

ACELRX PHARMACEUTICALS INC

Form 424B5

July 11, 2018

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Registration No. 333-218506

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

SUBJECT TO COMPLETION, DATED JULY 11, 2018

PROSPECTUS SUPPLEMENT

(To Prospectus dated June 14, 2017)

Shares

Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol "ACRX." On July 10, 2018, the last reported sale price of our common stock on the Nasdaq Global Market was \$3.45 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-4 of this prospectus supplement, on page 4 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 | TOTAL |
|--|------------------|--------------|
| Public Offering Price | \$ | \$ |
| Underwriting Discounts and Commissions ⁽¹⁾ | \$ | \$ |
| Proceeds to AcelRx Pharmaceuticals, Inc. before expenses | \$ | \$ |

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

Delivery of the shares of common stock is expected to be made on or about _____, 2018. We have granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ _____ and the total proceeds to us, before expenses, will be \$ _____.

Sole Book-Running Manager

Cantor

Lead Manager

H.C. Wainwright & Co.

Prospectus Supplement dated July , 2018

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PROSPECTUS

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and the underwriters are not, making an offer to sell these shares of common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents, regardless of when such documents are delivered. 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 in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized 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 we have referred you to in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

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 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 June 14, 2017, 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.

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 consolidated subsidiary, except where the context otherwise requires or as otherwise indicated.

“DSUVIA” is a trademark, and “ACELRX” and “ZALVISO” are registered trademarks, all owned by AcelRx Pharmaceuticals, Inc. This prospectus supplement also contains trademarks and trade names that are the property of their respective owners. We do not intend to use or display other companies’ trademarks and trade names to imply any relationship with, or endorsement or sponsorship of us by, any other companies. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus may be listed without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their right thereto.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of 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 common stock, you are assuming a high degree of risk. See “Risk Factors” beginning on page S-4 of this prospectus supplement, on page 4 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. Our product candidates, focused on the treatment of acute pain, are DSUVIA™ (known as DZUVEO™ outside of the United States) and Zalviso®. Each is a sublingual sufentanil formulation, designed to be delivered via a non-invasive route of sublingual administration exclusively for use in medically supervised settings. In May 2018, we announced the resubmission of the new drug application, or NDA, for DSUVIA to the U.S. Food and Drug Administration, or FDA. We anticipate a six-month review by the FDA, which assigned a Prescription Drug User Fee Act, or PDUFA, goal date of November 3, 2018. On June 27, 2018, we announced that the European Commission, or EC, had adopted the positive opinion of the Committee for Medicinal Products for Human Use for DZUVEO and approved DZUVEO, which means that DZUVEO can be commercialized in the European Economic Area (which includes the 28 European Union member states as well as Norway, Iceland and Liechtenstein), or EEA.

We anticipate developing a distribution capability and commercial organization to market and sell DSUVIA, if approved, in the United States by ourselves, and potentially, in EEA countries with strategic partners. In geographies where we decide not to commercialize ourselves, we may seek to out-license commercialization rights. We plan to resubmit our NDA for Zalviso in the second half of 2018. If we are successful in obtaining approval of Zalviso in the United States, we plan to potentially promote Zalviso either by ourselves or with strategic partners. Zalviso has been approved by the European Commission and is authorized for marketing in the EEA, and it is currently being commercialized by Grünenthal GmbH, or Grünenthal, and has been used by over 21,000 patients through March 31, 2018.

We have chosen sufentanil as the active ingredient for our current product candidates. Opioids have been utilized for pain relief for centuries and are the standard-of-care for the treatment of moderate-to-severe acute pain. Sufentanil, a

high-therapeutic index opioid, which has no active metabolites, is available as an injectable in several markets around the world and is used by anesthesiologists for induction of sedation or as an epidural; however, the injectable formulation is not suitable for the treatment of acute pain. Sufentanil has many pharmacological advantages over other opioids. Published studies demonstrate that sufentanil produces significantly less respiratory depressive effects relative to its analgesic effects compared to other opioids, including morphine and fentanyl. These third-party clinical results correlate well with preclinical trials demonstrating sufentanil's high therapeutic index, or the ratio of the toxic dose to the therapeutic dose of a drug, used as a measure of the relative safety of the drug for a particular treatment. Accordingly, we believe that sufentanil can be developed to provide an effective and well-tolerated treatment for acute pain.

