

PROSPECTUS



\$14,024,100
Common Stock

We have entered into a Capital on Demand™ Sales Agreement, or sales agreement, with JonesTrading Institutional Services LLC and William Blair & Company, L.L.C., each an Agent and collectively, the Agents, dated January 29, 2021, relating to the sale of shares of our common stock. Under the sales agreement, we may offer and sell shares of our common stock, \$0.001 par value per share, having an aggregate offering price of up to \$30,000,000 from time to time through or to the Agents, acting as our sales agents or as principals, in accordance with the terms of the sales agreement. Through the date of this prospectus, we have sold \$10,922,884 of shares of our common stock in accordance with the sales agreement under a prospectus supplement dated January 29, 2021.

As of the date of this prospectus, we are subject to General Instruction I.B.6 of Form S-3, which limits the amounts that we may sell under the registration statement of which this prospectus is a part. After giving effect to these limitations and the current public float of our common stock, we currently may offer and sell from and after the date hereof shares of our common stock having an aggregate offering price of up to \$14,024,100 under the sales agreement pursuant to this prospectus. If our public float increases such that we may sell additional amounts under the sales agreement and the registration statement of which this prospectus is a part, we will file a prospectus supplement prior to selling such additional amounts.

As of June 16, 2022, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$42,072,302, which we calculated based on 90,823,597 shares of outstanding common stock as of June 15, 2022, of which 73,604,447 shares were held by non-affiliates, and a price per share of \$0.5716 which was the closing price of our common stock on April 20, 2022. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell, pursuant to the registration statement of which this prospectus forms a part, securities with a value exceeding one-third of the aggregate market value of our outstanding common stock held by non-affiliates in any 12-month period, so long as the aggregate market value of our outstanding common stock held by non-affiliates remains below \$75.0 million. During the 12 calendar months prior to and including the date of this prospectus, we have not offered or sold any securities pursuant to General Instruction I.B.6 of Form S-3.

Our common stock is listed on The Nasdaq Capital Market under the trading symbol “ALRN.” On June 15, 2022, the last sale price of our common stock as reported on The Nasdaq Capital Market was \$0.40 per share.

Sales of our common stock, if any, under this prospectus will be made in sales deemed to be “at the market offerings” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act. The Agents are not required to sell any specific amount, but will act as our sales agents using commercially reasonable efforts, consistent with their normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Stock Market LLC. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

The compensation to the Agents for sales of common stock sold pursuant to the sales agreement will be an amount up to 3.0% of the gross sales price per share sold under the sales agreement. See “Plan of Distribution” beginning on page 19 of this prospectus for additional information regarding the compensation to be paid to the Agents. In connection with the sale of the common stock on our behalf, the Agents will be deemed to be “underwriters” within the meaning of the Securities Act and the compensation of the Agents will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to the Agents with respect to certain liabilities, including civil liabilities under the Securities Act.

Investing in our common stock involves certain risks. See “[Risk Factors](#)” beginning on page 9 of this prospectus and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to invest in our common stock.

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

JonesTrading

William Blair

June 16, 2022

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the “SEC,” utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$150,000,000. Under this prospectus, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$14,024,100, at prices and on terms to be determined by market conditions at the time of the offering in accordance with the sales agreement.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus and all of the information contained in the documents incorporated by reference herein, as well as the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.” These documents contain important information that you should consider when making your investment decision.

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the information incorporated by reference herein includes “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this prospectus or the information incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus and the information incorporated by reference herein include, among other things, statements about:

- our plans to develop and commercialize ALRN-6924, including the potential benefits thereof;
- our ongoing and future clinical trials for ALRN-6924, whether conducted by us or by any future collaborators, including the timing of initiation of these trials and of the anticipated results;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and investments;
- our expectations related to the use of proceeds from this offering.
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the timing of and our ability to obtain and maintain marketing approvals for ALRN-6924;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional product candidates with significant commercial potential;
- our plans to enter into collaborations for the development and commercialization of ALRN-6924 and any additional product candidates;
- potential benefits of any future collaboration;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;
- the impact the coronavirus pandemic may have on the timing of our clinical development and on our operations; and
- our ability to maintain our listing on The Nasdaq Capital Market.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included, or incorporated by reference, in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC that

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are incorporated herein by reference, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this prospectus, the documents incorporated by reference herein and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus and incorporated by reference herein are made as of the date hereof, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the documents we incorporate by reference herein. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under “Risk Factors” beginning on page 9 of this prospectus and our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus, before making an investment decision.

