

PROSPECTUS SUPPLEMENT
(To Prospectus dated July 8, 2020)

748,744 Shares of Common Stock
Pre-Funded Warrants to Purchase up to 2,632,898 Shares of Common Stock
Warrants to Purchase up to 4,227,052 Shares of Common Stock



We are offering 748,744 shares of our common stock, par value \$0.001 per share, pre-funded warrants to purchase 2,632,898 shares of common stock, and accompanying common warrants to purchase up to 4,227,052 shares of our common stock, or the common warrants, at a combined offering price of \$2.22625 per share of common stock and accompanying common warrant and \$2.22615 per pre-funded warrant and accompanying common warrant in a registered direct offering directly to an investor pursuant to this prospectus supplement and the accompanying prospectus and a securities purchase agreement with such investor. The common warrants have an exercise price per share equal to \$2.07, and will be exercisable following the six-month anniversary of the closing of this offering, and will expire on the six year anniversary of the closing of this offering. Each common warrant entitles the holder to purchase 1.25 shares of common stock, we have therefore allocated \$0.15625 of the combined offering price to each common warrant. We are also offering the shares of our common stock that are issuable from time to time upon exercise of the common warrants.

We are also offering the pre-funded warrants to purchase shares of common stock (and the shares of common stock issuable from time to time upon exercise of the pre-funded warrants), in lieu of shares of common stock to the investor. Each pre-funded warrant will be exercisable for one share of common stock at an exercise price of \$0.0001 per share of common stock. The offering price per pre-funded warrant and accompanying common warrant, is equal to the combined offering price per share of common stock and accompanying common warrant of \$2.22625 less \$0.0001. Each pre-funded warrant will be exercisable upon issuance and will expire when exercised in full.

The shares of our common stock and pre-funded warrants, as the case may be, each with the accompanying common warrants, can only be purchased together in this offering, but will be issued separately and will be immediately separable upon issuance. We refer to the shares of common stock issued in this offering, the pre-funded warrants and the accompanying common warrants to purchase common stock issued in this offering, collectively, as the securities. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the common warrants and the pre-funded warrants sold in this offering.

Our common stock is listed on The Nasdaq Global Market under the symbol "ACRX." On December 23, 2022, the last reported sale price of our common stock on The Nasdaq Global Market was \$2.07 per share. There is no established trading market for any of the common warrants and we do not expect a market to develop. We do not intend to apply for a listing for the pre-funded warrants or the common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants or the common warrants will be limited.

We engaged Cantor Fitzgerald & Co. to act as our sole placement agent, or the Placement Agent, in connection with this offering. The Placement Agent is not purchasing the securities offered by us in this offering and is not required to arrange the purchase or sale of any specific number or dollar amount of securities.

Investing in our securities involves a high degree of risk. Please read the section titled "Risk Factors" beginning on page S-6 of this prospectus supplement, on page 5 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

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

	PER SHARE AND ACCOMPANYING COMMON WARRANT	PER PRE- FUNDED WARRANT AND ACCOMPANYING COMMON WARRANT	TOTAL
Offering price	\$ 2.22625	\$ 2.22615	\$ 7,528,117
Placement Agent fees ⁽¹⁾	\$ 0.15584	\$ 0.15583	\$ 526,968
Proceeds to AcelRx Pharmaceuticals, Inc. before expenses ⁽²⁾	\$ 2.07041	\$ 2.07032	\$ 7,001,149

(1) See the section titled "Plan of Distribution" for additional disclosure regarding the Placement Agent fees.

(2) The above summary of offering proceeds does not give effect to any proceeds from the exercise of the pre-funded warrants or common warrants being issued in this offering.

Delivery of the shares of common stock, the pre-funded warrants and accompanying common warrants is expected to be made on or about December 29, 2022.

Sole Placement Agent
Cantor

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock, pre-funded warrants and common warrants and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated July 8, 2020, including the documents incorporated by reference therein, provides more general information that may not relate to this offering. 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, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date (for example, a document incorporated by reference in the accompanying prospectus), the statement in the document having the later date modifies or supersedes the earlier statement.

Before buying any of the common stock, pre-funded warrants and common warrants that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described in the sections titled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell or soliciting an offer to buy our common stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement, the accompanying prospectus and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement titled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

All references in this prospectus supplement and the accompanying prospectus to “AcelRx,” “AcelRx Pharmaceuticals,” “the company,” “we,” “us,” “our” or similar references refer to AcelRx Pharmaceuticals, Inc. and its wholly owned subsidiary, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement and the accompanying prospectus include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus supplement or the accompanying prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. For a more complete understanding of the company and this offering, you should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement, the accompanying prospectus and the information included in any free writing prospectus that we have authorized for use in connection with this offering. If you invest in our securities, you are assuming a high degree of risk. See “Risk Factors” beginning on page S-6 of this prospectus supplement, on page 5 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. DSUVIA® (known as DZUVEO® in Europe) is focused on the treatment of acute pain, and utilizes sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. In November 2018, the U.S. Food and Drug Administration, or FDA, approved DSUVIA for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In June 2018, the European Commission granted marketing approval of DZUVEO for the management of acute moderate to severe pain in adults in medically monitored settings. DSUVIA is a 30 mcg single-strength solid dosage form of sufentanil administered sublingually via a single-dose applicator by healthcare professionals. Sufentanil is an opioid analgesic currently also approved for IV and epidural anesthesia and analgesia. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration. Recent published studies have demonstrated that when administering DSUVIA there was an overall greater than 50% reduction in morphine milligram equivalents, or MME, administered, with an 80% reduction in MMEs administered post-op in the institution versus the control group. Near the end of 2021, we refocused our DSUVIA commercial efforts on procedural suites, and specifically in specialty settings such as plastic and cosmetic surgery, ear, nose and throat, and oral/maxillofacial surgery. As a result, procedural suites sales volume contribution to commercial sales, excluding sales to the Department of Defense, increased from 28% in the first quarter of 2021 to 74% in the third quarter of 2022, even with a significantly reduced commercial organization over this time period. As a result, we are seeing an increased interest from large national accounts in these specialty areas. We believe that the uptake of DSUVIA will be maximized through a partner with a larger commercial infrastructure and, as such, we are in discussions with potential partners that can execute a more robust commercial plan to support DSUVIA sales expansion, while further reducing our operating costs. The ultimate structure of a potential transaction with a third party may take multiple forms, however, our interest remains in participating in the potential long-term value created by a new potential partner.

