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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

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**FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

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**ACELRX PHARMACEUTICALS, INC.**  
(Exact name of Registrant as specified in its charter)

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**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**41-2193603**  
(I.R.S. Employer  
Identification Number)

**25821 Industrial Boulevard, Suite 400  
Hayward, CA 94545  
(650) 216-3500**

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

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**Vincent J. Angotti**  
Chief Executive Officer  
**25821 Industrial Boulevard, Suite 400  
Hayward, CA 94545  
(650) 216-3500**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

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If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

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**The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.**

**Subject to Completion, Dated April 15, 2022**

**PRELIMINARY PROSPECTUS**



**11,017,058 Shares Common Stock**

This prospectus relates to the proposed resale from time to time by the selling stockholders named herein, together with any of such stockholders' transferees, pledgees, donees or successors, of up to 11,017,058 shares of our common stock, par value \$0.001 per share, consisting of (i) 9,009,538 shares of our common stock issued to the selling stockholders, or the Closing Shares, (ii) 1,396,526 shares of our common stock we held back to satisfy any potential indemnification and other obligations of Lowell Therapeutics, Inc., a Delaware corporation, and its securityholders, or the Holdback Shares, and (iii) 610,994 shares of our common stock issued to Maxim Partners LLC, a financial advisor in the Merger (as defined below) to settle outstanding obligations, or the Advisor Shares. The selling stockholders acquired these shares from us pursuant to an Agreement and Plan of Merger, dated as of November 14, 2021, or the Merger Agreement, by and among, AcelRx and two of its direct wholly owned subsidiaries, AcelRx Intermediate Sub, Inc., a Delaware corporation, and AcelRx Consolidation Sub, LLC, a Delaware limited liability company, Lowell Therapeutics, Inc., and James Wilkie, solely in his capacity as the stockholder representative for the Lowell Therapeutic stockholders and option holders, or the Merger. We are not selling any of our common stock pursuant to this prospectus, and we will not receive any proceeds from the sale of our common stock offered by this prospectus by the selling stockholders.

The selling stockholders may offer and sell or otherwise dispose of the shares of our common stock described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling stockholders will bear all underwriting fees, commissions and discounts, if any, attributable to the sales of shares and any transfer taxes. We will bear all other costs, expenses and fees in connection with the registration of the shares. See "Plan of Distribution" for more information about how the selling stockholders may sell or dispose of their shares of our common stock.

Our common stock is listed on The Nasdaq Global Market under the trading symbol "ACRX." On April 14, 2022, the last reported sale price of the common stock was \$0.26 per share.

**Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 3 of this prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus.**

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

**The date of this prospectus is \_\_\_\_\_, 2022.**

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## ABOUT THIS PROSPECTUS

Neither we nor the selling stockholders have authorized anyone to provide you with any information other than that contained in, or incorporated by reference into, this prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of our common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should not assume that the information contained in or incorporated by reference in this prospectus is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

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 titled “Where You Can Find Additional Information.”

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.

## 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, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in this 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 management of acute moderate to severe pain in adults 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, and, in July 2021, 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. 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 itself or with strategic partners. Zalviso is approved in Europe and was commercialized by Gr✓nenthal GmbH, or Gr✓nenthal, through May 12, 2021. In July 2021, we also entered into a separate License and Commercialization 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.

#### **Acquisition of Lowell Therapeutics**

On January 7, 2022, we closed our acquisition of Lowell Therapeutics for merger consideration of approximately \$32.5 million plus net cash acquired, subject to certain other adjustments. Pursuant to the terms of the Merger Agreement, all options to purchase capital stock and all shares of Lowell Therapeutics capital stock issued and outstanding immediately before the effective time of the Merger were cancelled in exchange for the right to receive:

- 9,009,538 Closing Shares;
- \$3,519,129 of cash;
- 1,396,526 Holdback Shares; and

- up to \$26.0 million of contingent consideration payable in cash or common stock at our option, upon the achievement of regulatory and sales-based milestones.

In addition, we issued 610,994 Advisor Shares to Maxim Partners LLC, a financial advisor in the Merger, to settle outstanding obligations.

#### **Use of Proceeds**

We will not receive any of the proceeds from the sale of shares of our common stock by the selling stockholders in this offering. The selling stockholders will receive all of the proceeds from the sale of shares of our common stock hereunder.

