shares of common stock outstanding, excluding:

- 9,966,478 shares of common stock underlying options outstanding as of June 30, 2020, at a weighted average exercise price of \$11.49 per share;
- 80,000 shares of common stock underlying warrants outstanding as of June 30, 2020, at a weighted average exercise price of \$7.08 per share;
- 601,796 shares of common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2020;
- 4,205,999 shares of common stock available for future grant under our equity incentive plans as of June 30, 2020; and
- 2,489,963 shares of common stock available for future issuance under our employee stock purchase plan.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below, as well as the risk factors described under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC on August 10, 2020, and the other information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, including our financial statements and the related notes, as may be updated by our subsequent filings under the Securities Exchange Act of 1934, as amended ("Exchange Act"), and in any free writing prospectus that we have authorized for use in connection with this offering before acquiring shares of our common stock. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects, which may cause the trading price of our common stock to decline and you could lose all or part of your investment.

Risks Related to this Offering

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

Our management will have broad discretion in the application of the net proceeds from this offering, and could spend the proceeds in ways 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 and cause the price of our common stock to decline.

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

Purchasers of common stock in this offering will pay a price per share in this offering that exceeds the net tangible book value per share of our common stock. Assuming that an aggregate of 10,695,187 shares of common stock are sold at a public offering price of \$18.70 per share, the last reported sale price of our common shares on The Nasdaq Global Market on August 10, 2020, for aggregate net proceeds of approximately \$187.6 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us, if you purchase shares of our common stock in this offering, you will experience immediate dilution of \$13.55 per share, representing the difference between the assumed public offering price and our as adjusted net tangible book value per share as of June 30, 2020, after giving effect to this offering. See the section titled "Dilution" below for a more detailed illustration of the dilution you would incur if you purchase common stock in this offering.

You may experience further dilution if we issue additional equity securities in future fundraising transactions.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering. Further, we have a significant number of stock options, warrants and restricted stock units outstanding and we have additional shares reserved for issuance under our equity compensation plans and our employee stock purchase plan. The exercise of outstanding stock options and warrants and vesting of restricted stock units, and any other issuance of shares of common stock under our equity compensation plans or employee stock purchase plan, may result in further dilution of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering are forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry and involve known and unknown risks, uncertainties and other factors that may cause our company's or our industry's results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied in, or contemplated by, the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- the initiation, progress, timing, costs and results of preclinical studies and any clinical trials for our product candidates;
- our ability to advance our viral vector manufacturing and delivery capabilities;
- the timing or likelihood of regulatory filings, designations and approvals;
- our plans to explore potential applications of our gene therapy platform in other indications in ocular and rare diseases;
- our expectations regarding the clinical effectiveness and safety profile of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- our expectation regarding the potential market sizes for our product candidates;
- our intellectual property position;
- the potential benefits of our strategic collaborations and our ability to enter into strategic arrangements;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, our financial position, capital requirements, uses of cash and needs for additional financing and the period for which our cash resources will be sufficient to meet our operating requirements;
- the use of proceeds from this offering; and
- the safety, efficacy and projected development timeline and commercial potential of any product candidates.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading “Risk Factors” contained in this prospectus supplement and in any free writing prospectuses we may authorize for use in connection with this offering. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-

[Table of Contents](#)

looking statements. You should read this prospectus supplement and accompanying prospectus together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

We estimate that we will receive net proceeds from the sale of common stock in this offering of approximately \$187.6 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional common stock, we estimate that the net proceeds to us will be approximately \$215.8 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase (decrease) in the assumed public offering price of \$18.70 per share of common stock, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020, would increase (decrease) the net proceeds to us from this offering by approximately \$10.1 million, assuming that the assumed number of shares of common stock offered by us remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 100,000 shares of common stock in the number of shares of common stock offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$1.8 million, assuming that the assumed public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We will retain broad discretion over the use of the net proceeds from this offering. We currently intend to use the net proceeds from this offering for general corporate purposes. General corporate purposes may include, without limitation, the research and development of our gene therapy pipeline and our AAV vector discovery platform, process development, expansion and improvement in manufacturing capabilities, clinical development, acquisitions or in-licenses of complementary companies or businesses, working capital and capital expenditures. We currently expect the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to fund our planned operations to approximately mid-2022.