In July 2021, we entered into a License and Commercialization Agreement, with Laboratoire Aguettant, or Aguettant, for Aguettant to commercialize DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom. In July 2021, we also entered into a separate License and Commercialization Agreement, or DZUVEO Agreement, with Aguettant pursuant to which we obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States (i) an ephedrine pre-filled syringe containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection and (ii) a phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine hydrochloride for injection. Aguettant pre-filled syringes are focused on delivering commonly used medicines safely and efficiently. Perioperative medication errors continue, and pre-filled syringes are preferred for improving safety while containing costs.

In January 2022, we acquired Lowell Therapeutics, Inc., or Lowell, a privately held company, and, as a result, we acquired Niyad™, a regional anticoagulant for the extracorporeal circuit, such as the dialysis circuit during continuous renal replacement therapy, or CRRT, for acute kidney injury patients in the hospital, and for chronic kidney disease patients undergoing intermittent hemodialysis, or IHD, in dialysis centers. We plan to study Niyad, which has received Breakthrough Device Designation status from the FDA and an ICD-10 procedural code from the U.S. Centers for Medicare & Medicaid Services, under an investigational device exemption. While not approved for commercial use in the United States, the active drug component of Niyad, nafamostat, has been approved in Japan and South Korea as a regional anticoagulant for the dialysis circuit, disseminated intravascular coagulation and acute pancreatitis. Niyad is a lyophilized formulation of nafamostat, a broad-spectrum, synthetic serine protease inhibitor, which has a half-life of 8 minutes, with anticoagulant, anti-inflammatory and potential anti-viral activities. We believe Niyad's peak sales potential exceeds \$200 million annually in the United States for its use in CRRT and IHD, based on an estimated available market of 500,000 patients undergoing CRRT of \$575 million, and an estimated available market of 350,000 patients undergoing IHD of \$3.5 billion. If approved in the United States, Niyad would be the only FDA-approved regional anticoagulant for the extracorporeal circuit. Exposure of blood to the dialysis filter causes clotting, which is a major limitation to care during CRRT, as it leads to inefficient dialysis, causes blood loss and depletes limited resources. Circuit clotting is the most frequent cause of therapy interruption in circuit dialysis.

The current market landscape for anticoagulants used during CRRT includes heparin, a systemic anticoagulant used for anticoagulation of the patient and the circuit, and citrate, a regional anticoagulant used for anticoagulation of the circuit only and authorized under an Emergency Use Authorization, or EUA, in the United States. No anticoagulant is used in CRRT in 29% of cases, the default decision when physicians are concerned with the safety of heparin or citrate. According to our market research, when not using an anticoagulant for CRRT, frequent filter clogging was the most common issue, with 20-25% stating increased transfusions were needed. Niyad is much easier to administer than citrate, which has not received full FDA approval, and Niyad may be used in patients with liver failure whereas citrate is contraindicated. Our market research indicated physicians did not use citrate because of a number of concerns, including hypocalcemia, citrate lock, nursing time required to administer and monitor and calcium shortages, among other concerns.

Niyad is designed to provide short half-life titratable, regional anticoagulation without the shortcomings of heparin or citrate. In a 1991 clinical study undertaken by Ohtake Y, et. al. to elucidate the relationship between various anticoagulants and the incidences of bleeding complication during continuous hemofiltration, or CHF, and continuous hemodiafiltration, or CHDF, the incidence of bleeding during CHF and/or CDHF with heparin was 66.7% as compared to 4.3% with nafamostat. We are evaluating nafamostat as an anticoagulant for the extracorporeal circuit. The FDA has provided guidance for a single registrational study and endpoints for Niyad. The study will be a prospective, randomized, placebo-controlled study at up to 10 clinical sites of 160 adult patients who cannot tolerate heparin or are at risk for bleeding. The primary endpoint will be the mean post-filter activated clotting time over the first 24 hours versus placebo. We believe that decades of nafamostat studies on anticoagulation of the extracorporeal circuit can support Niyad development. An EUA submission for Niyad is pending.

In addition, we acquired LTX-608, a proprietary nafamostat formulation for direct IV infusion that we intend to develop for the treatment of acute respiratory distress syndrome, or ARDS, and disseminated intravascular coagulation, or DIC, an indication for which nafamostat is approved in Japan and South Korea.

Nafamostat has the potential for six years of data exclusivity upon FDA approval of a premarket approval application prior to the issuance of pending patents. We currently have a patent pending for Niyad claims drawn to priming of the extracorporeal circuit and blood flow when using nafamostat and multiple LTX-608 patents pending including claims drawn to use of nafamostat in DIC, as an antiviral agent (e.g., COVID treatment), in ARDS and other conditions.

To extend our financial resources, we have realigned our cost structure from a focus on commercialization to a focus on advancing our recently acquired late-stage development pipeline, namely the pre-filled syringes and Niyad product candidates. This realignment has generated potential annual savings of approximately \$9 million and we continue to assess how we can further reduce our annual expenses. As a result, we have also decided to not focus any development resources on Zalviso® in the United States and do not expect to resubmit the Zalviso new drug application in the foreseeable future. In addition, due to the termination of our agreements with Gr✓nenthal GmnH for Zalviso in Europe and the related withdrawal of our Marketing Authorization in Europe in July 2022, we do not expect any revenues from Zalviso in Europe in the foreseeable future. Accordingly, we recorded a non-cash impairment charge of \$4.9 million for the nine months ended September 30, 2022 related to Zalviso property and equipment. Future development of Zalviso will be contingent upon identification of a strategic partner.