We have created a proprietary sublingual (under the tongue) formulation of sufentanil intended for the treatment of moderate-to-severe acute pain. The sublingual formulation is designed to retain the therapeutic value of sufentanil with a novel delivery device to provide a non-invasive route of administration. Sufentanil is highly lipophilic that has shown rapid absorption in the mucosal tissue, or fatty cells, found under the tongue, resulting in rapid transit across the blood-brain barrier to reach the mu-opioid receptors in the brain. The sublingual route of delivery used by DSUVIA and Zalviso has been found in clinical studies to provide a predictable onset of analgesia. The sublingual delivery system also eliminates the risk of intravenous, or IV, complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV infusion pump, or IV line, DSUVIA and Zalviso may allow for ease of patient mobility.

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Financial Update

Our financial statements for the quarter ended June 30, 2018 will not be available until after this offering is completed and consequently will not be available to you prior to investing in this offering. Based upon preliminary estimates and information available to us as of the date of this prospectus supplement, we estimate that we had approximately \$50 million of cash, cash equivalents and short-term investments as of June 30, 2018, which we believe will be sufficient to fund our operations through at least the next 12 months. This estimate of our cash, cash equivalents and short-term investments as of June 30, 2018 is preliminary, has not been reviewed and is subject to change upon completion of our financial statement closing procedures. Additional information and disclosure would be required for a more complete understanding of our financial position and results of operations as of June 30, 2018.

Corporate Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005 and changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006. Our principal executive offices are located at 351 Galveston Drive, Redwood City, California 94063, 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 | shares |
| Common stock to be outstanding immediately after this offering | shares (or exercised in full) shares if the underwriters' option to purchase additional shares is |
| Option to purchase additional shares | We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement. |
| Use of proceeds | We intend to use the net proceeds from this offering for general corporate purposes, including funding of early commercialization efforts. See "Use of Proceeds" on page S-7 of this prospectus supplement. |
| Listing | Our common stock is listed on the Nasdaq Global Market under the symbol "ACRX." |
| Risk Factors | An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-4 of this prospectus supplement, on page 4 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement. |

Outstanding Shares

The number of shares of common stock outstanding immediately after this offering is based on 50,991,444 shares of common stock outstanding as of March 31, 2018. This number excludes:

176,730 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2018, at a weighted average exercise price of \$3.07 per share;

10,375,368 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted average exercise price of \$3.84 per share;

2,335,743 shares of common stock issued and sold under our existing Sales Agreement since March 31, 2018, at a weighted average sales price of \$3.26 per share; and

up to an aggregate of 3,433,647 shares of common stock reserved for future issuance under our 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan.

In addition, the number of shares outstanding immediately after this offering excludes shares of common stock that we may sell pursuant to our an Controlled Equity OfferingSM Sales Agreement, or the Sales Agreement, that we entered into with Cantor Fitzgerald & Co., or Cantor, on June 21, 2016. Under the Sales Agreement, we may issue and sell shares of our common stock having an aggregate offering price of up to \$40 million from time to time after the expiration of the 60-day lock-up period applicable to us and described in “Underwriting” in such amounts as we may determine, subject to certain limitations contained therein and under applicable securities laws. As of the date of this prospectus, we had issued and sold an aggregate of 7.7 million shares of common stock pursuant to the Sales Agreement, for which we had received net proceeds of approximately \$23.1 million, after deducting commissions, fees and expenses of \$0.7 million.

Except as otherwise indicated, all information included or incorporated by reference in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

RISK FACTORS

An investment 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 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 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. 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.

Risks Relating to this Offering

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

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. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

You may experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the public offering price per share of our common stock is higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of approximately \$ per share, based upon the public offering price of \$ per share and our net tangible book value as of March 31, 2018, after giving effect to this offering. See “Dilution” for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. In addition, we have a significant number of stock options outstanding. To the extent that outstanding stock options or warrants have been or may be exercised, investors purchasing our common stock in this offering may experience further dilution.

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 Sales Agreement with Cantor, or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share paid by any investor 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 that are superior to those of 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.