Aileron Therapeutics, Inc.

Overview

We are a clinical-stage chemoprotection oncology company that aspires to make chemotherapy safer and thereby more effective to save more patients’ lives. ALRN-6924, our first-in-class MDM2/MDMX dual inhibitor, is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle. ALRN-6924 is the only reported chemoprotective agent in clinical development to employ a biomarker strategy, in which we exclusively focus on treating patients with p53-mutated cancers. Our targeted strategy is designed to selectively protect multiple healthy cell types throughout the body from chemotherapy without protecting cancer cells. As a result, healthy cells are spared from chemotherapeutic destruction while chemotherapy continues to kill cancer cells. By reducing or eliminating multiple chemotherapy-induced side effects, ALRN-6924 may improve patients’ quality of life and help them better tolerate chemotherapy. Enhanced tolerability may result in fewer dose reductions or delays of chemotherapy and the potential for improved efficiency. Our vision is to bring chemoprotection to all patients with p53-mutated cancer regardless of type of cancer or chemotherapy.

Risks Related to Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the “Risk Factors” section of this prospectus immediately following this prospectus summary and our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q. These risks include the following:

- Our business depends entirely on the successful development and commercialization of our product candidate, ALRN-6924. Our clinical trials of ALRN-6924 may not be successful. If our trials prove unsuccessful or if we are unable to obtain approval for and commercialize ALRN-6924 or experience significant delays in doing so, our business will be materially harmed.
- We will need substantial additional funding to continue our operations. Our cash, cash equivalents and investments are not sufficient to enable us to complete the development or commercialization of ALRN-6924. If we are unable to raise capital when needed, we may be forced to delay, reduce and/or eliminate our research and drug development programs, reduce headcount, and future commercialization efforts, or take other actions that could adversely affect our business.
- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. Even if we are able to develop and commercialize ALRN-6924, we may never generate revenues that are significant or large enough to achieve profitability.
- The COVID-19 pandemic has affected and may continue to affect our ability to conduct our ongoing and planned clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has adversely impacted economies worldwide, which could result in adverse effects on our business and operations.

- The approach we are taking to discover and develop novel drugs is unproven and may never lead to marketable products.
- We are pursuing the development of ALRN-6924 as a chemoprotective agent in combination with approved chemotherapeutics. If the U.S. Food and Drug Administration, or the FDA, revokes approval of any such chemotherapeutic, or if safety, efficacy, manufacturing or supply issues arise with any chemotherapeutic that we use in combination with ALRN-6924 in the future, we may be unable to further develop and/or market ALRN-6924, or we may experience significant regulatory delays, and our business could be materially harmed.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, interim results of a clinical trial, do not necessarily predict final results and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities. In addition, results of clinical trials of ALRN-6924 when used with one chemotherapy or in one patient population may not be predictive of the results of other clinical trials of ALRN-6924 when used with a different chemotherapy or in a different patient population.
- Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of ALRN-6924 or any other product candidate that we may develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs, experience delays in completing, or ultimately be unable to complete, the development of ALRN-6924 or any other product candidate that we may develop or be unable to obtain marketing approval.
- We are conducting clinical trials of ALRN-6924 and plan to conduct additional clinical trials of ALRN-6924 at sites outside the United States. The FDA's acceptance of data from clinical trials outside of the United States is subject to conditions. Accordingly, the FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.
- We may not be able to initiate or continue clinical trials for ALRN-6924 or any other product candidate that we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. We do not yet know exactly how many patients will have the genetic profile that ALRN-6924 or other future product candidates are designed to address. In particular, because our clinical trials are targeted at a subset of patients in indications with p53-mutated cancers, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.
- If serious adverse or unacceptable side effects are identified during the development of ALRN-6924 or any other product candidate that we may develop or we observe limited efficacy of ALRN-6924 or any other product candidate that we may develop, we may need to abandon or limit the development of ALRN-6924 or other product candidates that we may develop.
- The FDA or comparable foreign regulatory authorities may, under certain circumstances, require that a companion diagnostic be approved for use with ALRN-6924. If we are unable to successfully develop and obtain approval for such a diagnostic, either on our own or through a third party, or if we experience significant delays in doing so, we may not obtain marketing approval for ALRN-6924 in a timely manner, or at all.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