Corporate Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005 and changed our name to AcelRx Pharmaceuticals, Inc. on January 6, 2006. Our principal executive offices are located at 25821 Industrial Boulevard, Suite 400, Hayward, California 94545, and our telephone number is (650) 216-3500. Our website address is www.acelrx.com. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

THE OFFERING

Common stock offered by us	748,744 shares.
Pre-funded warrants offered by us	We are also offering 2,632,898 pre-funded warrants to purchase shares of common stock, in lieu of shares of common stock that would otherwise result in any such purchaser's beneficial ownership exceeding 9.99% of our outstanding common stock. Each pre-funded warrant is exercisable for one share of our common stock. The purchase price of each pre-funded warrant and each accompanying common warrant (as described below) is equal to the price at which a share of common stock and accompanying common warrant is being sold in this offering, minus \$0.0001 per share, and the exercise price of each pre-funded warrant is \$0.0001 per share. The pre-funded warrants are exercisable immediately and may be exercised at any time until all of the pre-funded warrants are exercised in full. This offering also relates to the shares of common stock issuable upon exercise of any pre-funded warrants sold in this offering. There is no established trading market for the pre-funded warrants and we do not expect a market to develop. We do not intend to apply for a listing for any of the pre-funded warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See the section titled "Description of Securities We Are Offering" for a discussion on the terms of the pre-funded warrants.
Common warrants offered by us	We are also offering common warrants to purchase an aggregate of 4,227,052 shares of our common stock. Each share of common stock and each pre-funded warrant is being sold together with a common warrant to purchase 1.25 shares of our common stock. The exercise price of each common warrant will be \$2.07 per whole share. Each common warrant will be exercisable following the six-month anniversary of the closing date of this offering and will expire six years from the date of issuance. This prospectus supplement also relates to the offering of the common stock issuable upon exercise of such common warrants. There is no established trading market for the common warrants and we do not expect a market to develop. We do not intend to apply for a listing for any of the common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the common warrants will be limited. See the section titled "Description of Securities We Are Offering" for a discussion on the terms of the common warrants.
Common stock to be outstanding immediately after this offering	8,154,710 shares, assuming no exercise of any pre-funded warrants or common warrants issued in this offering. Assuming all the pre-funded warrants were immediately exercised, there would be 10,787,608 shares of common stock outstanding after this offering.

Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting Placement Agent fees and paying estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants issued in this offering, will be approximately \$6.7 million. We intend to use the net proceeds from this offering for working capital and general corporate purposes, including general and administrative expenses, research and development expenses and capital expenditures. See the section titled "Use of Proceeds" on page S-11 of this prospectus supplement.
Risk factors	An investment in our securities involves a high degree of risk. See the section titled "Risk Factors" beginning on page S-6 of this prospectus supplement, on page 5 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.
The Nasdaq Global Market symbol	Our common stock is listed on The Nasdaq Global Market under the symbol "ACRX." We do not intend to apply for listing of the pre-funded warrants or the common warrants on any securities exchange or other nationally recognized trading system.

The number of shares of common stock outstanding immediately after this offering is based on 7,405,966 shares of common stock outstanding as of September 30, 2022, and excludes as of such date:

- 964,983 shares of common stock issuable upon the exercise of warrants, with a weighted average exercise price of \$19.00 per share;
- 672,255 shares of common stock issuable upon the exercise of options, with a weighted average exercise price of \$54.06 per share;
- 86,678 shares of common stock issuable upon the vesting of restricted stock units;
- 61,053 shares of common stock issuable upon the exercise of share price performance options, with a weighted average exercise price of \$37.60 per share; and
- an aggregate of 543,525 shares of common stock reserved for future issuance under our Amended and Restated 2020 Equity Incentive Plan and Amended and Restated 2011 Employee Stock Purchase Plan.

Upon the closing of this offering we have agreed to amend a warrant held by Armistice Capital Master Fund Ltd. to purchase up to 750,000 shares of common stock to reduce the exercise price to \$2.07 per share. This warrant, as amended, will be exercisable following the six-month anniversary of the closing of this offering, and will expire on the six year anniversary of the closing of this offering. Upon the closing of this offering, the exercise price of a warrant to purchase up to 81,150 shares of common stock held by Lincoln Park Capital Fund, LLC will automatically be reduced to \$2.07 per share. No other terms of this warrant will be affected by this offering.

In addition, the number of shares outstanding immediately after this offering excludes additional shares of common stock that we may sell pursuant to a Controlled Equity OfferingSM Sales Agreement that we entered into with Cantor Fitzgerald & Co. in May 2019. Under the Controlled Equity OfferingSM Sales Agreement, we may issue and sell shares of our common stock from time to time in such amounts as we may determine, subject to certain limitations contained in the Controlled Equity OfferingSM Sales Agreement and under applicable securities laws. As of the date of this prospectus supplement, we may sell up to \$35.9 million of our common stock pursuant to the Controlled Equity OfferingSM Sales Agreement after the expiration of the 90-day lock-up period applicable to us and described in the section titled "Plan of Distribution."

Except as otherwise noted, all the information in this prospectus supplement further assumes:

- no exercise of the pre-funded warrants and common warrants issued in this offering; and
- no exercise of outstanding stock options or warrants, or settlement of outstanding restricted stock units.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks described below together with the other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flows could be harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Risks Relating to this Offering

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

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

There is no public market for the pre-funded warrants or common warrants being offered in this offering.

There is no established public trading market for the pre-funded warrants or the common warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants or the common warrants on any securities exchange or nationally recognized trading system, including The Nasdaq Global Market. Without an active market, the liquidity of the pre-funded warrants and the common warrants will be limited.

A holder of pre-funded warrants and common warrants purchased in this offering will have no rights as a common stockholder until such holder exercises its pre-funded warrants or common warrants and acquires shares of our common stock, except as set forth in such pre-funded warrants or common warrants.

Until investors acquire shares of our common stock upon exercise of the pre-funded warrants or the common warrants purchased in this offering, such warrants will not provide investors any rights as a common stockholder, except as set forth in the pre-funded warrants or the common warrants. Upon exercise of the pre-funded warrants or the common warrants, the holder will be entitled to exercise the rights of a common shareholder only as to matters for which the record date occurs after the exercise date.