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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated herein 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 our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these 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” these terms or other comparable terminology and similar expressions intended to identify forward-looking statements. These forward-looking statements may also use different phrases. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These statements reflect our current views with respect to future events, are based on current expectations, assumptions, estimates and projections about our business and our industry, and are subject to risks and uncertainties. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus supplement and the accompanying prospectus, including the information incorporated herein and therein by reference, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

our ability to consummate this offering in the size and manner described herein;

our ability to obtain, without further delays, and maintain regulatory approval of DSUVIA in the United States and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

our ability to commercialize DZUVEO in Europe, including our ability to potentially secure a strategic partner to whom we would out-license our commercialization rights;

our ability to successfully execute the pathway towards a resubmission of the ZALVISO NDA and subsequently obtain, without further delays, and maintain regulatory approval of ZALVISO in the United States and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

the outcome of any potential FDA Advisory Committee meeting held for any of our product candidates;

our ability to manufacture and supply ZALVISO to Grünenthal in accordance with their forecast and our Manufacture and Supply Agreement with Grünenthal;

the status of our Collaboration and License Agreement with Grünenthal or any other future potential collaborations, including potential milestones and royalty payments under such agreement and obligations under our Purchase and Sale Agreement with PDL BioPharma, Inc.;

our plans to research, develop and commercialize our product candidates;

our ability to attract additional collaborators with development, regulatory and commercialization expertise;

our ability to successfully retain our key scientific, engineering, medical or management personnel and hire new personnel as needed;

the size and growth potential of the markets for our product candidates, and our ability to serve those markets;

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our ability to successfully commercialize our product candidates;

the rate and degree of market acceptance of our product candidates;

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;

our ability to manufacture and supply DSUVIA, if approved, in support of any potential U.S. commercial launch;

our ability to manufacture and supply DZUVEO in support of the European commercial launch;

our ability to obtain adequate government or third-party payer reimbursement;

regulatory developments in the United States and foreign countries;

the performance of our third-party suppliers and manufacturers;

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 our product candidates.

We discuss in greater detail, and incorporate by reference into this prospectus supplement in their entirety, many of these risks under the headings “Risk Factors” on page S-4 of this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2017 and in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018. 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.

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.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase additional shares of common stock, in each case based on the public offering price of \$ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for general corporate purposes, including funding of early commercialization efforts.

The amounts and timing of our use of the net proceeds from this offering 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 high-quality, short-term, interest-bearing instruments.

DIVIDEND POLICY

To date, we have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our existing credit facility. Regardless of the restrictions under our existing credit facility or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

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DILUTION

Our net tangible book value as of March 31, 2018 was approximately \$(46.9) million, or \$(0.92) per share of common stock. We calculate tangible book value per share by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of March 31, 2018. If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share paid by purchasers of shares of our common stock in this offering and our as adjusted net tangible book value per share immediately after this offering.

After giving effect to the sale of _____ shares of our common stock in this offering at the public offering price of \$ _____ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2018 would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of \$ _____ per share to new investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

| | | |
|---|----|--------|
| Public offering price per share | | \$ |
| Net tangible book value per share as of March 31, 2018 | \$ | (0.92) |
| Increase per share attributable to investors purchasing our common stock in this offering | | |
| As adjusted net tangible book value per share after this offering | | |
| Dilution per share to investors purchasing our common stock in this offering | | \$ |

If the underwriters exercise in full their option to purchase _____ additional shares of common stock at the public offering price of \$ _____ per share, the as adjusted net tangible book value after this offering would be \$ _____ per share, representing an increase in net tangible book value of \$ _____ per share to existing stockholders and

immediate dilution of \$ _____ per share to new investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 50,991,444 shares of common stock outstanding as of March 31, 2018 and exclude:

176,730 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2018, at a weighted average exercise price of \$3.07 per share;

10,375,368 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted average exercise price of \$3.84 per share;

2,335,743 shares of common stock issued and sold under our existing Sales Agreement since March 31, 2018, at a weighted average sales price of \$3.26 per share; and

up to an aggregate of 3,433,647 shares of common stock reserved for future issuance under our 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan.

In addition, the number of shares outstanding immediately after this offering excludes shares of common stock that we may sell pursuant to the Sales Agreement with Cantor. Under the Sales Agreement, we may issue and sell shares of our common stock having an aggregate offering price of up to \$40 million from time to time after the expiration of the 60-day lock-up period applicable to us and described in “Underwriting” in such amounts as we may determine, subject to certain limitations contained therein and under applicable securities laws. As of the date of this prospectus, we had issued and sold an aggregate of 7.7 million shares of common stock pursuant to the Sales Agreement, for which we had received net proceeds of approximately \$23.1 million, after deducting commissions, fees and expenses of \$0.7 million.