#### **The Nasdaq Global Market Listing**

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

#### **Company 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](http://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 and should not be considered part of this prospectus.

## RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described under the heading “Risk Factors” contained in our most recent Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q and other filings we make with the Securities and Exchange Commission, or the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus and the documents incorporated by reference. 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 titled “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, 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;
- 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® (sufentanil sublingual tablet, 30 mcg);
- 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 satisfactorily comply with FDA regulations concerning the advertising and promotion of DSUVIA;
- the size and growth potential of the markets for DSUVIA, and, if approved, Zalviso® (sufentanil sublingual tablet system) 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, 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;
- our ability to satisfy the required conditions and otherwise complete our planned acquisition of Lowell Therapeutics, Inc., or Lowell, pursuant to the Agreement and Plan of Merger, or Merger Agreement, on a timely basis or at all;
- the expected benefits and potential value created by the proposed Merger Agreement with Lowell for our stockholders;
- potential legal proceedings relating to the proposed acquisition of Lowell and the outcome of any such legal proceedings;
- our ability to achieve all or any of the anticipated benefits of the proposed acquisition of Lowell on a timely basis or at all;
- the integration and performance of any assets or businesses we acquire;
- our ability to develop and commercialize products and product candidates that we in-license;

- 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, 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 Laboratoire Aguettant, or Aguettant, in accordance with their forecasts and the License and Commercialization Agreement, or the DZUVEO Agreement, with Aguettant;
- the status of the DZUVEO Agreement or any other future potential collaborations, including potential milestones and revenue share payments under the DZUVEO Agreement;
- our, or Aguettant's, ability to maintain regulatory approval of DZUVEO in the European Union, or EU;
- our ability to timely and efficiently close-out our relationship with Gr✓nenthal GmbH, or Gr✓nenthal, following the termination of our Collaboration and License Agreement and the Manufacture and Supply Agreement;
- our ability to fulfill our obligations under the Purchase and Sale Agreement with SWK Funding, LLC, or SWK, (assignee of PDL BioPharma, Inc., or PDL) including our obligation to use commercially reasonable efforts to negotiate a replacement license agreement for Zalviso with a third party;
- our ability to successfully execute the pathway towards a resubmission of the Zalviso 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;
- 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, 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 its entirety, many of these risks under the headings “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2021, 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.

These risks are not exhaustive. Other sections of this prospectus 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 from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur.

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. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus or to conform these statements to actual results or to changes in our expectations.

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, 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 relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and achievements may be different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

## USE OF PROCEEDS

All the shares of our common stock to be sold pursuant to this prospectus will be sold by the selling stockholders. We will not receive any of the proceeds from such sales.

## DESCRIPTION OF CAPITAL STOCK

### Summary

Our authorized capital stock consists of 200,000,000 shares of common stock and 10,000,000 shares of preferred stock, \$0.001 par value. As of March 31, 2022, we had 147,109,007 shares of common stock issued and outstanding and no shares of preferred stock issued and outstanding.

A description of the material terms and provisions of our amended and restated certificate of incorporation and amended and restated bylaws affecting the rights of holders of our capital stock is set forth below. The description is intended as a summary, and is qualified in its entirety by reference to our amended and restated certificate of incorporation and our amended and restated bylaws which are incorporated by reference into the registration statement of which this prospectus is a part.

### Common Stock

*Voting Rights.* Each holder of 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, the 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 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.* Holders of common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to shares of common stock.

*Fully Paid and Nonassessable.* All of outstanding shares of common stock are fully paid and nonassessable.

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

*Certificate of Incorporation and Bylaws.* Our amended and restated certificate of incorporation and amended and restated 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 certificate of incorporation, 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 certificate of incorporation 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 Certificate of Incorporation 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 certificate of incorporation provides that our stockholders may not take action by written consent and 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.

#### **Listing on The Nasdaq Global Market**

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.: 1-800-736-3001. The transfer agent's address is 250 Royall Street, Canton, Massachusetts 02021.