The pre-funded warrants and the common warrants are speculative in nature.

The pre-funded warrants and the common warrants do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price for a limited period of time. Specifically, commencing on the date of issuance, holders of the pre-funded warrants may acquire the common stock issuable upon exercise of such warrants at an exercise price of \$0.0001 per share of common stock, and following the six-month anniversary of the closing date of this offering, holders of the common warrants may acquire the common stock issuable upon exercise of such common warrants at an exercise price of \$2.07 per share. Moreover, following this offering, the market value of the pre-funded warrants and the common warrants is uncertain and there can be no assurance that the market value of the pre-funded warrants or the common warrants will equal or exceed their offering price. There can be no assurance that the market price of the common stock will ever equal or exceed the exercise price of the pre-funded warrants or the common warrants, and consequently, whether it will ever be profitable for holders of the pre-funded warrants to exercise the pre-funded warrants or the holders of the common warrants to exercise the common warrants.

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, including pursuant to the Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co., or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

In addition, we have a significant number of outstanding stock options, restricted stock units and warrants exercisable into shares of our common stock. To the extent that outstanding stock options or warrants are exercised, or restricted stock units vest and settle, investors purchasing our securities in this offering may experience further dilution in the future. Furthermore, a significant portion of our total outstanding shares are eligible to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock in a negative manner, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

Provisions of the common warrants could discourage an acquisition of us by a third party.

Certain provisions of the common warrants could make it more difficult or expensive for a third party to acquire us. The common warrants prohibit us from engaging in certain transactions constituting “fundamental transactions” unless, among other things, the surviving entity assumes our obligations under the common warrants. Further, the common warrants provide that, in the event of certain transactions constituting “fundamental transactions,” with some exceptions, holders of such warrants will have the right, at their option, to receive from us or a successor entity the same type or form of consideration (and in the same proportion) that is being offered and paid to the holders of our common stock in the fundamental transaction in the amount of the Black-Scholes value (as described in such common warrants) of the unexercised portion of the applicable common warrants on the date of the consummation of the fundamental transaction. These and other provisions of the common warrants could prevent or deter a third party from acquiring us even where the acquisition could be beneficial to the holders of our common stock.

The common warrants have certain anti-dilutive rights.

The common warrants include full ratchet anti-dilutive rights in the event any shares of common stock or other equity or equity equivalent securities payable in common stock are granted, issued or sold (or we enter into any agreement to grant, issue or sell), or in accordance with the terms of the applicable warrants, are deemed to have granted, issued or sold, in each case, at a price less than the exercise price, which automatically decreases the exercise price of the common warrants upon the occurrence of such event, as described in greater detail in the applicable warrants, subject to a minimum exercise price of \$1.50 per share. Such anti-dilution rights, if triggered, could result in a significant decrease in the exercise price of the common warrants, which could result in significant dilution to existing shareholders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering 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. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- the accuracy of our estimates regarding the sufficiency of our cash resources, future revenues, expenses, capital requirements and needs for additional financing, and our ability to obtain additional financing and continue as a going concern;
- our ability to manage our operating costs and reduce our cash burn;
- the uncertainties and impact arising from the worldwide COVID-19 pandemic, including restrictions on the ability of our sales force to contact and communicate with target customers and resulting delays and challenges to our commercial sales of DSUVIA;
- our success in commercializing DSUVIA in the United States, including the marketing, sales and distribution of the product, whether alone or with contract sales organizations and other collaborators;
- our ability to identify and secure potential partnerships with a third party having sufficient commercial resources to develop and potentially grow the DSUVIA franchise;
- our ability to satisfactorily comply with FDA regulations concerning the advertising and promotion of DSUVIA;
- the size and growth potential of the markets for DSUVIA, and our other product candidates in the United States, and our ability to serve those markets;
- our ability to maintain regulatory approval of DSUVIA in the United States, including effective management of and compliance with the DSUVIA Risk Evaluation and Mitigation Strategies program;
- acceptance of DSUVIA by physicians, patients and the healthcare community, including the acceptance of pricing and placement of DSUVIA on payers’ formularies;
- our ability to realize the expected benefits and potential value created by the acquisition of Lowell for our stockholders on a timely basis or at all;
- our ability to develop, file for and obtain regulatory approval for, and then successfully launch and commercialize products and product candidates that we have in-licensed or acquired;
- our ability to file for and secure a potential EUA for our lead nafamostat product candidate, Niyad;
- our ability to develop sales and marketing capabilities in a timely fashion, whether alone through recruiting qualified employees, by engaging a contract sales organization, or with potential future collaborators;
- successfully establishing and maintaining commercial manufacturing and supply chain relationships with third-party service providers;
- our ability to manage effectively, and the impact of any costs associated with potential governmental investigations, inquiries, regulatory actions or lawsuits that may be, or have been, brought against us;
- continued demonstration of an acceptable safety profile of DSUVIA;
- effectively competing with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;

- our ability to manufacture and supply DZUVEO to Aguettant in accordance with their forecasts and the DZUVEO Agreement, including compliance with any import/export controls or restrictions;
- the status of the DZUVEO Agreement or any other future potential collaborations, including potential milestones and revenue share payments under the DZUVEO Agreement;
- Aguettant’s ability to successfully launch and commercialize DZUVEO in the European Union;
- our, or Aguettant’s, ability to maintain regulatory approval of DZUVEO in the European Union;
- our ability to obtain adequate government or third-party payer reimbursement;
- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- our ability to identify and secure potential commercial partners to develop and then commercialize our developmental product candidates;
- our ability to successfully retain our key commercial, scientific, engineering, medical or management personnel and hire new personnel as needed;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers, including any supply chain impacts or work limitations;
- the success of competing therapies that are or become available;
- our liquidity and capital resources; and
- our ability to obtain and maintain intellectual property protection for our approved products and product candidates.