- We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.
- We contract with third parties for the manufacture of our ALRN-6924 for our ongoing clinical trials and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of ALRN-6924 or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We may seek to enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 or other product candidates. If we are unable to enter into collaborations or those collaborations into which we enter are not successful, the development, marketing and/or commercialization of ALRN-6924 or such other product candidates that are the subject of such collaborations would be harmed.
- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us, or any future collaborators, from obtaining approvals for the commercialization of ALRN-6924 or any other product candidate that we may develop. As a result, we cannot predict when or if, and in which territories or for which indications, we, or any future collaborators, will obtain marketing approval to commercialize ALRN-6924 or any other product candidate that we may develop.
- Even if ALRN-6924 receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.
- If we fail to maintain compliance with the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would adversely affect the liquidity of our common stock and our ability to raise additional capital or enter into strategic transactions.

Corporate Information

We were incorporated under the laws of the State of Delaware on August 6, 2001 under the name Renegade Therapeutics, Inc. We changed our name to Aileron Therapeutics, Inc. in February 2007. Our principal executive offices are located at 285 Summer Street, Suite 101, Boston, Massachusetts 02210, and our telephone number is (617) 995-0900. Our website address is <http://www.aileronrx.com>. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

In this prospectus, unless otherwise stated or the context otherwise requires, references to “Aileron,” “the company,” “we,” “us,” “our” and similar references refer to Aileron Therapeutics, Inc. Aileron and other trademarks or service marks of Aileron appearing in this prospectus are the property of Aileron. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

As a company with less than \$1.07 billion of revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company until December 31, 2022 or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million as of the last business day of our most recently completed second fiscal quarter or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. For so long as we remain a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not smaller reporting companies.

THE OFFERING

Common Stock Offered by Us	Shares of our common stock having an aggregate offering price of up to \$14,024,100.
Manner of Offering	“At the market offering” that may be made from time to time through or to JonesTrading Institutional Services LLC and William Blair & Company, L.L.C., as sale agents or principals. See “Plan of Distribution.”
Use of Proceeds	We intend to use the net proceeds from this offering primarily for general corporate purposes. See “ Use of Proceeds ” on page 13 of this prospectus.
Risk Factors	You should read the “Risk Factors” section of this prospectus and the other information included in, or incorporated by reference in, this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Capital Market Symbol	ALRN

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus and the risk factors in our most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q and in our other filings with the SEC that we make from time to time, which are incorporated by reference in this prospectus, together with other information in this prospectus, the information and documents incorporated by reference in this prospectus or free writing prospectus that we authorize for use in connection with this offering. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to This Offering

Our management has broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds of this offering in ways with which you may not agree or in ways that may not yield a return.

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. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

In addition, the issuance from time to time of shares of our common stock in this offering, or our ability to issue these shares of common stock in this offering, could result in resales of our common stock by our current stockholders concerned about the potential dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

Because we do not anticipate paying any cash dividend on our capital stock for the foreseeable future, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain.

We have never declared nor paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

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

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

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

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different levels of dilution and different outcomes in their investment results. We will have

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discretion, subject to market demand and the terms of the sales agreement, to vary the timing, prices and number of shares sold in this offering. In addition, subject to the final determination by our board of directors or any restrictions we may place in any applicable placement notice, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

