

PROSPECTUS SUPPLEMENT
(To Sales Agreement Prospectus Dated July 15, 2019)



\$4,194,699

Common Stock

We have entered into a Capital on Demand™ Sales Agreement, or the sales agreement, with JonesTrading Institutional Services LLC, or JonesTrading, dated July 1, 2019, relating to the sale of shares of our common stock. Under this prospectus supplement and the accompanying prospectus we may offer and sell shares of our common stock, \$0.001 par value per share, having an aggregate offering price of up to \$4,194,699 from time to time through JonesTrading, acting as our agent, in accordance with the terms of the sales agreement. This prospectus supplement updates and supplements the prior sales agreement prospectus dated July 15, 2019.

Our common stock is listed on The Nasdaq Capital Market under the trading symbol “ALRN.” On September 24, 2020, the last sale price of our common stock as reported on The Nasdaq Capital Market was \$1.26 per share.

As of September 24, 2020, the aggregate market value of our outstanding shares of common stock held by non-affiliates was approximately \$48,404,893, which was calculated based on 31,637,185 shares held by non-affiliates on such date and a price per share of \$1.53 as of a date within 60 days prior to the date of this prospectus supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding one-third of the aggregate market value of our 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 million. During the 12 calendar months prior to and including the date of this prospectus supplement, we have offered and sold \$11,940,265 of securities pursuant to General Instruction I.B.6 of Form S-3.

Sales of our common stock, if any, under this prospectus supplement and the accompanying 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, including sales made directly on or through The Nasdaq Capital Market, the existing trading market for our common stock. JonesTrading is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts, consistent with its 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 JonesTrading 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 S-14 of this prospectus supplement for additional information regarding the compensation to be paid to JonesTrading. In connection with the sale of the common stock on our behalf, JonesTrading will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of JonesTrading will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to JonesTrading 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 S-8 of this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference in this prospectus supplement and the accompanying 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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.



September 25, 2020

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Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and accompanying prospectus are 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 supplement and accompanying prospectus, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$4,194,699, at prices and on terms to be determined by market conditions at the time of the offering in accordance with the sales agreement.

This document is in two parts. 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 this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus and all of the information contained in the documents incorporated by reference herein and therein, 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 JonesTrading has not, authorized anyone to provide you with any information other than that contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus or in any related free writing prospectus filed by us with the SEC. We have not, and JonesTrading has not, authorized anyone to provide you with different information. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus supplement and the accompanying 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 supplement, the accompanying prospectus, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include “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 supplement, the accompanying prospectus or the information incorporated by reference herein or therein, 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 supplement, the accompanying prospectus and the information incorporated by reference herein and therein include, among other things, statements about:

- our plans to develop and commercialize ALRN-6924 and other product candidates, 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 our product candidates;
- 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 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 operations;
- our ability to continue as a going concern; 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

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we make. We have included important factors in the cautionary statements included, or incorporated by reference, in this prospectus supplement and the accompanying 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 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 supplement and the accompanying prospectus, the documents incorporated by reference in herein and therein and the documents that we have filed as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are 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 supplement and the accompanying 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 SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference herein and therein. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus supplement and accompanying prospectus carefully, especially the risks of investing in our common stock discussed under “Risk Factors” beginning on page S-8 of this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus, before making an investment decision.

Aileron Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company that is focused on transforming the experience of chemotherapy for cancer patients, enabling them to fight cancer without the fear or burden of chemotherapy-induced side effects. We are advancing ALRN-6924, our first-in-class dual MDM2/MDMX inhibitor currently in clinical development, to provide a single medicine to protect multiple healthy cell types throughout the body from chemotherapy while ensuring chemotherapy continues to destroy cancer cells.

In addition to potentially reducing or eliminating multiple side effects, ALRN-6924 may also improve patients’ quality of life and help them better tolerate chemotherapy, potentially allowing patients to complete their treatment without dose reductions or delays. Our long-term vision is to provide chemoprotection for patients with p53-mutated cancers, which represents approximately 50% of cancer patients, regardless of cancer type or chemotherapeutic drug.