These risks are not exhaustive. Other sections of this prospectus supplement may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

All statements other than statements of historical facts contained in this prospectus supplement, including statements regarding our future financial condition, business strategy and plans, and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail, and incorporate by reference into this prospectus supplement and the accompanying prospectus in their entirety, many of these risks under the section titled “Risk Factors” on page S-6 of this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2021 and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, as updated by our subsequent filings under the Exchange Act, which are incorporated herein by reference, as may be updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. You should read this prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. These forward-looking statements are made as of the date of this prospectus supplement and unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

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

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering, after deducting Placement Agent fees and paying estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants issued in this offering, will be approximately \$6.7 million. If all the pre-funded warrants and common warrants are exercised for cash at an exercise price of \$0.0001 per share and \$2.07 per share, respectively, then our net proceeds will be approximately \$15.5 million, after deducting Placement Agent fees and paying estimated offering expenses payable by us. We cannot predict when or if the pre-funded warrants or the common warrants will be exercised. It is possible that the pre-funded warrants or the common warrants may expire and/or may never be exercised.

We currently intend to use the net proceeds from this offering, if any, and excluding the proceeds, if any, from the exercise of the pre-funded warrants and the common warrants issued in this offering, for working capital and general corporate purposes, including general and administrative expenses, research and development expenses and capital expenditures.

The amounts and timing of our use of the net proceeds from this offering, if any, will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and collaboration efforts and technological advances. 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. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

DESCRIPTION OF SECURITIES WE ARE OFFERING

Common Stock

The material terms and provisions of our common stock are described in the section titled “Description of Capital Stock” starting on page 9 of the accompanying prospectus.

Common Warrants

The following is a summary of the material terms and provisions of the common warrants that are being offered hereby. This summary is subject to and qualified in its entirety by the form of common warrant, which has been provided to the investors in this offering and which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement and the accompanying prospectus form a part. Prospective investors should carefully review the terms and provisions of the form of common warrant for a complete description of the terms and conditions of the common warrants.

Duration and Exercise Price

The common warrants offered hereby will have an exercise price of \$2.07 per share. The common warrants will be exercisable following the six-month anniversary of the closing of this offering and will expire six years from the date of issuance. The exercise price of the common warrants and the number of shares of common stock issuable upon exercise of the common warrants are subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock. The common warrants include anti-dilutive adjustment rights in the event we issue shares of common stock or common stock equivalents in the future with a value less than the then exercise price of such common warrants, subject to certain customary exceptions, and further subject to a minimum exercise price of \$1.00 per share. Common warrants will be issued in certificated form only.

Exercisability

The common warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder’s common warrants to the extent that the holder would own more than 4.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise, which may be increased to 9.99% upon election by the holder and written notice to us.

Cashless Exercise

The common warrants may be exercised by delivery of the aggregate exercise price or by means of a cashless exercise, provided however, that if, at the time a holder exercises its common warrants, a registration statement registering the issuance of the shares of common stock underlying the common warrants under the Securities Act, is not then effective or available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder must elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the common warrants.

Transferability

A common warrant may be transferred at the option of the holder upon surrender of the common warrant to us together with the appropriate instruments of transfer.

Fractional Shares

No fractional shares of common stock will be issued upon the exercise of the common warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

Trading Market

There is no established trading market for any of the common warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the common warrants will be limited.

Rights as a Stockholder

Except as otherwise provided in the common warrants or by virtue of the holders' ownership of shares of our common stock, the holders of common warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until such common warrant holders exercise their common warrants.

Fundamental Transaction

In the event of a fundamental transaction, as described in the common warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the common warrants will be entitled to receive upon exercise of the common warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the common warrants immediately prior to such fundamental transaction. In addition, the holders of the common warrants have, at the option of the applicable holder, the right to receive from us or a successor entity the same type or form of consideration (and in the same proportion) that is being offered and paid to the holders of our common stock in the fundamental transaction in the amount of the Black Scholes value (as described in the common warrants) of the unexercised portion of the common warrant on the date of the consummation of the fundamental transaction.

Waivers and Amendments

No term of the common warrants may be amended or waived without the written consent of the holder of such common warrant.

Pre-Funded Warrants

The following is a summary of the material terms and provisions of the pre-funded warrants that are being offered hereby. This summary is subject to and qualified in its entirety by the form of pre-funded warrant, which has been provided to the investors in this offering and which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement and the accompanying prospectus form a part. Prospective investors should carefully review the terms and provisions of the form of pre-funded warrant for a complete description of the terms and conditions of the pre-funded warrants.

Duration and Exercise Price

The pre-funded warrants offered hereby will have an exercise price of \$0.0001 per share. The pre-funded warrants will be exercisable immediately upon the closing of this offering. The exercise price of the pre-funded warrants and the number of shares of common stock issuable upon exercise of the pre-funded warrants are subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock. The pre-funded warrants will not expire until they are fully exercised.

Exercisability

The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder's pre-funded warrants to the extent that the holder would own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise.

Cashless Exercise

The pre-funded warrants may be exercised by delivery of the aggregate exercise price or by means of a cashless exercise, provided however, that if at the time a holder exercises its pre-funded warrants, a registration statement registering the issuance of the shares of common stock underlying the pre-funded warrants under the Securities Act, is not then effective or available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder must elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the pre-funded warrant.

Transferability

A pre-funded warrant may be transferred at the option of the holder upon surrender of the pre-funded warrant to us together with the appropriate instruments of transfer.

Fractional Shares

No fractional shares of common stock will be issued upon the exercise of the pre-funded warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

Trading Market

We do not intend to list the pre-funded warrants on The Nasdaq Global Market, any other national securities exchange or any other nationally recognized trading system.

Rights as a Stockholder

Except as otherwise provided in the pre-funded warrants or by virtue of the holders' ownership of shares of our common stock, the holders of pre-funded warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until such pre-funded warrant holders exercise their pre-funded warrants.

Fundamental Transactions

Upon the consummation of a fundamental transaction (as described in the pre-funded warrants, and generally including any reorganization, recapitalization or reclassification of our shares of common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding shares of common stock, or any person or group becoming the beneficial owner of 50% of the voting power of our outstanding shares of common stock), the holders of the pre-funded warrants will be entitled to receive, upon exercise of the pre-funded warrants, the kind and amount of securities, cash or other property that such holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction, without regard to any limitations on exercise contained in the pre-funded warrants.