The price of our common stock is volatile and may fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is volatile. During the period from June 28, 2017 to June 15, 2022, the closing price of our common stock ranged from a high of \$14.91 per share to a low of \$0.29 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of other companies. As a result of this volatility, our stockholders may not be able to sell their shares at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of ALRN-6924 and any of our other product candidates that may develop;
- regulatory actions with respect to ALRN-6924 or our competitors' products and product candidates;
- the effect of the COVID-19 pandemic on both the healthcare system and the patient population;
- the success of existing or new competitive products or technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- establishment or termination of collaborations for ALRN-6924 or development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to ALRN-6924 or development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other risk factors described in our most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q and in our other filings with the SEC that we make from time to time.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 35,325,189 shares of our common stock are sold at a price of \$0.40 per share pursuant to this prospectus, which was the last reported sale price of our common stock on The Nasdaq Capital Market on June 15, 2022, for aggregate net proceeds of \$13.0 million, after deducting commissions and estimated aggregate offering expenses payable by us, you would experience immediate dilution of \$0.01 per share, representing the difference between our pro forma as adjusted net tangible book value per share as of March 31, 2022, after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options may result in further dilution of your investment. See the section entitled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order 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 public offering price for the shares in this offering. We may sell shares or other securities in any other offering at prices that are less than the price 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 paid by investors in this offering.

Additionally, if and when we sell shares of our common stock to Lincoln Park Capital Fund LLC, or Lincoln Park, pursuant to our purchase agreement, dated September 21, 2020, with Lincoln Park, or the Purchase Agreement, you may experience dilution as a result of such sales.

If we fail to maintain compliance with the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would adversely affect the liquidity of our common stock and our ability to raise additional capital or enter into strategic transactions.

On December 6, 2021, we received a deficiency letter from the Listing Qualifications Department, or the Staff, of the Nasdaq Stock Market, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum \$1.00 per share requirement for continued inclusion on the Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2), or the Bid Price Rule. The deficiency letter does not result in the immediate delisting of our common stock from the Nasdaq Capital Market. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), or the Compliance Period Rule, we were initially provided an initial period of 180 calendar days, or until June 7, 2022 to regain compliance with the Bid Price Rule and on June 7, 2020, we were provided an additional period of 180 calendar days, or until December 5, 2022, or the Compliance Date. If, at any time before the Compliance Date, the bid price for the Company’s common stock closes at \$1.00 or more per share for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that we are in compliance with the Bid Price Rule, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H). As of the date of this prospectus, we have not yet regained compliance with the Bid Price Rule

If we do not comply with the Bid Price Rule by the Compliance Date, then Nasdaq will provide notice to us that our common stock will be delisted. At that time, we may appeal the Staff’s delisting determination to a Nasdaq Listing Qualifications Panel, or the Panel. We expect that its common stock would remain listed pending the Panel’s decision. There can be no assurance that, if we do appeal the Staff’s delisting determination to the Panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Rule, including seeking to effect a reverse stock split. On

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June 15, 2022, we held our 2022 annual meeting of stockholders at which stockholders approved, amongst other things, an amendment to our restated certificate of incorporation to effect a reverse stock split at a ratio of not less than 1-for-5 and not greater than 1-for-25, with the exact ratio to be set within that range at the discretion of our board of directors prior to December 31, 2022 without further approval or authorization of our stockholders and with our board of directors able to elect to abandon such proposed amendment and not effect the reverse stock split authorized by stockholders, in its sole discretion. However, there can be no assurance that we will be able to regain compliance with the Bid Price Rule.

There are many factors that may adversely affect our minimum bid price. Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the Bid Price Rule in the long term. Any potential delisting of our common stock from the Nasdaq Capital Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Capital Market would also make it more difficult for our stockholders to sell our common stock in the public market.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$14,024,100 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with the Agents as a source of financing.

We currently estimate that we will use the net proceeds from this offering primarily for general corporate purposes, which may include working capital and capital expenditures, research and development expenses, including clinical trial costs, general and administrative expenses, potential acquisition of, or investment in, companies, technologies, products or assets that complement our business, and repayment and refinancing of debt.

The amounts and timing of our actual use of the net proceeds may vary significantly depending on numerous factors, including the progress of our research and development efforts, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our programs, and any unforeseen cash needs. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the timing and application of these proceeds.

We may temporarily invest the 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.

DILUTION

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

Our net tangible book value as of March 31, 2022 was approximately \$36.1 million, or \$0.40 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the 90,823,597 shares of common stock outstanding as of March 31, 2022. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering.