## SELLING STOCKHOLDERS

We have prepared this prospectus to allow the selling stockholders to offer and sell from time to time up to 11,017,058 shares of our common stock, consisting of (i) 9,009,538 Closing Shares, (ii) 1,396,526 Holdback Shares and (iii) 610,994 Advisor Shares. As of the date of this prospectus, we have not released the Holdback Shares to the selling stockholders. We are registering the offer and sale of the shares beneficially owned by the selling stockholders to satisfy certain registration obligations that we granted the selling stockholders in connection with our acquisition of Lowell Therapeutics.

The following table sets forth (i) the name of each selling stockholder; (ii) the number of shares beneficially owned by each of the selling stockholders; (iii) the number of shares that may be offered under this prospectus, or the Registrable Securities; and (iv) the number of shares of common stock beneficially owned by each of the selling stockholders assuming all of the shares covered hereby are sold. We do not know how long the selling stockholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale or other disposition of any shares. Except as disclosed in the footnotes to the table below, to our knowledge, none of the selling stockholders has, or during the three years prior to the date of this prospectus has had, any position, office or other material relationships with us or any of our affiliates.

Only the Closing Shares and the Advisor Shares have been issued as of the date of this prospectus. The Holdback Shares if any, will be issued in accordance with the terms, and subject to the contingencies, set forth in the Merger Agreement.

The information set forth in the table below is based upon information obtained from the selling stockholders. Beneficial ownership of the selling stockholders is determined in accordance with Rule 13d-3(d) under the Exchange Act. The percentage of shares beneficially owned prior to, and after, the offering is based on 147,109,007 shares of our common stock outstanding as of March 31, 2022, and assumes the issuance of 1,396,526 Holdback Shares to the selling stockholders.

As used in this prospectus, the term “selling stockholders” includes the selling stockholders listed in the table below, together with any additional selling stockholders listed in a prospectus supplement, and their donees, pledgees, assignees, transferees, distributees and successors-in-interest that receive shares in any non-sale transfer after the date of this prospectus.

Name of Selling Stockholder <sup>(1)</sup>	Beneficial Ownership Prior to This Offering			Beneficial Ownership After This Offering	
	Shares	% of Total Voting Power Before This Offering	Number of Shares Being Offered	Shares	% of Total Voting Power After This Offering
Abhishek Srinivas <sup>(2)</sup>	43,145	*	43,145	—	—
Akila Chandrasekar <sup>(3)</sup>	22,507	*	22,507	—	—
Andrew Seacat <sup>(4)</sup>	19,318	*	19,318	—	—
BioAltum Consulting, LLC <sup>(5)</sup>	313,593	*	313,593	—	—
Brian Howell <sup>(6)</sup>	657	*	657	—	—
Carey Chern <sup>(7)</sup>	28,763	*	28,763	—	—
CuriRx, Inc. <sup>(8)</sup>	22,614	*	22,614	—	—
David L. Hall <sup>(9)</sup>	68,796	*	68,796	—	—
Diana Chirita <sup>(10)</sup>	71,910	*	71,910	—	—
Edward S. Price <sup>(11)</sup>	171,996	*	171,996	—	—
Elaine Liong <sup>(12)</sup>	316,254	*	316,254	—	—
Feng Zeng <sup>(13)</sup>	57,528	*	57,528	—	—
Gnat, LLC <sup>(14)</sup>	335,244	*	335,244	—	—
GreenLeap Ventures, LLC <sup>(15)</sup>	546,522	*	546,522	—	—
Gregor Zenas Kent <sup>(16)</sup>	343,897	*	343,897	—	—
Innovative BioTherapies, Inc. <sup>(17)</sup>	11,306	*	11,306	—	—
Jack and Barbara Irvin 2006 Trust <sup>(18)</sup>	35,954	*	35,954	—	—
James Michael Rolke <sup>(19)</sup>	85,974	*	85,974	—	—
James Wilkie <sup>(20)</sup>	2,993,906	2.0	2,993,906	—	—
John J. Fee <sup>(21)</sup>	13,831	*	3,831	10,000	*
Jon S. Saxe and Myrna G. Marshall 1997 Trust <sup>(22)</sup>	85,987	*	85,987	—	—
Jonathan Hong-Min Chow <sup>(23)</sup>	34,406	*	34,406	—	—
Kyto Technology & Life Science, Inc. <sup>(24)</sup>	528,122	*	528,122	—	—
La Jolla Pharmaceutical Company <sup>(25)</sup>	1,555,531	1.1	1,555,531	—	—
Lakhmir Chawla <sup>(26)</sup>	1,658,530	1.1	1,658,530	—	—
Martha C. Farmer <sup>(27)</sup>	131,015	*	131,015	—	—
Maxim Partners LLC <sup>(28)</sup>	724,884	*	724,884	—	—
Michelle Marie Merrigan <sup>(29)</sup>	54,907	*	54,907	—	—
Peter Raymond Rock <sup>(30)</sup>	45,014	*	45,014	—	—
Rayyan Daghistani <sup>(31)</sup>	223,369	*	223,369	—	—
Russo Family Trust <sup>(32)</sup>	104,330	*	104,330	—	—
Securitas Biosciences LLC <sup>(33)</sup>	171,990	*	171,990	—	—
Sharon Xia Gao <sup>(34)</sup>	16,960	*	16,960	—	—
Sota Kurita <sup>(35)</sup>	1,685	*	1,685	—	—
The 1991 Baghramian Family Revocable Trust <sup>(36)</sup>	61,085	*	54,585	6,500	*
Thomas Lee Vogelsong <sup>(37)</sup>	132,028	*	132,028	—	—