Waivers and Amendments

No term of the pre-funded warrant may be amended or waived without the written consent of the holder of such pre-funded warrant.

PLAN OF DISTRIBUTION

We have engaged Cantor Fitzgerald & Co. to act as our exclusive Placement Agent to solicit offers to purchase the securities offered by this prospectus supplement and the accompanying prospectus. The Placement Agent is not purchasing or selling any such securities, nor is it required to arrange for the purchase and sale of any specific number or dollar amount of such securities. Therefore, we may not sell all of the securities being offered. The terms of this offering were subject to market conditions and negotiations between us and the prospective investor. We have entered into a securities purchase agreement directly with the investor who has agreed to purchase our securities in this offering. We will only sell securities in this offering to such investor.

Delivery of the securities offered hereby is expected to take place on or about December 29, 2022, subject to satisfaction of customary closing conditions

Fees and Expenses

We have agreed to pay the Placement Agent a cash fee equal to 7.0% of the aggregate gross proceeds from the offering. The following table shows the per share and total cash fees we will pay to the Placement Agent in connection with the sale of our securities offered pursuant to this prospectus supplement and the accompanying prospectus, assuming the purchase of all of the securities offered hereby.

	Per Share and Accompanying Common Warrant	Per Pre-Funded Warrant and Accompanying Common Warrant	Total
Offering price	\$ 2.22625	\$ 2.22615	\$ 7,528,117
Placement Agent fees ⁽¹⁾	\$ 0.15584	\$ 0.15583	\$ 526,968
Proceeds to us, before expenses	\$ 2.07041	\$ 2.07032	\$ 7,001,149

⁽¹⁾ Includes a cash fee of 7.0% of the aggregate gross proceeds of this offering. We have also agreed to reimburse the Placement Agent up to \$100,000 of certain of their fees and expenses.

In addition, we have granted Cantor Fitzgerald & Co. the right of first refusal to participate in the distributions of future public offerings, private placements and other financing transactions, subject to certain limitations. The right of first refusal will have a duration of less than three years, in accordance with FINRA Rule 5110(g)(6)(A).

H.C. Wainwright & Co., LLC is acting as independent financial advisor to us in connection with this offering, and we will pay a customary advisory fee which is included in our estimated total fees and expenses for this offering.

From time to time, the Placement Agent or its affiliates may provide in the future various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. For example, in May 2019, we entered into an “at-the-market” sales agreement with Cantor Fitzgerald & Co.

No Sale of Similar Securities

From the date hereof until 90 days after the closing of this offering, or the restricted period, neither we nor our subsidiary shall (i) issue, enter into any agreement to issue, or announce the issuance or proposed issuance of any shares of common stock or common stock equivalents, or (ii) file or amend any registration statement or prospectus, other than as necessary to maintain the registration of the securities offered hereby.

The foregoing restrictions shall not apply in respect of (i) the issuance of securities to our directors, officers, employees and consultants pursuant to employee benefit plans, equity incentive plans or other employee compensation plans existing on the date hereof and as described in this prospectus supplement and the documents that are incorporated by reference herein or pursuant to Nasdaq Rule 5635(c)(4), (ii) securities pursuant to the exercise, exchange or conversion of any options, warrants, restricted stock units, rights or convertible securities outstanding on the date hereof, (iii) securities issued in connection with any joint venture, commercial or collaborative relationship or the acquisition or license by us of the securities, businesses, property or other assets of another person, provided that such issuance is approved by the majority of the disinterested directors of our board of directors and provided that such securities are issued as “restricted securities” (as defined in Rule 144 under the Securities Act) and carry no registration rights that require or permit the filing of any registration statement in connection therewith during the restricted period, and (iv) issuances to one or more lenders in connection with the our entry into a debt financing transaction, provided that such issuances shall only be in the form of warrants to purchase shares of our common stock.

Listing of Common Stock

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

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare, Inc and its telephone number is 1-800-736-3001. The transfer agent's address is 150 Royall Street, Canton, Massachusetts 02021.

LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon the validity of the issuance of the securities being sold in this offering. Latham & Watkins LLP, San Diego, California, is representing the Placement Agent in connection with this offering.

EXPERTS

WithumSmith+Brown, PC, independent registered public accounting firm, has audited our consolidated financial statements and related schedule for the year ended December 31, 2021 included in our Annual Report on Form 10-K for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Such financial statements are incorporated by reference in reliance on WithumSmith+Brown, PC's report, given on their authority as experts in accounting and auditing.

OUM & Co. LLP, independent registered public accounting firm, has audited our consolidated financial statements and related schedule for the year ended December 30, 2020 included in our Annual Report on Form 10-K for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Such financial statements are incorporated by reference in reliance on OUM & Co. LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 that was declared effective by the SEC under the Securities Act on July 8, 2020, and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement. We incorporate by reference into this prospectus supplement and the registration statement of which this prospectus supplement is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-35068):

- our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on [March 10, 2022](#), and Amendment No. 1 to Annual Report on Form 10-K/A, filed with the SEC on [April 20, 2022](#);
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2022, June 30, 2022, and September 30, 2022, filed with the SEC on [May 16, 2022](#), [August 11, 2022](#) and [November 14, 2022](#), respectively;
- our Current Reports on Form 8-K filed with the SEC on [January 12, 2022](#), [February 14, 2022](#), [March 1, 2022](#), [March 31, 2022](#), [May 9, 2022](#), [June 2, 2022](#), [July 15, 2022](#) (as amended on [July 25, 2022](#) and [July 26, 2022](#)), [July 28, 2022](#), [August 4, 2022](#), [August 12, 2022](#), [September 23, 2022](#), [October 25, 2022](#) and [December 5, 2022](#); and
- the description of our common stock in our registration statement on [Form 8-A](#) filed with the SEC on February 1, 2011, as updated by [Exhibit 4.1](#) to our Annual Report on Form 10-K for the year ended December 31, 2021, and any amendments or reports filed for the purpose of updating such description.