Our expected use of the net proceeds from this offering represents our current intentions based upon our present plans and business conditions. The amounts and timing of our actual use of net proceeds will vary depending on numerous factors and any unforeseen delays or cash needs. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone or not pursue our planned development activities if the net proceeds of this offering and our other sources of cash are less than, or do not last as long as, expected.

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

DILUTION

Our net tangible book value as of June 30, 2020, was approximately \$282.6 million, or \$3.50 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of June 30, 2020. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering, and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the assumed sale of our common stock in the aggregate amount of \$200 million at an assumed public offering price of \$18.70 per share, the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2020 would have been \$470.2 million, or \$5.15 per share of common stock. This amount represents an immediate increase in net tangible book value of \$1.65 per share to our existing stockholders and an immediate dilution in net tangible book value of \$13.55 per share to new investors in this offering. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$18.70
Net tangible book value per share as of June 30, 2020	\$ 3.50
Increase in net tangible book value per share attributable to investors purchasing our common stock in this offering	<u>1.65</u>
As adjusted net tangible book value per share after giving effect to this offering	<u>5.15</u>
Dilution per share to investors purchasing our common stock in this offering	<u>\$13.55</u>

Each \$1.00 increase (decrease) in the assumed public offering price of \$18.70 per share of common stock, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020, would increase (decrease) our as adjusted net tangible book value per share after this offering by approximately \$0.11, and increase (decrease) dilution to new investors by approximately \$0.89 per share, assuming that the assumed number of shares of common stock offered by us remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase of 100,000 shares of common stock in the number of shares of common stock offered by us would increase the as adjusted net tangible book value per share after this offering by approximately \$0.01 and decrease the dilution to new investors by \$0.01 per share, and each decrease of 100,000 shares of common stock in the number of shares of common stock offered by us would decrease the as adjusted net tangible book value per share after this offering by approximately \$0.02 and increase the dilution to new investors by \$0.02 per share, assuming in each case that the assumed public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriters' option to purchase up to \$30 million of additional shares of common stock within 30 days of the date of the final prospectus supplement for this offering, based upon an assumed public offering price of \$18.70 per share of common stock, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020, the exercise of other outstanding options and warrants having a per share exercise price less than the public offering price per share in this offering, the vesting of restricted stock units, or the issuance of shares of common stock under our equity compensation plans or employee stock purchase plan. If the underwriters exercise in full their option to purchase additional shares, based upon an assumed public offering price of \$18.70 per share of common stock, our net tangible book value on June 30, 2020, after giving effect to this offering, would have been approximately \$498.4 million, or approximately \$5.36 per share, representing an immediate dilution of \$13.34 per share to new investors purchasing

[Table of Contents](#)

shares of common stock in this offering and an immediate increase in net tangible book value of \$1.86 per share to our existing stockholders.

The above discussion and table are based on the number of shares outstanding as of June 30, 2020. As of that date, we had 80,638,975 shares of common stock outstanding, excluding:

- 9,966,478 shares of common stock underlying options outstanding as of June 30, 2020, at a weighted average exercise price of \$11.49 per share;
- 80,000 shares of common stock underlying warrants outstanding as of June 30, 2020, at a weighted average exercise price of \$7.08 per share;
- 601,796 shares of common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2020;
- 4,205,999 shares of common stock available for future grant under our equity incentive plans as of June 30, 2020; and
- 2,489,963 shares of common stock available for future issuance under our employee stock purchase plan.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe that we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and capitalization as of June 30, 2020:

- on an actual basis; and
- on an as adjusted basis to reflect the assumed sale by us of 10,695,187 shares of our common stock in this offering at the assumed public offering price of \$18.70 per share of common stock, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 10, 2020, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the data set forth in the table below in conjunction with our financial statements, including the related notes, and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” from our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2020, which are incorporated by reference into this prospectus supplement and the accompanying prospectus.