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- \* Denotes less than 1%.
- (1) Certain of the selling stockholders are currently employees following our acquisition of Lowell.
  - (2) Consists of (i) 40,847 shares of our common stock and (ii) 2,298 Holdback Shares.
  - (3) Consists of (i) 18,676 shares of our common stock and (ii) 3,831 Holdback Shares.
  - (4) Consists of (i) 16,700 shares of our common stock and (ii) 2,618 Holdback Shares.
  - (5) Consists of (i) 297,076 shares of our common stock and (ii) 16,517 Holdback Shares. Lakhmir Chawla is the Principal of BioAltum Consulting, LLC and may be deemed to be the beneficial owner of the Registrable Securities held by BioAltum Consulting, LLC.
  - (6) Consists solely of 657 Holdback Shares.
  - (7) Consists of (i) 27,231 shares of our common stock and (ii) 1,532 Holdback Shares.
  - (8) Consists of (i) 19,549 shares of our common stock and (ii) 3,065 Holdback Shares. Indu Javeri is the President and Chief Executive Officer of CuriRx, Inc. and may be deemed to be the beneficial owner of the Registrable Securities held by CuriRx, Inc.
  - (9) Consists of (i) 65,063 shares of our common stock and (ii) 3,733 Holdback Shares.
  - (10) Consists of (i) 68,079 shares of our common stock and (ii) 3,831 Holdback Shares.
  - (11) Consists of (i) 162,663 shares of our common stock and (ii) 9,333 Holdback Shares.
  - (12) Consists of (i) 270,266 shares of our common stock and (ii) 45,988 Holdback Shares.
  - (13) Consists of (i) 54,463 shares of our common stock and (ii) 3,065 Holdback Shares.
  - (14) Consists solely of 335,244 Holdback Shares. Joseph P. Galda is deemed to have power to vote or dispose of the Registrable Securities.
  - (15) Consists of (i) 517,404 shares of our common stock and (ii) 29,188 Holdback Shares. Joseph Brannan Musumeci is deemed to have power to vote or dispose of the Registrable Securities.
  - (16) Consists of (i) 325,235 shares of our common stock and (ii) 18,662 Holdback Shares.
  - (17) Consists of (i) 9,774 shares of our common stock and (ii) 1,532 Holdback Shares. H. David Humes is deemed to have power to vote or dispose of the Registrable Securities.
  - (18) Consists of (i) 34,039 shares of our common stock and (ii) 1,915 Holdback Shares. Jack D. Irvin and Barbara Ann Irvin are deemed to have power to vote or dispose of the Registrable Securities.
  - (19) Consists of (i) 81,309 shares of our common stock and (ii) 4,665 Holdback Shares.
  - (20) Consists of (i) 2,636,370 shares of our common stock and (ii) 357,536 Holdback Shares.
  - (21) Consists of (i) 10,000 shares of our common stock and (ii) 3,831 Holdback Shares.
  - (22) Consists of (i) 81,321 shares of our common stock and (ii) 4,666 Holdback Shares. Jon S. Saxe and Myrna G. Marshall are deemed to have power to vote or dispose of the Registrable Securities.