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 our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2020, which is incorporated by reference herein. These risks include the following:

- We will need substantial additional funding to continue our operations. 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.
- As of August 5, 2020, after considering various risks and uncertainties as prescribed by accounting standard ASU No. 2014-15 (subtopic 205-40), we concluded that there was substantial doubt about our ability to continue as a going concern.
- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We are dependent on the success of our lead 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.
- The COVID-19 pandemic may affect our ability to conduct our ongoing clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this

pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of 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 in combination with other approved therapeutics. If the FDA revokes approval of any such therapeutic, or if safety, efficacy, manufacturing or supply issues arise with any therapeutic 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.
- Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of our product candidates 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 our product candidates or be unable to obtain marketing approval.
- The FDA's acceptance of data from clinical trials outside of the United States is subject to certain conditions, including that the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice; the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful; and that the trials are conducted in compliance with all applicable U.S. laws and regulations
- If serious adverse or unacceptable side effects are identified during the development of our product candidates or we observe limited efficacy of our product candidates, we may need to abandon or limit the development of one or more of our product candidates.
- 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 our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We may enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 and our other stabilized cell-permeating peptide product candidates. If those collaborations are not successful, the development, marketing and/or commercialization of our product candidates that are the subject of such collaborations would be harmed.
- 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.

Corporate Information

We were incorporated under the laws of the State of Delaware on August 6, 2001 under the name Renegade Therapeutics, Inc. We commenced principal operations in 2006 and we subsequently changed our name to

Aileron Therapeutics, Inc. in February 2007. Our principal executive offices are located at 490 Arsenal Way, Suite 210, Watertown, Massachusetts 02472, 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 supplement or the accompanying prospectus. We have included our website address in this prospectus supplement solely as an inactive textual reference.

In this prospectus supplement, 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 supplement are the property of Aileron. The other trademarks, trade names and service marks appearing in this prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement 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 \$4,194,699.
Manner of Offering	“At the market” offering that may be made from time to time through our sales agent, JonesTrading. 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 S-11 of this prospectus supplement
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and the other information included in, or incorporated by reference in, this prospectus supplement and the accompanying prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq 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 supplement and the accompanying 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 supplement and the accompanying prospectus, together with other information in this prospectus supplement and the accompanying prospectus, the information and documents incorporated by reference in this prospectus supplement and the accompanying 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

Sale of a substantial number of shares of our common stock, including by us, could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. Moreover, holders of a substantial number of shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

On September 21, 2020, we entered into a purchase agreement with Lincoln Park Capital Fund, LLC, or Lincoln Park, pursuant to which we may issue and sell from time to time at our sole discretion and subject to certain conditions up to \$15.0 million of shares of our common stock to Lincoln Park from time to time (of which \$500,000 has been purchased to date by Lincoln Park). We have agreed with Lincoln Park to file a registration statement on Form S-1 registering the resale by Lincoln Park of shares sold by us to Lincoln Park pursuant to the purchase agreement.

In connection with our April 2019 private placement, we entered into a registration rights agreement, pursuant to which we registered for resale the shares purchased in the private placement and shares issuable upon exercise of warrants issued in the private placement. In August 2020, we registered for resale certain shares issued in our June 2020 public offering.

We have filed a registration statement registering the sale of shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Sales under these registration statements also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the size of future issuances or the effect, if any, that this offering or any future issuances may have on the market price for our common stock.

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

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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.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

There are limitations on our ability to issue securities under the registration statement of which this prospectus supplement and accompanying prospectus form a part, which may have an adverse effect on our liquidity.

The aggregate market value of our outstanding shares of common stock held by non-affiliates as of the date of this prospectus supplement was \$48,404,893 based on 31,637,185 shares of outstanding common stock that were held by non-affiliates on September 24, 2020, and a per share price of \$1.53 as of a date within 60 days prior to the date of this prospectus supplement. Accordingly, pursuant to General Instruction I.B.6. of Form S-3, in no event may we use a Form S-3 to sell securities with a value exceeding one-third of the aggregate market value of our 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 million. During the twelve calendar months prior to and including the date of this prospectus supplement, we have offered and sold \$11,940,265 million of shares of our common stock pursuant to General Instruction I.B.6. of Form S-3. As a result, so long as we remain subject to General Instruction I.B.6, we are only eligible to offer and sell up to an aggregate of \$4,194,699 of shares of our common stock on Form S-3 pursuant to such instruction through June 2021.