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

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

AcelRx Pharmaceuticals, Inc.
25821 Industrial Boulevard, Suite 400
Hayward, CA 94545
(650) 216-3500
Attn: Secretary

S-17



\$150,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants

From time to time, we may offer and sell up to an aggregate amount of \$150,000,000 of any combination of the securities described in this prospectus, either individually or in combination. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

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

Our common stock is listed on The Nasdaq Global Market under the trading symbol "ACRX." On June 9, 2020, the last reported sale price of our common stock was \$1.47 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The Nasdaq Global Market or other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 5 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

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

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is July 8, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under this shelf registration statement, we may, from time to time, offer and sell, either individually or in combination, in one or more offerings, up to a total dollar amount of \$150,000,000 of any combination of the securities described in this prospectus.

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

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

You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus, the accompanying prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

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

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

PROSPECTUS SUMMARY

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

AcelRx Pharmaceuticals, Inc.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. DSUVIA® (known as DZUVEO in Europe) and Zalviso®, are both focused on the treatment of acute pain, and each utilize sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. On November 2, 2018, the U.S. Food and Drug Administration, or FDA, approved DSUVIA for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In June 2018, the European Commission, or EC, granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. We are further developing a distribution capability and commercial organization to continue to market and sell DSUVIA in the United States. In geographies where we decide not to commercialize products by ourselves, we may seek to out-license commercialization rights. We currently intend to commercialize and promote DSUVIA/DZUVEO outside the United States with one or more strategic partners, although we have not yet entered into any such arrangement. The timing of the resubmission of the Zalviso new drug application, or NDA, is in part dependent upon the finalization of the FDA’s new opioid approval guidelines and process. We intend to seek regulatory approval for Zalviso in the United States and, if successful, potentially promote Zalviso either by ourselves or with strategic partners. Zalviso is approved in Europe.

Company Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006. Our corporate address is 351 Galveston Drive, Redwood City, California 94063, and our telephone number is (650) 216-3500.

Unless the context indicates otherwise, as used in this prospectus, the terms “AcelRx,” “AcelRx Pharmaceuticals, Inc.,” “we,” “us” and “our” refer to AcelRx Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, up to a total dollar amount of \$150,000,000, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity date, if applicable;
- original issue discount, if any;

- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exercise, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- material or special U.S. federal income tax considerations, if any.

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

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

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

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

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

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

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

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

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

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

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

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including commercialization activities, general and administrative expenses, research and development expenses, capital expenditures, for making scheduled payments under our debt facility, or any other purpose we describe in the applicable prospectus supplement. See “Use of Proceeds” in this prospectus.

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including commercialization activities, general and administrative expenses, research and development expenses, capital expenditures, for making scheduled payments under our debt facility, or any other purpose we describe in the applicable prospectus supplement.

The Nasdaq Global Market Listing

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

RISK FACTORS

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Many important factors affect our ability to achieve our objectives, including:

- the expected benefits and potential value created by the co-promotion agreement with Tetrphase Pharmaceuticals, Inc.;
- our estimates regarding the sufficiency of our cash resources, expenses, capital requirements and needs for additional financing, and our ability to obtain additional financing;
- the uncertainties and impact arising from the worldwide COVID-19 pandemic, including restrictions on the ability of our sales force to contact and communicate with target customers and resulting delays and challenges to our commercial sales of DSUVIA;
- our success in commercializing DSUVIA® (sufentanil sublingual tablet, 30 mcg) in the United States, including the marketing, sales, and distribution of the product;
- the size and growth potential of the markets for DSUVIA, and Zalviso, if approved in the United States, and our ability to serve those markets;
- our ability to maintain regulatory approval of DSUVIA in the United States, including effective management of and compliance with the DSUVIA Risk Evaluation and Mitigation Strategies, or REMS, program;
- acceptance of DSUVIA by physicians, patients and the healthcare community, including the acceptance of pricing and placement of DSUVIA on payers’ formularies;
- the integration and performance of any businesses we acquire;
- our ability to develop sales and marketing capabilities in a timely fashion, whether alone through recruiting qualified employees, by engaging a contract sales organization, or with potential future collaborators;
- successfully establishing and maintaining commercial manufacturing with third parties;
- our ability to manage effectively, and the impact of any costs associated with, potential governmental investigations, inquiries, regulatory actions or lawsuits that may be brought against us;
- continued demonstration of an acceptable safety profile of DSUVIA;
- effectively competing with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;
- our ability to maintain regulatory approval of DZUVEO™ in the European Union, or EU, and enter into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe;
- our ability to manufacture and supply DZUVEO in Europe to any future strategic partner;
- our ability to manufacture and supply Zalviso to Gr✓nenthal GmbH, or Gr✓nenthal, in accordance with their forecast and the Manufacture and Supply Agreement with Gr✓nenthal during its remaining term;
- our ability to negotiate a replacement license agreement for the Collaboration and License Agreement with Gr✓nenthal;
- the status of the Collaboration and License Agreement with Gr✓nenthal and any other future potential collaborations, including potential milestones and royalty payments under the Gr✓nenthal agreement and obligations under the Purchase and Sale Agreement with PDL BioPharma, Inc., or PDL;

- our ability to successfully execute the pathway towards a resubmission of the Zalviso® (sufentanil sublingual tablet system) New Drug Application, or NDA, and subsequently obtain and maintain regulatory approval of Zalviso in the United States and comply with any related restrictions, limitations, and/or warnings in the label of Zalviso, if approved;
- the outcome of any potential FDA Advisory Committee meeting held for Zalviso;
- our ability to successfully commercialize Zalviso, if approved in the United States;
- the rate and degree of market acceptance of Zalviso, if approved in the United States;
- our ability to obtain adequate government or third-party payer reimbursement;
- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- our ability to successfully retain our key commercial, scientific, engineering, medical or management personnel and hire new personnel as needed;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers, including any supply chain impacts or work limitations resulting from shelter-in-place orders related to COVID-19;
- the success of competing therapies that are or become available;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our liquidity and capital resources; and
- our ability to obtain and maintain intellectual property protection for DSUVIA/DZUVEO and Zalviso.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail, and incorporate by reference into this prospectus in their entirety, many of these risks under the heading “Risk Factors” in our most recent annual report on Form 10-K, and in our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Exchange Act, which are incorporated herein by reference, as may be updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

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

Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including commercialization activities, general and administrative expenses, research and development expenses, capital expenditures, for making scheduled payments under our debt facility, or any other purpose we describe in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 200,000,000 shares of our common stock, \$0.001 par value, or Common Stock, and 10,000,000 shares of preferred stock, \$0.001 par value, or Preferred Stock. A description of material terms and provisions of our amended and restated certificate of incorporation, as amended, or our Charter, and our amended and restated bylaws, or Bylaws, affecting the rights of holders of our capital stock is set forth below. The description is intended as a summary, and is qualified in its entirety by reference to the Charter and Bylaws.