  - (23) Consists of (i) 32,540 shares of our common stock and (ii) 1,866 Holdback Shares.
  - (24) Consists of (i) 499,877 shares of our common stock and (ii) 28,245 Holdback Shares. Paul Russo and Simon Westbrook are deemed to have power to vote or dispose of the Registrable Securities.
  - (25) Consists of (i) 1,344,703 shares of our common stock and (ii) 210,828 Holdback Shares. Larry Edwards is the Chief Executive Officer of La Jolla Pharmaceutical Company and Michael Hearne is the Chief Financial Officer of La Jolla Pharmaceutical Company, both Larry Edwards and Michael Hearne are deemed to have power to vote or dispose of the Registrable Securities.
  - (26) Consists of (i) 1,442,059 shares of our common stock and (ii) 216,471 Holdback Shares.
  - (27) Consists of (i) 118,686 shares of our common stock and (ii) 12,329 Holdback Shares.
  - (28) Consists of (i) 709,448 shares of our common stock and (ii) 15,436 Holdback Shares. Michael Rabinowitz is deemed to have power to vote or dispose of the Registrable Securities. Maxim Group LLC was a financial advisor in the Merger. Maxim Group LLC, a registered broker-dealer, is a subsidiary of Maxim Partners LLC. Based on information provided by the selling securityholder, the selling securityholder acquired the Registrable Securities as compensation for services rendered as financial advisor in the Merger, and at the time of the acquisition of the Registrable Securities, the selling securityholder did not have any agreements or understandings with any person to distribute such Registrable Securities.
  - (29) Consists of (i) 45,905 shares of our common stock and (ii) 9,002 Holdback Shares.
  - (30) Consists of (i) 37,352 shares of our common stock and (ii) 7,662 Holdback Shares.
  - (31) Consists of (i) 211,249 shares of our common stock and (ii) 12,120 Holdback Shares.
  - (32) Consists of (i) 98,711 shares of our common stock and (ii) 5,619 Holdback Shares. Paul Russo is the trustee of the Russo Family Trust and may be deemed to be the beneficial owner of the Registrable Securities held by the Russo Family Trust.
  - (33) Consists of (i) 162,657 shares of our common stock and (ii) 9,333 Holdback Shares. Matias Fernando Cristobal Vidal is deemed to have power to vote or dispose of the Registrable Securities.
  - (34) Consists of (i) 14,662 shares of our common stock and (ii) 2,298 Holdback Shares.
  - (35) Consists solely of 1,685 Holdback Shares.
  - (36) Consists of (i) 58,150 shares of our common stock and (ii) 2,935 Holdback Shares. Mike Baghrmian is deemed to have power to vote or dispose of the Registrable Securities.
  - (37) Consists of (i) 124,968 shares of our common stock and (ii) 7,060 Holdback Shares.