After giving effect to the sale of our common stock pursuant to this prospectus in the aggregate amount of \$14,024,100 at an assumed offering price of \$0.40 per share, the last reported sale price of our common stock on The Nasdaq Capital Market on June 15, 2022, and after deducting commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2022 would have been approximately \$49.1 million, or \$0.39 per share. This represents an immediate decrease in net tangible book value of \$0.01 per share to existing stockholders and dilution of \$0.01 per share of as adjusted net tangible book value to new investors based on the assumed average sale price of \$0.40 per share. The following table illustrates this dilution to the investors purchasing shares of common stock in this offering:

Assumed offering price per share		\$ 0.40
Net tangible book value per share as of March 31, 2022	0.40	
Decrease in as adjusted net tangible book value per share attributable to investors purchasing shares of our common stock in this offering	(0.01)	
As adjusted net tangible book value per share after giving effect to this offering		0.39
Dilution per share to investors purchasing shares of our common stock in this offering		\$ 0.01

The information discussed above is illustrative only and will vary based on the actual offering price, the actual number of shares we offer in this offering, and other terms of this offering determined at the time shares of our common stock are sold pursuant to this prospectus. The shares sold in this offering, if any, will be sold from time to time at various prices.

The table does not include:

- 12,935,323 shares of common stock that have been reserved for issuance in connection with warrants outstanding as of March 31, 2022, at an exercise price of \$2.00 per share;
- 11,957,497 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2022, at a weighted-average exercise price of \$1.51 per share; and
- 5,102,686 and 150,000 shares of common stock available for future issuance, as of March 31, 2022, under our 2021 Stock Incentive Plan and our 2017 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans.

In addition, the discussion and table above assumes no additional sales of our common stock under the Purchase Agreement with Lincoln Park, pursuant to which we may sell, at our discretion, up to \$14.5 million of shares of our common stock from time to time during the 36-month term of the Purchase Agreement.

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To the extent that options or warrants outstanding as of March 31, 2022 have been or may be exercised or other shares are issued, investors purchasing shares of our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. 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.

DESCRIPTION OF COMMON STOCK

The following description of our common stock is intended as a summary only and therefore is not complete. This description is based upon, and is qualified by reference to, our certificate of incorporation and our bylaws, each as amended from time to time, and by applicable provisions of Delaware corporate law. You should read our certificate of incorporation and bylaws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 300,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share. The following description of our common stock and provisions of our certificate of incorporation and amended and restated by-laws are summaries and are qualified by reference to our certificate of incorporation and by-laws. Copies of these documents are filed with the SEC as exhibits to our registration statement of which this prospectus forms a part. As of June 15, 2022, 90,823,597 shares of common stock were outstanding and no shares of preferred stock were outstanding.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Any matter other than the election of directors to be voted upon by the stockholders will be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except when a different vote is required by law, our certificate of incorporation or our bylaws.

Dividends. Holders of our common stock are entitled to receive proportionately any dividends as may be declared and paid on our common stock from funds lawfully available therefore as and when determined by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

Liquidation and Dissolution. In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Other Rights. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of 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 and issue in the future. Outstanding shares of our common stock are non-assessable. Holders of our common stock are not, and will not be, subject to any liability as stockholders.

Listing on The Nasdaq Capital Market. Our common stock is listed on The Nasdaq Capital Market under the symbol “ALRN.”

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

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. The issuance of preferred stock could impede the completion of a merger, tender offer, or other takeover attempt.

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Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

Provisions of Our Certificate of Incorporation and Bylaws and Delaware Law That May Have Anti-Takeover Effects

Certain provisions of our certificate of incorporation and bylaws may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. Such provisions could limit the price that certain investors might be willing to pay in the future for shares of our common stock and may limit the ability of stockholders to remove current management or directors or approve transactions that stockholders may deem to be in their best interest and, therefore, could adversely affect the price of our common stock.

Staggered Board; Removal of Directors. Our certificate of incorporation and bylaws divide our board of directors into three classes with staggered three-year terms. In addition, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action by Written Consent; Special Meetings. Our certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Our certificate of incorporation and bylaws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board of directors, our chief executive officer or our board of directors.