	As of June 30, 2020	
	Actual	As Adjusted
	(unaudited)	
	(in thousands, except share data)	
Cash, cash equivalents and short-term investments	\$ 280,139	\$ 467,759
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized, no shares issued and outstanding, actual and as adjusted	—	—
Common stock, \$0.0001 par value; 300,000,000 shares authorized, 80,638,975 shares issued and outstanding, actual; 91,334,162 shares issued and outstanding as adjusted	8	9
Additional paid-in capital	720,288	907,907
Accumulated other comprehensive loss	(598)	(598)
Accumulated deficit	(437,135)	(437,135)
Total stockholders' equity	282,563	470,183
Total capitalization	\$ 282,563	\$ 470,183

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of June 30, 2020. As of that date, we had 80,638,975 shares of common stock outstanding, excluding:

- 9,966,478 shares of common stock underlying options outstanding as of June 30, 2020, at a weighted average exercise price of \$11.49 per share;
- 80,000 shares of common stock underlying warrants outstanding as of June 30, 2020, at a weighted average exercise price of \$7.08 per share;
- 601,796 shares of common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2020;
- 4,205,999 shares of common stock available for future grant under our equity incentive plans as of June 30, 2020; and
- 2,489,963 shares of common stock available for future issuance under our employee stock purchase plan.

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

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion is not a complete analysis of all potential U.S. federal income tax consequences relating thereto, and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences (such as gift and estate taxes) other than income taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended (the "Code"), such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, certain former U.S. citizens or long-term residents, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, corporations organized outside of the United States, any state thereof or the District of Columbia that are nonetheless treated as United States income taxpayers for United States federal tax purposes, persons that hold our common stock as part of a "straddle," "hedge," "conversion transaction," "synthetic security" or integrated investment or other risk reduction strategy, persons who acquire our common stock through the exercise of an option or otherwise as compensation, persons subject to the alternative minimum tax or federal Medicare contribution tax on net investment income, "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds, partnerships and other pass-through entities or arrangements, and investors in such pass-through entities or arrangements. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service ("IRS") with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment).

Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income, estate and other tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a "Non-U.S. Holder" is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, nor a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation). A "U.S. Holder" means a beneficial owner of our common stock that is for U.S. federal income tax purposes any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity treated as a corporation for U.S. federal income tax purposes created or organized in or under the laws of the U.S., any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

[Table of Contents](#)

- a trust if it (1) is subject to the primary supervision of a court within the U.S. and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

In the case of a holder of our common stock that is classified as a partnership for U.S. federal income tax purposes, the tax treatment of a person treated as a partner in such partnership for U.S. federal income tax purposes generally will depend on the status of the partner, the activities of the partner and the partnership and certain determinations made at the partner level. A person treated as a partner in a partnership or who holds our common stock through another transparent entity should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other transparent entity, as applicable.

Distributions

Distributions, if any, made on our common stock to a Non-U.S. Holder to the extent treated as made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty, subject to the discussion below regarding foreign accounts. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN (in the case of individuals) or IRS Form W-8BEN-E (in the case of entities), or other appropriate form, including a U.S. taxpayer identification number, or in certain circumstances, a foreign tax identifying number, and certifying the Non-U.S. Holder's entitlement to benefits under that treaty. This certification must be provided to us or our paying agent prior to the payment of dividends and must be updated periodically. In the case of a Non-U.S. Holder that is an entity, Treasury Regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty and you do not timely file the required certification, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent) prior to the payment of such dividends. In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular rates applicable to U.S. residents. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments. Non-U.S. Holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce the Non-U.S. Holder's adjusted basis in our common stock, but not below zero, and then will be treated as gain to the extent of any excess, and taxed in the same

manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met or (c) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder's holding period. In general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprise (by fair market value) at least half of our business assets. We believe that we have not been and we are not, and do not anticipate becoming, a U.S. real property holding corporation. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder's holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market. If any gain on your disposition is taxable because we are a United States real property holding corporation and your ownership of our common stock exceeds five percent, you will be taxed on such disposition generally in the manner applicable to U.S. persons.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular U.S. federal income tax rates, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. Gain described in (b) above will be subject to U.S. federal income tax at a flat 30% rate or such lower rate as may be specified by an applicable income tax treaty, which gain may be offset by certain U.S.-source capital losses (even though you are not considered a resident of the U.S.), provided that the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any distributions we pay on our common stock (even if the payments are exempt from withholding), including the amount of any such distributions, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such distributions are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Distributions to a Non-U.S. Holder that are classified as dividends paid by us (or our paying agents) may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E, or IRS Form W-ECI, or otherwise establishes an exemption. Notwithstanding the foregoing, backup withholding may apply if the payor has actual knowledge, or reason to know, that the holder is a U.S. person who is not an exempt recipient.

[Table of Contents](#)

U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be credited against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

Foreign Accounts

Sections 1471 through 1474 of the Code (commonly referred to as FATCA) impose a U.S. federal withholding tax of 30% on certain payments, including dividends paid on and, subject to the proposed Treasury regulations described below, the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). FATCA also generally imposes a federal withholding tax of 30% on certain payments, including dividends paid on and the gross proceeds of a disposition of our common stock to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. An intergovernmental agreement between the United States and an applicable foreign country may modify those requirements. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Holders are encouraged to consult with their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

The withholding provisions described above currently apply to payments of dividends. Under proposed Treasury Regulations, the preamble to which states that taxpayers may rely on them, this withholding tax will not apply to payments of gross proceeds from a sale or other disposition of common stock.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY RECENT CHANGE IN APPLICABLE LAW.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC, Cowen and Company, LLC, SVB Leerink LLC and Piper Sandler & Co. are the representatives of the underwriters.

<u>Underwriters</u>	<u>Number of Shares</u>
Goldman Sachs & Co. LLC	
Cowen and Company, LLC	
SVB Leerink LLC	
Piper Sandler & Co.	
Total	

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional _____ shares from us. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase _____ additional shares.

<u>Paid by Adverum</u>	<u>No Exercise</u>	<u>Full Exercise</u>
Per Share	\$	\$
Total	\$	\$

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$ _____ per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We and our directors and executive officers have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representatives. Among the exceptions, certain directors and executive officers are permitted to sell up to an aggregate of approximately 60,000 shares of common stock pursuant to existing Rule 10b5-1 trading plans during such 90-day period. In addition, a significant stockholder, Versant Ventures IV, LLC and certain of its related entities (collectively, Versant), have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representatives. Among the exceptions, Versant may enter into a Rule 10b5-1 trading plan that provides for the distribution to its limited partners and general partner of up to 2,000,000 shares of

Table of Contents

common stock in the aggregate (representing approximately 28.3% of Versant's shares of our common stock) provided that such distribution may not occur earlier than the 31st day after the date of this prospectus supplement or at a time when the prior day closing price per share is less than the offering price per share to the public set forth on the cover of this prospectus supplement.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover 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 cover 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 additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the 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.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our common stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

European Economic Area

In relation to each Member State of the European Economic Area (each a "Member State"), no common shares (the "Shares") have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the Shares which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of Shares may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

[Table of Contents](#)

provided that no such offer of Shares shall require us or any representative to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to any Shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

United Kingdom

Each Underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA)) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Canada

The securities may be sold in Canada 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 securities must be made in accordance with an exemption form, 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 offering memorandum (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 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.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (“Companies (Winding Up and Miscellaneous Provisions) Ordinance”) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (“Securities and Futures Ordinance”), or (ii) to “professional investors” as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances

[Table of Contents](#)

which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation’s securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (“Regulation 32”).

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be

[Table of Contents](#)

offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 – 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 – 1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$380,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

[Table of Contents](#)

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

LEGAL MATTERS

Cooley LLP will pass upon the validity of the common stock offered hereby. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. is representing 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, 2019, and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus supplement and accompanying prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>.