## PLAN OF DISTRIBUTION

We are registering the shares of our common stock held by the selling stockholders from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of our common stock.

The term “selling securityholders” includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from a selling securityholder as a gift, pledge, partnership distribution or other transfer. The selling securityholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on the principal trading market for our common stock or any other stock exchange, market or trading facility on which our common stock is traded or in private transactions. These sales may be at fixed or negotiated prices. A selling stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker dealer solicits purchasers;
- block trades in which the broker dealer will attempt to sell the common stock as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker dealer as principal and resale by the broker dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- distribution to employees, members, limited partners or stockholders of the selling securityholders;
- in transactions through broker dealers that agree with the selling stockholders to sell a specified number of such common stock at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- by pledge to secured debts and other obligations;
- delayed delivery arrangements;
- to or through underwriters or broker-dealers;
- in “at the market” offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or at prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents;
- in privately negotiated transactions;
- in options transactions
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell the shares of our common stock under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

In addition, a selling securityholder that is an entity may elect to make a pro rata in-kind distribution of securities to its members, partners or stockholders pursuant to the registration statement of which this prospectus is a part by delivering a prospectus with a plan of distribution. Such members, partners or stockholders would thereby receive freely tradeable securities pursuant to the distribution through a registration statement. To the extent a distributee is our affiliate (or to the extent otherwise required by law), we may, at our option, file a prospectus supplement in order to permit the distributees to use the prospectus to resell the securities acquired in the distribution.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of our common stock, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with Financial Industry Regulatory Authority, or FINRA, Rule 5110; and in the case of a principal transaction a markup or markdown in compliance with FINRA Rule 2121.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of our common stock in the course of hedging the positions they assume. The selling stockholders may also sell our common stock short and deliver these shares to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these shares. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling stockholders may also pledge securities to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged securities pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by the selling stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling securityholders in amounts to be negotiated immediately prior to the sale.

The selling stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of our common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares of our common stock.

We are required to pay certain fees and expenses incurred by us incident to the registration of the shares of our common stock. We and the selling stockholders have agreed to indemnify each other against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares of our common stock may not simultaneously engage in market making activities with respect to our common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of our common stock by the selling stockholders or any other person. We will make copies of this prospectus available to the selling stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

At the time a particular offer of securities is made, if required, a prospectus supplement will be distributed that will set forth the number of securities being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallocated or paid to any dealer, and the proposed selling price to the public.

## LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon the validity of the shares of our common stock offered by this prospectus.

## EXPERTS

WithumSmith+Brown, PC, 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, 2021, as set forth in their report, which is incorporated by reference in this prospectus 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 included in our Annual Report on Form 10-K for the year ended December 31, 2020, as set forth in their report, which is 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 reports, 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.acerlx.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, 2021, filed with the SEC on [March 10, 2022](#);
- our Current Reports on Form 8-K, which were filed with the SEC on [January 12, 2022](#); [February 14, 2022](#), [March 1, 2022](#) and [March 31, 2022](#); 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.  
25821 Industrial Boulevard, Suite 400  
Hayward, California 94545  
Attn: Investor Relations  
(650) 216-3500

## PART II

### INFORMATION NOT REQUIRED IN THE PROSPECTUS

#### Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an estimate of the fees and expenses, other than the underwriting discounts and commissions, payable by us in connection with the issuance and distribution of the securities being registered. All the amounts shown are estimates, except for the SEC registration fee.

	<b>Amount</b>
SEC registration fee	\$ 269
Financial Industry Regulatory Authority filing fee	(1)
Accounting fees and expenses	25,000
Legal fees and expenses	100,000
Transfer agent and registrar fees and expenses	15,000
Miscellaneous fees and expenses	731
<b>Total</b>	<b>\$ 141,000</b>

(1) This fee is calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

#### Item 15. Indemnification of Directors and Officers

The following summary is qualified in its entirety by reference to the complete copy of the Delaware General Corporation Law, AcelRx's amended and restated certificate of incorporation, as amended, and AcelRx's amended and restated bylaws.

Section 145 of the Delaware General Corporation Law authorizes a court to award, or a corporation's board of directors to grant indemnity to directors and officers under certain circumstances and subject to certain limitations. The terms of Section 145 of the Delaware General Corporation Law are sufficiently broad to permit indemnification under certain circumstances for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

As permitted by the Delaware General Corporation Law, AcelRx's amended and restated certificate of incorporation, as amended, contains provisions that eliminate the personal liability of its directors for monetary damages for any breach of fiduciary duties as a director, except liability for the following:

- any breach of the director's duty of loyalty to AcelRx or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- under Section 174 of the Delaware General Corporation Law (regarding unlawful dividends and stock purchases); or
- any transaction from which the director derived an improper personal benefit.

As permitted by the Delaware General Corporation Law, AcelRx's amended and restated bylaws provide that:

- AcelRx is required to indemnify its directors and executive officers to the fullest extent permitted by the Delaware General Corporation Law, subject to very limited exceptions;
- AcelRx may indemnify its other employees and agents as set forth in the Delaware General Corporation Law;
- AcelRx is required to advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to very limited exceptions; and

- the rights conferred in the bylaws are not exclusive.