Assuming the sale of the \$4,194,699 of shares of common stock offered pursuant to this prospectus supplement, we will be limited in our ability to sell additional securities on Form S-3, unless and until the market value of our outstanding common stock held by non-affiliates increases substantially. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy, and we could be forced to delay, reduce or eliminate certain research and development programs or any future commercialization efforts.

The trading price of our common stock has been, and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control.

Our stock price is volatile. During the period from June 28, 2017 to September 24, 2020, 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 smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the public offering price and you may lose some or all of your investment.

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

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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 pursuant to our purchase agreement with Lincoln Park, you may experience dilution as a result of such sales.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$4,194,699 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 JonesTrading as a source of financing.

We currently estimate that we will use the net proceeds from this offering primary 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 supplement, 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 this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share 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 June 30, 2020 was approximately \$16.7 million, or \$0.43 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the 39,261,576 shares of common stock outstanding as of June 30, 2020. 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.

Our pro forma net tangible book value as of June 30, 2020 was \$17.1 million, or \$0.43 per share of common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to (i) our issuance and sale of 367,647 shares of our common stock to Lincoln Park in a private placement at a price per share of \$1.36, resulting in net proceeds of \$0.5 million on September 21, 2020 and (ii) our issuance of 220,588 shares of our common stock in a private placement as consideration to Lincoln Park for entering into a purchase agreement with us on September 21, 2020. Pro forma net tangible book value per share represents pro forma net tangible book value divided by 39,849,811 shares of common stock outstanding, after giving effect to the pro forma adjustments described above.

After giving effect to the sale of our common stock pursuant to this prospectus supplement and accompanying prospectus in the aggregate amount of \$4,194,699 at an assumed offering price of \$1.26 per share, the last reported sale price of our common stock on The Nasdaq Capital Market on September 24, 2020 and after deducting commissions and estimated aggregate offering expenses payable by us, our pro forma as adjusted net tangible book value as of June 30, 2020 would have been approximately \$21.1 million, or \$0.49 per share. This represents an immediate increase in net tangible book value of \$0.06 per share to existing stockholders and dilution of \$0.77 per share of pro forma as adjusted net tangible book value to new investors based on the assumed average sale price of \$1.26 per share. The following table illustrates this dilution to the investors purchasing shares of common stock in this offering:

Public offering price per share	\$1.26
Historical net tangible book value per share as of June 30, 2020	\$0.43
Increase per share attributable to the pro forma adjustments described above	—
Pro forma net tangible book value per share as of June 30, 2020	0.43
Increase in as adjusted net tangible book value per share attributable to investors purchasing shares of our common stock in this offering	0.06
Pro forma as adjusted net tangible book value per share after giving effect to this offering	0.49
Dilution per share to investors purchasing shares of our common stock in this offering	<u>\$0.77</u>

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 supplement. 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 June 30, 2020, at an exercise price of \$2.00 per share;
- 4,689,952 shares of common stock issuable upon exercise of stock options outstanding as of June 30, 2020, at a weighted-average exercise price of \$2.45 per share; and

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- 358,416 and 150,000 shares of common stock available for future issuance, as of June 30, 2020, under our 2017 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.

To the extent that options or warrants outstanding as of June 30, 2020 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.

PLAN OF DISTRIBUTION

We have entered into a Capital on Demand™ Sales Agreement, or sales agreement, with JonesTrading, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$15,000,000 from time to time through JonesTrading acting as our sales agent. Prior to the date of this prospectus supplement, we have issued and sold an aggregate of 1,263,059 shares of common stock for gross proceeds of \$762,000 under the sales agreement. Sales of our common stock, if any, under this prospectus supplement and the accompanying 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. We may not sell shares of common stock having an aggregate offering price in excess of \$4,194,699 under this prospectus supplement.