Exclusive Forum Selection. Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL or our certificate of incorporation or bylaws, or (4) any action asserting a claim against us governed by the internal affairs doctrine. These choice of forum provisions will not apply to claims arising under the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Advance Notice Requirements for Stockholder Proposals. Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to our board of directors. Stockholders at an annual meeting may consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

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These provisions of Delaware law, our certificate of incorporation and our bylaws may have the effect of deterring hostile takeovers or delaying changes in our control or in our management. These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and in the policies they implement, and to discourage certain types of transactions that may involve an actual or threatened change of our control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Delaware Business Combination Statute. We are subject to Section 203 of the DGCL (“Section 203”), which prohibits a Delaware corporation from engaging in business combinations with an interested stockholder. An interested stockholder is generally defined as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation or any entity or person affiliated with or controlling or controlled by such entity or person (“interested stockholder”). Section 203 provides that an interested stockholder may not engage in business combinations with the corporation for a period of three years after the date that such stockholder 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 stockholder;
- 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 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 (i) by persons who are directors and also officers and (ii) 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; or
- 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 defines business combinations to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, lease, transfer, pledge or other disposition of 10% or more of the assets of the corporation to or with 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; or
- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

PLAN OF DISTRIBUTION

We have entered into a Capital on Demand™ Sales Agreement, or sales agreement, with JonesTrading Institutional Services LLC and William Blair & Company, L.L.C., each an Agent and collectively, the Agents, dated January 29, 2021, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$30,000,000 from time to time through or to the Agents acting as agents or principals. Through the date of this prospectus, we have sold \$10,922,884 of shares of our common stock in accordance with the sales agreement under a prospectus supplement dated January 29, 2021. We currently may offer and sell from and after the date hereof shares of our common stock having an aggregate offering price of up to \$14,024,100 under the sales agreement pursuant to this prospectus.

Sales of our common stock, if any, under this prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415(a)(4) promulgated under the Securities Act.

Each time we wish to issue and sell common stock, we will notify an Agent of the number of shares to be issued, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed such Agent, unless such Agent declines to accept the terms of the notice, such Agent has agreed, subject to the terms and conditions of the sales agreement, to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. We may instruct the Agents not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or the Agents may suspend the offering of shares of common stock being made through the Agents under the sales agreement upon proper notice to the other party.

We will pay the Agents commissions for their services in acting as agents in the sale of our common stock. The Agents will be entitled to compensation at a commission rate of up to 3.0% of the aggregate gross sales price of the shares sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse the Agents for certain specified expenses, including the fees and disbursements of their legal counsel in an amount not to exceed \$35,000, as provided in the sales agreement. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to the Agents under the terms of the sales agreement, will be approximately \$125,000.

Settlement for sales of common stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and the Agents in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of our transfer agent, Computershare Trust Company, N.A. or by such other means as we and the Agents may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, the Agents will be deemed to be “underwriters” within the meaning of the Securities Act and the compensation of the Agents will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to the Agents against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the termination of such sales agreement as permitted therein.

The Agents and their affiliates have in the past and may in the future provide various investment banking and other financial services for us and our affiliates for which services they may in the future receive customary fees.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. We are filing a copy of the sales agreement as an exhibit to the registration statement of which this prospectus forms a part.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Duane Morris LLP, New York, New York, is acting as counsel for the Agents in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.aileronrx.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's internet site.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-38130) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- (1) Our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 28, 2022, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2022 Annual Meeting of Stockholders filed with the SEC on April 29, 2022;
- (2) Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2022, filed with the SEC on May 5, 2022;
- (3) Our Current Reports on Form 8-K filed with the SEC on [January 5, 2022](#), [April 29, 2022](#), [June 7, 2022](#), [June 8, 2022](#) and [June 16, 2022](#); and
- (4) The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on June 23, 2017, as the description therein has been updated and superseded by the description of our capital stock contained in [Exhibit 4.2](#) to our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, as filed with the SEC on March 28, 2022, and including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

Aileron Therapeutics, Inc.
285 Summer Street, Suite 101
Boston, Massachusetts 02210
(617) 995-0900

\$14,024,100



Common Stock

PROSPECTUS

JonesTrading

William Blair

June 16, 2022