AcelRx has entered, and intends to continue to enter, into separate indemnification agreements with its directors and executive officers to provide these directors and executive officers additional contractual assurances regarding the scope of the indemnification set forth in AcelRx's amended and restated certificate of incorporation, as amended, and amended and restated bylaws and to provide additional procedural protections. At present, there is no pending litigation or proceeding involving a director or executive officer of AcelRx regarding which indemnification is sought. The indemnification provisions in AcelRx's amended and restated certificate of incorporation, as amended, amended and restated bylaws and the indemnification agreements entered into or to be entered into between AcelRx and each of its directors and executive officers may be sufficiently broad to permit indemnification of AcelRx's directors and executive officers for liabilities arising under the Securities Act. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of AcelRx pursuant to the foregoing provisions, or otherwise, AcelRx has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

AcelRx currently carries liability insurance for its directors and officers.

## Item 16. Exhibits

Exhibit Number	Description	Incorporated by Reference			
		Schedule Form	File Number	Exhibit	Filing Date
2.1	<a href="#">Agreement and Plan of Merger, dated as of November 14, 2021, by and among the Registrant, Lowell, Merger Sub 1, Merger Sub 2 and the Stockholder Representative.</a>	10-Q	001-35068	2.1	11/15/2021
3.1	<a href="#">Amended and Restated Certificate of Incorporation of the Registrant.</a>	8-K	001-35068	3.1	2/18/2011
3.2	<a href="#">Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.</a>	8-K	001-35068	3.1	6/25/2019
3.3	<a href="#">Amended and Restated Bylaws of the Registrant.</a>	S-1	333-170594	3.4	1/7/2011
4.1	Reference is made to Exhibits 3.1 through 3.3.				
4.2	<a href="#">Specimen Common Stock Certificate of the Registrant.</a>	S-1	333-170594	4.2	1/31/2011
5.1	<a href="#">Opinion of Cooley LLP.</a>				
23.1	<a href="#">Consent of WithumSmith+Brown, PC, Independent Registered Public Accounting Firm.</a>				
23.2	<a href="#">Consent of OUM &amp; Co. LLP, Independent Registered Public Accounting Firm.</a>				
107	<a href="#">Filing Fee Table</a>				

## Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
  - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
  - (ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
  - (iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

*provided, however*, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
  - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
  - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
  - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
  - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
  - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) That, for the purpose of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Hayward, State of California, on April 15, 2022.

### ACELRX PHARMACEUTICALS, INC.

By: /s/ Vincent J. Angotti  
Vincent J. Angotti  
Chief Executive Officer

### Power of Attorney

**KNOW ALL PERSONS BY THESE PRESENTS**, that each person whose signature appears below constitutes and appoints Vincent J. Angotti and Raffi Asadorian, and each of them, as true and lawful attorneys-in-fact and agents, with full powers of substitution and resubstitution, for them and in their name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, and generally to do all such things in their names and behalf in their capacities as officers and directors to enable AcelRx Pharmaceuticals, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed below by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ VINCENT J. ANGOTTI</u> Vincent J. Angotti	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	April 15, 2022
<u>/s/ RAFFI ASADORIAN</u> Raffi Asadorian	Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	April 15, 2022
<u>/s/ ADRIAN ADAMS</u> Adrian Adams	Chairman	April 15, 2022
<u>/s/ RICHARD AFABLE</u> Richard Afable, M.D.	Director	April 15, 2022
<u>/s/ MARINA BOZILENKO</u> Marina Bozilenko	Director	April 15, 2022
<u>/s/ JILL M. BROADFOOT</u> Jill M. Broadfoot	Director	April 15, 2022

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<hr/> <i>/s/ STEPHEN J. HOFFMAN</i> Stephen J. Hoffman, Ph.D., M.D.	Director	April 15, 2022
<hr/> <i>/s/ PAMELA P. PALMER</i> Pamela P. Palmer, M.D., Ph.D.	Director	April 15, 2022
<hr/> <i>/s/ HOWARD B. ROSEN</i> Howard B. Rosen	Director	April 15, 2022
<hr/> <i>/s/ MARK WAN</i> Mark Wan	Director	April 15, 2022



John T. McKenna  
+1 650 843 5059  
jmckenna@cooley.com

April 15, 2022

AcelRx Pharmaceuticals, Inc.  
25821 Industrial Blvd, Suite 400  
Hayward, CA 94545

Ladies and Gentlemen:

You have requested our opinion, as counsel to AcelRx Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), with respect to certain matters in connection with the filing by the Company of a Registration Statement on Form S-3 (the "**Registration Statement**") with the Securities and Exchange Commission, including a related prospectus (the "**Prospectus**"), covering the registration for resale of 11,017,058 shares of Common Stock, \$0.001 par value, of the Company (the "**Shares**"). We have been advised that (i) the Shares have been or may be issued by the Company pursuant to that certain Agreement and Plan of Merger, dated as of November 14, 2021, by and among the Company, AcelRx Intermediate Sub, Inc., AcelRx Consolidation Sub, LLC, Lowell Therapeutics, Inc., a Delaware corporation ("**Target**"), and the stockholder representative for the Target's stockholders and option holders (the "**Merger Agreement**"), and (ii) certain of the Shares have been issued by the Company pursuant to an agreement between Target and Maxim Group LLC.

In connection with this opinion, we have examined and relied upon the Registration Statement, the Prospectus, the Company's Amended and Restated Certificate of Incorporation, as amended, and Amended and Restated Bylaws, each as currently in effect, the Merger Agreement and originals or copies certified to our satisfaction of such records, documents, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below. We have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals and the conformity to originals of all documents submitted to us as copies; the accuracy, completeness and authenticity of certificates of public officials; and the due execution and delivery of all documents by all persons other than the Company where due execution and delivery are prerequisites to the effectiveness thereof. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not independently verified such matters.

With respect to Shares issuable by the Company pursuant to the Merger Agreement in the future contingent upon satisfaction of any potential indemnification and other obligations of Target and its securityholders (the "**Holdback Shares**"), we express no opinion to the extent that future issuances of securities of the Company, including the Holdback Shares, and/or antidilution adjustments to outstanding securities of the Company cause the number of Holdback Shares to be greater than the number of shares of Common Stock that then remain authorized but unissued or committed to be issued.

Our opinion is expressed only with respect to the General Corporation Law of the State of Delaware. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, other than the Holdback Shares, have been validly issued and are fully paid and nonassessable, and the Holdback Shares, when issued pursuant to the Merger Agreement, will be validly issued, fully paid and nonassessable.

Cooley LLP 3175 Hanover Street Palo Alto, CA 94304-1130  
t: (650) 843-5000 f: (650) 849-7400 cooley.com

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We consent to the reference to our firm under the caption “Legal Matters” in the Prospectus and to the filing of this opinion as an exhibit to the Registration Statement.

Sincerely,

Cooley LLP

By:           /s/ John T. McKenna            
John T. McKenna

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement on Form S-3 of our report dated March 10, 2022, relating to the consolidated financial statements and schedule of AcclRx Pharmaceuticals, Inc., included in its Annual Report on Form 10-K for the year ended December 31, 2021. We also consent to the reference to our firm under the heading “Experts” in such Registration Statement.

/s/ WithumSmith+Brown, PC

San Francisco, California  
April 15, 2022

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference, in the Prospectus constituting a part of this Registration Statement on Form S-3, of our report dated March 15, 2021 relating to the consolidated financial statements and schedule of AcetRx Pharmaceuticals, Inc., which appears in its Annual Report on Form 10-K for the year ended December 31, 2021.

We also consent to the reference to us under the caption “Experts” in the Prospectus.

/s/ OUM & CO. LLP

San Francisco, California

April 15, 2022

## CALCULATION OF REGISTRATION FEE

Title of each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Unit (1)	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(1)
Common Stock, par value \$0.001 per share	11,017,058(2)	\$0.26	\$2,864,436.00	\$266.00

- (1) Estimated solely for the purposes of calculating the registration fee. Pursuant to Rule 457(c) under the Securities Act, the registration fee has been calculated based upon the average of the high and low prices, as reported by The Nasdaq Global Market, for shares of our common stock on April 11, 2022.
- (2) Consists of up to 11,017,058 shares of our common stock registered for resale by the selling securityholders named in this registration statement, consisting of (i) 9,009,538 shares of our common stock issued to the selling stockholders, (ii) 1,396,526 shares of our common stock to be held back to satisfy any potential indemnification and other obligations of Lowell Therapeutics, Inc., a Delaware corporation, and its securityholders and (iii) 610,994 shares of our common stock issued to Maxim Partners LLC.