Common Stock

Voting Rights. Each holder of our Common Stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. In all matters other than the election of directors, the affirmative vote of the majority of shares present in person, by remote communication, or represented by proxy at a meeting of the stockholders and entitled to vote generally on the subject matter shall be the act of the stockholders. Directors shall be elected by a plurality of the votes of the shares present in person, by remote communication, or represented by proxy at a meeting of the stockholders and entitled to vote generally on the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors to be elected at any particular time.

Dividends. Subject to preferences that may be applicable to any then outstanding Preferred Stock, holders of our Common Stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

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

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

Fully Paid and Nonassessable. All of our outstanding shares of Common Stock are, and the shares of Common Stock to be issued pursuant to any offering we may make pursuant to this prospectus and any related prospectus supplement will be, fully paid and nonassessable.

Preferred Stock

Our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue Preferred Stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors can also increase or decrease the number of shares of any series, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of Preferred Stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the Common Stock. The issuance of Preferred Stock, while providing flexibility in connection with financings, possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring, discouraging or preventing a change in control of our company, may adversely affect the market price of our Common Stock and the voting and other rights of the holders of Common Stock, and may reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

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

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

Anti-Takeover Effects of Provisions of our Charter and Bylaws and Delaware Law

Charter and Bylaws. Our Charter and Bylaws include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- *Issuance of undesignated preferred stock.* Under our Charter, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by the board of directors. The existence of authorized but unissued shares of Preferred Stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.
- *Classified board.* Our Charter provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of the board.

- *Board of directors vacancies.* Our Charter and Bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.
- *Stockholder action; special meetings of stockholders.* Our Charter provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our Bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, or our chief executive officer. These provisions may prevent stockholders from corporate actions as stockholders at times when they otherwise would like to do so.
- *Advance notice requirements for stockholder proposals and director nominations.* Our Bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at our annual meeting of stockholders.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage certain types of transactions that may involve an actual or threatened acquisition of us. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. This section prevents some Delaware corporations from engaging, under some circumstances, in a business combination, which includes a merger or sale of at least 10% of the corporation's assets with any interested stockholder, meaning a stockholder who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of the corporation's outstanding voting stock, unless:

- the transaction is approved by the board of directors prior to the time that the interested stockholder became an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder's becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced; or
- at or subsequent to such time that the stockholder became an interested stockholder the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders by at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

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

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

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not “opted out” of these provisions and do not plan to do so. The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare, Inc.: 1-800-736-3001. The transfer agent's address is 150 Royall Street, Canton, Massachusetts 02021.

Listing on The Nasdaq Global Market

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

DESCRIPTION OF DEBT SECURITIES

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

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

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

General

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

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

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

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

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

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

Conversion or Exchange Rights

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

Consolidation, Merger or Sale

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

Events of Default under the Indenture

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

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

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

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

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

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

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

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

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

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

Modification of Indenture; Waiver

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

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

- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

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

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

Discharge

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

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

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

Form, Exchange and Transfer

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

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

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

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

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

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

Information Concerning the Trustee

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

Payment and Paying Agents

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

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

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

Governing Law

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

DESCRIPTION OF WARRANTS

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

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

General

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

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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

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

Exercise of Warrants

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

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

Governing Law

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

Enforceability of Rights by Holders of Warrants

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

LEGAL OWNERSHIP OF SECURITIES

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

Book-Entry Holders

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

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

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

Street Name Holders

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

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

Legal Holders

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

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

Special Considerations For Indirect Holders

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

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

Global Securities

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

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

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

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

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

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

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depository in any way;
- the depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

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

Special Situations When a Global Security Will Be Terminated

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

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

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

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

PLAN OF DISTRIBUTION

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

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

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

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

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

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

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

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

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

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

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

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

LEGAL MATTERS

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

EXPERTS

OUM & Co. LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019, and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Such financial statements are incorporated by reference in reliance on OUM & Co. LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Our website address is <http://www.ace1rx.com>. Information contained on or accessible through our website is not a part of this prospectus and is not incorporated by reference herein, and the inclusion of our website address in this prospectus is an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary):

- our [Annual Report on Form 10-K for the year ended December 31, 2019, which was filed with the SEC on March 16, 2020, as amended by Amendment No. 1 to the Annual Report on Form 10-K/A for the year ended December 31, 2019, which was filed with the SEC on April 17, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, which was filed with the SEC on May 11, 2020](#);
- our [Current Reports on Form 8-K which were filed on January 13, 2020, March 16, 2020 \(solely with respect to Items 1.01 and 8.01\), April 8, 2020 \(solely with respect to Item 5.02\), April 30, 2020, May 22, 2020, May 27, 2020, May 29, 2020, and June 4, 2020](#); and
- [the description of our common stock in our registration statement on Form 8-A filed with the SEC on February 1, 2011, including any amendments or reports filed for the purpose of updating such description](#).

All filings filed by us pursuant to the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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

AcelRx Pharmaceuticals, Inc.
351 Galveston Drive
Redwood City, CA 94063

Attn: Investor Relations
(650) 216-3500



748,744 Shares of Common Stock
Pre-Funded Warrants to Purchase up to 2,632,898 Shares of Common Stock
Warrants to Purchase up to 4,227,052 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Sole Placement Agent
Cantor

December 27, 2022