Each time we wish to issue and sell common stock, we will notify JonesTrading 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 JonesTrading, unless JonesTrading declines to accept the terms of the notice, JonesTrading 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 JonesTrading 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 JonesTrading may suspend the offering of shares of common stock being made through JonesTrading under the sales agreement upon proper notice to the other party.

We will pay JonesTrading commissions for its services in acting as agent in the sale of our common stock. JonesTrading will be entitled to compensation at a commission rate of up to 3.0% of the aggregate gross sales price of the shares sold. JonesTrading may effect sales to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from JonesTrading and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal. 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 JonesTrading for certain specified expenses, including the fees and disbursements of its 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 JonesTrading under the terms of the sales agreement, will be approximately \$250,000.

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 JonesTrading 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 supplement and the accompanying prospectus will be settled through the facilities of our transfer agent, Computershare Trust Company, N.A. or by such other means as we and JonesTrading 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, JonesTrading will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of JonesTrading will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to JonesTrading 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.

JonesTrading and its affiliates 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 filed a copy of the sales agreement as an exhibit to the registration statement of which this prospectus supplement and accompanying prospectus form 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 JonesTrading 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, 2019 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) 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 supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying 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 supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate 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), 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, 2019, filed with the SEC on March 30, 2020, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2020 Annual Meeting of Stockholders filed with the SEC on April 28, 2020;
- (2) Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2020 and June 30, 2020, filed with the SEC on [May 11, 2020](#) and [August 5, 2020](#), respectively;
- (3) Our Current Reports on Form 8-K filed with the SEC on [April 22, 2020](#) (Item 8.01 only), [June 1, 2020](#) (Item 8.01 only), [June 5, 2020](#), [June 11, 2020](#), [June 18, 2020](#), [September 14, 2020](#) and [September 22, 2020](#); and
- (4) The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on June 23, 2017, 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.
490 Arsenal Way, Suite 210
Watertown, Massachusetts 02472
(617) 995-0900

PROSPECTUS



\$13,265,506

Common Stock

We have entered into a Capital on Demand™ Sales Agreement, or the sales agreement, with JonesTrading Institutional Services LLC, or JonesTrading, dated July 1, 2019, relating to the sale of shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, under this prospectus we may offer and sell shares of our common stock, \$0.001 par value per share, having an aggregate offering price of up to \$13,265,506 from time to time through JonesTrading, acting as our agent.

Our common stock is listed on The Nasdaq Global Market under the trading symbol "ALRN." On June 28, 2019, the last sale price of our common stock as reported on The Nasdaq Global Market was \$0.72 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, including sales made directly on or through The Nasdaq Global Market, the existing trading market for our common stock. JonesTrading is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts, consistent with its 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 JonesTrading 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 SA-14 for additional information regarding the compensation to be paid to JonesTrading. In connection with the sale of the common stock on our behalf, JonesTrading will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of JonesTrading will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to JonesTrading 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 SA-7 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 purchase 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.



July 15, 2019

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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 \$13,265,506, at prices and on terms to be determined by market conditions at the time of the offering in accordance with the sales agreement. The \$13,265,506 of shares of our common stock that may be sold under this prospectus are included in the \$150,000,000 of shares of common stock that may be sold under the registration statement.

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 in this prospectus, 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.

To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference in this prospectus, on the other hand, you should rely on the information in this prospectus, 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 this 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 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 JonesTrading has not, authorized anyone to provide you with any information other than that contained in or incorporated by reference in this prospectus, any prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not, and JonesTrading has 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, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the documents incorporated by reference herein 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, 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 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 contained in this prospectus and incorporated by reference herein include, among other things, statements about:

- our plans to develop and commercialize ALRN-6924 and other product candidates, 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 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 our product candidates;
- 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 product candidates;
- potential benefits of any future collaboration;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

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 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.

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You should read this prospectus, the documents incorporated by reference in this prospectus 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.