We maintain a website at www.adverum.com. Information contained in or accessible through our website does not constitute a part of this prospectus supplement or the accompanying prospectus and is not incorporated by reference into this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information in this prospectus supplement and the accompanying prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement and the accompanying prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. We incorporate by reference into this prospectus supplement, the accompanying prospectus and the registration statement of which this prospectus supplement and the accompanying prospectus are a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-36579), excluding any portions of any Form 8-K that are not deemed “filed” pursuant to the General Instructions of Form 8-K:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2019, filed with the SEC on March 12, 2020 (our “Form 10-K”);
- the information specifically incorporated by reference in our Form 10-K from our proxy statement on [Schedule 14A](#) filed with the SEC on April 28, 2020, and additional definitive materials on [Schedule 14A](#) filed with the SEC on June 19, 2020;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2020, filed with the SEC on May 28, 2020;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended June 30, 2020, filed with the SEC on August 10, 2020;
- our Current Reports on Form 8-K filed with the SEC on [February 12, 2020](#) (other than the information in Item 2.02), [April 20, 2020](#), [May 8, 2020](#), [June 15, 2020](#), and [June 29, 2020](#); and
- the description of our common stock set forth in our registration statement on [Form 8-A](#), filed with the SEC on July 28, 2014, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act. Information in such future filings updates and supplements the information provided in this prospectus supplement and the accompanying prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Adverum Biotechnologies, Inc.
800 Saginaw Drive
Redwood City, CA 94063
(650) 656-9323
Attn: Investor Relations

Prospectus



**Common Stock
Preferred Stock
Debt Securities
Warrants**

From time to time, we may offer and sell any combination of the securities described in this prospectus, either individually or in combination. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on the Nasdaq Global Market under the trading symbol "ADVM." On August 7, 2019, the last reported sale price of our common stock was \$11.71 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the Nasdaq Global Market or other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. Before making an investment decision, you should review carefully the risks described under the heading "[Risk Factors](#)" on page 6 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

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

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. The supplements to this prospectus will provide the specific terms of the plan of distribution. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is August 8, 2019.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	i
PROSPECTUS SUMMARY	1
RISK FACTORS	6
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	7
USE OF PROCEEDS	8
DESCRIPTION OF CAPITAL STOCK	8
DESCRIPTION OF DEBT SECURITIES	13
DESCRIPTION OF WARRANTS	20
LEGAL OWNERSHIP OF SECURITIES	22
PLAN OF DISTRIBUTION	25
LEGAL MATTERS	27
EXPERTS	27
WHERE YOU CAN FIND ADDITIONAL INFORMATION	28
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	28

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process 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 statement, we may, from time to time, offer and sell, either individually or in combination, in one or more offerings, any combination of the securities described in this prospectus. There is no limit on the aggregate amount of the securities that we may offer pursuant to the registration statement of which this prospectus is a part.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference,” before buying any of the securities being offered.

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

You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we

[Table of Contents](#)

have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus, the accompanying prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you. This prospectus is 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 appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains and incorporates by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe that these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled “Where You Can Find Additional Information.”

PROSPECTUS SUMMARY

This summary highlights selected information appearing elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Adverum Biotechnologies, Inc.

Overview

We are a clinical-stage gene therapy company targeting unmet medical needs in ocular and rare diseases. We develop gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Our core capabilities include clinical development, novel vector discovery, and in-house manufacturing expertise, specifically in scalable process development, assay development, and current Good Manufacturing Practices (“cGMP”) quality control. Since our inception, we have devoted our efforts to performing research and development activities, filing patent applications, hiring personnel and raising capital to support these activities.

Risks Associated with our Business

Our business is subject to numerous risks. You should read these risks before you invest in our common stock. In particular, our risks include, but are not limited to, the following:

- We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability;
- We expect that our cash, cash equivalents, and short-term investments will be sufficient to fund our lead gene therapy programs into 2021. If this expectation proves to be wrong, we may be forced to delay, limit or terminate certain of our development efforts;
- We will need to raise additional funding, which may not be available on acceptable terms, or at all. If we fail to obtain additional capital necessary to fund our operations, we will be unable to successfully develop and commercialize our product candidates;
- Our business will depend substantially on the success of one or more of our product candidates. If we are unable to develop, obtain regulatory approval for, or successfully commercialize, any or all of our product candidates, our business will be materially harmed;
- Our gene therapy platform is based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval;
- The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval;
- Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates;

- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected;
- The occurrence of serious complications or side effects in connection with use of our product candidates, either in preclinical studies or clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business prospects, financial condition and results of operations; and
- We will rely on third parties to conduct some preclinical testing and all of our planned clinical trials. If these third parties do not meet our deadlines or otherwise fail to conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

Corporate Information

We were incorporated in Delaware in 2006 under the name “Avalanche Biotechnologies, Inc.” We completed the initial public offering of our common stock in August 2014. On May 11, 2016, upon the completion of our acquisition of Annapurna Therapeutics SAS, we changed our name to “Adverum Biotechnologies, Inc.” Our common stock is currently listed on the Nasdaq Global Market under the symbol “ADV.M.” We are an “emerging growth company” under the Jumpstart Our Business Startups Act of 2012, and therefore we are subject to reduced public company reporting requirements.

Our principal executive offices are located at 1035 O’Brien Drive, Menlo Park, CA 94025, and our telephone number is (650) 272-6269. Our internet address is www.adverum.com. The information on our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our internet address is included in this prospectus as an inactive textual reference only.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. There is no limit on the aggregate amount of the securities that we may offer pursuant to the registration statement of which this prospectus is a part. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity date, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exercise, exchange or sinking fund terms, if any;

- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- material or special U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. In this prospectus, we have summarized certain general features of the common stock under “Description of Capital Stock—Common Stock.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. In this prospectus, we have summarized certain general features of the preferred stock under “Description of Capital Stock—Preferred Stock.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under “Description of Debt Securities.” We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities. In this prospectus, we have summarized certain general features of the warrants under “Description of Warrants.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Use of Proceeds

Unless otherwise specified in connection with a particular offering of securities, the net proceeds from the sale of the securities offered by this prospectus will be used for general corporate purposes. General corporate

purposes may include, without limitation, the research and development of our gene therapy pipeline and our AAV vector discovery platform, process development and manufacturing improvements, acquisitions or in-licenses of complementary companies or businesses, working capital and capital expenditures. See “Use of Proceeds” in this prospectus.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the symbol “ADVM.” The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the Nasdaq Global Market or other securities exchange of the securities covered by the applicable prospectus supplement.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled “Risk Factors” contained in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. 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. Please also read carefully the section below entitled “Special Note Regarding Forward-Looking Statements.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- the initiation, progress, timing, costs and results of preclinical studies and any clinical trials for our product candidates;
- our ability to advance our viral vector manufacturing and delivery capabilities;
- the timing or likelihood of regulatory filings, designations and approvals;
- our plans to explore potential applications of our gene therapy platform in other indications in ocular and rare diseases;
- our expectations regarding the clinical effectiveness of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- our expectation regarding the potential market sizes for our product candidates;
- our intellectual property position;
- the potential benefits of our strategic collaborations and our ability to enter into strategic arrangements;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- the safety, efficacy and projected development timeline and commercial potential of any product candidates.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading “Risk Factors” contained in the applicable prospectus supplement, in any free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, any applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

Unless otherwise specified in connection with a particular offering of securities, the net proceeds from the sale of the securities offered by this prospectus will be used for general corporate purposes. General corporate purposes may include, without limitation, the research and development of our gene therapy pipeline and our AAV vector discovery platform, process development and manufacturing improvements, acquisitions or in-licenses of complementary companies or businesses, working capital and capital expenditures. We may temporarily invest such net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 300,000,000 shares of common stock, \$0.0001 par value per share, and 5,000,000 shares of preferred stock, \$0.0001 par value per share. A description of material terms and provisions of our certificate of incorporation and bylaws affecting the rights of holders of our capital stock is set forth below. The description is intended as a summary, and is qualified in its entirety by reference to our certificate of incorporation and the bylaws.

Common Stock

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. In the election of directors, a plurality of the votes cast at a meeting of stockholders is sufficient to elect a director. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In all other matters, except as noted below under “—Amendment of our Amended and Restated Certificate of Incorporation or our Amended and Restated Bylaws” and “—Election and Removal of Directors” and except where a higher threshold is required by law, a majority of the votes cast affirmatively or negatively (excluding abstentions and broker non-votes) will decide such matters.