This prospectus incorporates by reference certain statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the documents we incorporate by reference. 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 SA-7 of this prospectus, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.

Aileron Therapeutics, Inc.

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of stabilized cell-permeating alpha-helical peptides to address intracellular targets in oncology and other therapeutic areas. Our lead product candidate, ALRN-6924, is a cell-permeating peptide that disrupts the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers. Based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, we believe that there may be a significant opportunity to develop ALRN-6924 in combination with other drugs for a wide variety of cancers.

Our clinical development program for ALRN-6924 is currently focused on our ongoing Phase 2a clinical trial of the combination of ALRN-6924 and palbociclib (Ibrance), marketed by Pfizer, Inc., for the treatment of MDM2-amplified advanced solid tumors and our planned Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent, to protect against chemotherapy-induced bone marrow toxicity. Our first planned clinical trial to assess the myelopreservation opportunity will be in small cell lung cancer patients who will be treated with the chemotherapy topotecan.

We believe that by using our proprietary stabilized cell-permeating peptide platform, we can develop first-in-class molecules, like ALRN-6924, that contain a novel set of properties. As such, our stabilized cell-permeating peptide drugs may be able to address historically undruggable targets, such as intracellular protein-protein interactions like p53 and MDM2/MDMX, that underlie many diseases with high unmet medical need. We believe that stabilized cell-permeating peptide therapeutics have the potential to become a major class of drugs, like small molecules and monoclonal antibodies, for oncology and other therapeutic areas, and may significantly improve treatment paradigms and clinical outcomes for patients.

Corporate Information

We were incorporated under the laws of the State of Delaware on August 6, 2001 under the name Renegade Therapeutics, Inc. We commenced principal operations in 2006 and we subsequently changed our name to Aileron Therapeutics, Inc. in February 2007. Our principal executive offices are located at 490 Arsenal Way, Suite 210, Watertown, Massachusetts 02472, 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 for up to five years from the date of the closing of our initial public offering, 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 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 company.

THE OFFERING

Common Stock Offered by Us	Shares of our common stock having an aggregate offering price of up to \$13,265,506.
Manner of Offering	“At the market” offering that may be made from time to time through our sales agent, JonesTrading. 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.”
Risk Factors	You should read the “Risk Factors” section of this prospectus and the other information included in, or incorporated by reference into, this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global 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, and in any prospectus supplement 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

Sale of a substantial number of shares of our common stock, including by us, could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. Moreover, holders of a substantial number of shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

We have filed a registration statement registering the sale of shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the size of future issuances or the effect, if any, that this offering or any future issuances may have on the market price for our common stock.

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.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$13,265,506 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 JonesTrading as a source of financing.

We currently estimate that we will use the net proceeds from this offering primary 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.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, capital requirements, business prospects and other factors our board of directors may deem relevant.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital 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 150,000,000 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 capital 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 May 31, 2019, 26,713,617 shares of common stock were outstanding and no shares of preferred stock were outstanding.

Common Stock

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. Other matters shall 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 as otherwise disclosed below. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of 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. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

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 purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock.

Registration Rights

Resale Registration Rights

In connection with the March 2019 private placement, we entered into a registration rights agreement with the purchasers under which we agreed to file a registration statement covering the resale of the 11,838,582 shares of common stock issued in the March 2019 private placement, 14,032,064 shares of common stock issuable upon exercise of the warrants issued in the March 2019 private placement and 178,106 shares of common stock held by one of the selling stockholders as of the date of execution of the registration rights agreement.

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Investor Rights Agreement

We are a party to an investor rights agreement with certain former holders of our preferred stock that provides such holders with the right to require us to register their shares under the Securities Act under specified circumstances as described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act.

Demand Registration Rights

Subject to specified limitations set forth in the investor rights agreement, at any time the holder or holders of at least thirty percent of senior preferred registrable securities, as defined in the investor rights agreement, acting together, may demand in writing that we register at least twenty percent of the outstanding registrable securities, as defined in the investor rights agreement, under the Securities Act or any lesser percentage so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public of least \$10.0 million. We are not obligated to file a registration statement pursuant to this demand provision on more than two occasions, subject to specified exceptions.