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

Our amended and restated certificate of incorporation authorizes our board of directors, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be

[Table of Contents](#)

greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control of our company or other corporate action.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if applicable;
- the provisions for a sinking fund, if applicable;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Anti-takeover Effects of Provisions of our Certificate of Incorporation and Bylaws and Delaware Law

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

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our charter documents provide that a special meeting of stockholders may be called only by the secretary of our company at the direction of the board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Election and Removal of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors. Our charter documents provide that directors may be removed from office at any time (i) with cause by the affirmative vote of the holders of a majority of the voting power of all the then outstanding shares of our voting stock entitled to vote at an election of directors or (ii) without cause by the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all the then outstanding shares of our voting stock entitled to vote at an election of directors.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the

Table of Contents

time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 of the DGCL defines business combination to include the following:

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

Section 203 of the DGCL defines an “interested stockholder” as an entity or person who, together with the entity’s or person’s affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation. A Delaware corporation may “opt out” of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change of control attempts of us.

Amendment of our Amended and Restated Certificate of Incorporation or our Amended and Restated Bylaws

The amendment of any of the above provisions in our amended and restated certificate of incorporation, except for the provision making it possible for our board of directors to issue preferred stock, or the amendment of any provision in our amended and restated bylaws (other than by action of the board of directors), would require approval by holders of at least 66 2/3% of our then outstanding voting stock

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Delaware as Sole and Exclusive Forum

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of Adverum, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of Adverum to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or (iv) any action asserting a claim governed by the internal

[Table of Contents](#)

affairs doctrine shall be the Court of Chancery of the State of Delaware, in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants.

Transfer Agent and Registrar

American Stock Transfer & Trust Company is the transfer agent and registrar for our common stock. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219. The main telephone number is (800) 937-5449.

Listing on the Nasdaq Global Market

Our common stock is listed on the Nasdaq Global Market the symbol "ADVM." The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the Nasdaq Global Market or any securities market or other exchange of the preferred stock covered by such prospectus supplement.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

Table of Contents

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities;
- the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities, and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

[Table of Contents](#)

- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

[Table of Contents](#)

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

Table of Contents

- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities—General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;

Table of Contents

- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and in any related free writing prospectuses that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

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

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;

Table of Contents

- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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

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

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

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

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

[Table of Contents](#)

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under the section entitled "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We

do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depository in any way;
- the depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depository, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

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

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

[Table of Contents](#)

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters or agents that are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in the common stock on the Nasdaq Global Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Cooley LLP will pass upon the validity of the securities offered by this prospectus, and any supplement thereto, unless otherwise indicated in the applicable prospectus supplement. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements for the year ended December 31, 2018, 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.

The 2017 consolidated financial statements incorporated in this Prospectus by reference from the Company's Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such consolidated financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-36579):

- our Annual Report on [Form 10-K](#), for the year ended December 31, 2018, filed with the SEC on March 6, 2019;
- our Amendment No. 1 to Annual Report on [Form 10-K/A](#), for the year ended December 31, 2018, filed with the SEC on April 30, 2019;
- our Quarterly Report on [Form 10-Q](#), for the quarter ended March 31, 2019, filed with the SEC on May 8, 2019;
- our Quarterly Report on [Form 10-Q](#), for the quarter ended June 30, 2019, filed with the SEC on August 8, 2019;
- our Current Reports on Form 8-K filed with the SEC on [March 1, 2019](#), [April 24, 2019](#), [May 2, 2019](#), [July 31, 2019](#) and [August 1, 2019](#); and
- the description of our common stock set forth in our registration statement on [Form 8-A](#), filed with the SEC on July 28, 2014, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus, which will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later-filed document modify or replace such earlier statements. We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral

[Table of Contents](#)

request, a copy of any or all of the documents incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to:

Adverum Biotechnologies, Inc.
1035 O'Brien Drive,
Menlo Park, CA 94025
Attn: Investor Relations
(650) 272-6269

\$200,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Goldman Sachs & Co. LLC

Cowen

SVB Leerink

Piper Sandler