In addition, at any time when we are eligible to file a registration statement on Form S-3 under the Securities Act, subject to specified limitations, a holder or holders of the senior preferred registrable securities may demand in writing that we register on Form S-3 all or part of the registrable securities held by them so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public of least \$1.0 million

Incidental Registration Rights

If, at any time, we propose to file a registration statement to register any of our common stock under the Securities Act, either for our own account or for the account of any of our stockholders that are not holders of registrable securities, and on a form that would also permit the registration of registrable securities, the holders of our registrable securities are entitled to notice of registration and, subject to specified exceptions, we will be required to use our best efforts to register the registrable securities then held by them that they request that we register.

Expenses

Pursuant to the investor rights agreement, we are required to pay all registration expenses, including registration fees, printing expenses, fees and disbursements of our counsel and accountants and reasonable fees and disbursements not to exceed \$30,000 of one counsel representing the selling stockholders, other than any underwriting discounts and commissions, related to any demand or incidental registration.

The investor rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover Effects of Delaware Law and Our Charter and Bylaws

Delaware law contains, our certificate of incorporation and our 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.

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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, our chief executive officer or our board of directors.

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.

Delaware Business Combination Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Certificate of Incorporation and Bylaws

The General Corporation Law of the State of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or 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 any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above under "—Staggered Board; Removal of Directors" and "—Stockholder Action by Written Consent; Special Meetings."

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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 behalf of our company, (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 our stockholders, (3) any action asserting a claim against our company arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or (4) any action asserting a claim against our company governed by the internal affairs doctrine. 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.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of the Nasdaq Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Stock Options and Warrants

As of May 31, 2019, we had outstanding warrants to purchase 12,935,323 shares of our common stock at an exercise price of \$2.00 per share and outstanding warrants to purchase 1,096,741 shares of our common stock at an exercise price of \$0.01 per share.

As of May 31, 2019, we had outstanding options to purchase 3,853,304 shares of our common stock at a weighted average price \$4.65 per share. The stock options expire 10 years after their grant date.

Listing on the Nasdaq Global Market

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

Transfer Agent and Registrar

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

PLAN OF DISTRIBUTION

We have entered into a Capital on Demand™ Sales Agreement, or sales agreement, with JonesTrading, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$13,265,506 from time to time through JonesTrading acting as our sales agent. 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 JonesTrading 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 JonesTrading, unless JonesTrading declines to accept the terms of the notice, JonesTrading 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 JonesTrading 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 JonesTrading may suspend the offering of shares of common stock being made through JonesTrading under the sales agreement upon proper notice to the other party.

We will pay JonesTrading commissions for its services in acting as agent in the sale of our common stock. JonesTrading will be entitled to compensation at a commission rate of up to 3.0% of the aggregate gross sales price of the shares sold. JonesTrading may effect sales to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from JonesTrading and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal. 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 JonesTrading for certain specified expenses, including the fees and disbursements of its 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 JonesTrading under the terms of the sales agreement, will be approximately \$250,000.

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 JonesTrading 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 JonesTrading 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, JonesTrading will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of JonesTrading will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to JonesTrading 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.

JonesTrading and its affiliates 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, Newark, New Jersey, is acting as counsel for JonesTrading 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, 2018 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) 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 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 <https://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 we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

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 Securities Exchange Act of 1934, as amended, or 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.

- Our Annual Report on Form 10-K and Form 10-K/A for the year ended December 31, 2018, filed with the SEC on [March 29, 2019](#) and [May 8, 2019](#), respectively, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2019 Annual Meeting of Stockholders 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 Current Reports on Form 8-K filed with the SEC on [March 1, 2019](#), [April 1, 2019](#), [April 3, 2019](#), [June 5, 2019](#), [June 20, 2019](#) and [June 24, 2019](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on June 23, 2017, 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.
490 Arsenal Way, Suite 210
Watertown, Massachusetts 02472
(617) 995-0900

\$4,194,699



Common Stock

Prospectus Supplement



September 25, 2020