To the extent that options or warrants outstanding as of March 31, 2018 have been or are exercised, or other shares are issued, including pursuant to the Sales Agreement with Cantor, investors purchasing shares of common stock in this offering could experience further dilution. In addition, we may choose to raise capital in addition to the amounts remaining available to be sold under our Sales Agreement with Cantor due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity securities, the issuance of those securities could result in further dilution to our stockholders.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated _____, 2018, between us and Cantor Fitzgerald & Co., 499 Park Avenue, New York, New York 10022, as representative of the underwriters named below, or the Representative, and the sole book-running manager of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally, or not jointly, to purchase from us, the shares of common stock shown opposite its name below:

| <u>Underwriter</u> | <u>Number of Shares</u> |
|----------------------------|-------------------------|
| Cantor Fitzgerald & Co. | |
| H.C. Wainwright & Co., LLC | |

Total

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of _____ shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to certain conditions, to purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment as indicated in the table above.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallocate, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the initial offering, the Representative may change the offering price and other selling terms.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

| | Per Share | | Total | |
|--|--|---|--|---|
| | Without Option to Purchase Additional Shares | With Option to Purchase Additional Shares | Without Option to Purchase Additional Shares | With Option to Purchase Additional Shares |
| Public offering price | \$ | \$ | \$ | \$ |
| Underwriting discounts and commissions | \$ | \$ | \$ | \$ |
| Proceeds to us, before expenses | \$ | \$ | \$ | \$ |

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have also agreed to reimburse the underwriters for up to \$ of certain of their counsels' fees and expenses, which reimbursed fee is deemed underwriting compensation for this offering by FINRA.

Listing

Our common stock is listed on The Nasdaq Global Market under the trading symbol "ACRX."

No Sales of Similar Securities

We, our officers and our directors have agreed, subject to certain specified exceptions, not to directly or indirectly, for a period of 60 days after the date of the underwriting agreement:

sell, offer to sell, contract to sell or lend, effect any short sale or establish or increase a “put equivalent position” (as defined in Rule 16a-1(h) under the Exchange Act) or liquidate or decrease any “call equivalent position” (as defined in Rule 16a-1(b) under the Exchange Act), pledge, hypothecate or grant any security interest in, or in any other way transfer or dispose of, in each case whether effected directly or indirectly, any shares of common stock or options or warrants or other rights to acquire common stock or any securities exchangeable or exercisable for or convertible into common stock currently or hereafter owned either of record or beneficially,

enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of any shares of common stock or options or warrants or other rights to acquire common stock or any securities exchangeable or exercisable for or convertible into common stock, or

publicly announce an intention to do any of the foregoing.

In addition, we and each such person agrees that, without the prior written consent of Cantor Fitzgerald & Co., we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions in the immediately preceding paragraph do not apply in certain circumstances, including, with respect to our directors and officers, transfers:

as a bona fide gift or gifts;

by will or intestate succession;

to any trust for the benefit of the undersigned or the immediate family of the undersigned (within the meaning of Rule 16a-1(e) under the Exchange Act);

to an affiliate of the party or distributions to partners, members of stockholders of the party, if such transfer is not for value;

to us in full or partial payment of exercise or purchase prices or to satisfy tax withholding obligations upon settlement, vesting or exercise of any equity award or warrant granted by us pursuant to our equity incentive plans disclosed in this prospectus;

pursuant to a sale or an offer to purchase 100% of our outstanding common stock, whether pursuant merger, tender offer or otherwise, provided that in the event such merger, tender offer or other transaction is not completed, such securities held by a party will remain subject to the lock-up agreement;

pursuant to a trading plan pursuant to Rule 10b-5 under the Exchange Act entered into prior to the date of the lock-up agreement, or the entrance into a trading plan pursuant to Rule 10b-5 under the Exchange Act, provided that any such plan entered into after the date of the lock-up agreement does not permit the sale of any common stock during the restricted period and no public announcement or filing is made regarding such plan during the restricted period; and

In our case, the restrictions described above do not apply in certain circumstances, including certain issuances upon exercise, vesting or conversion of stock options, restricted stock units, warrants, rights or convertible securities outstanding on the date of the lock-up agreement or pursuant to our equity incentive plans disclosed in this prospectus.

Cantor Fitzgerald & Co. may, in its sole discretion and at any time or from time to time before the termination of the 60-day period release all or any portion of the securities subject to lock-up agreements.

Market Making, Stabilization and Other Transactions

The underwriters may make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, may end any of these activities at any time.

Passive Market Making

The underwriters may also engage in passive market making transactions in our common stock on the NASDAQ in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters are not required to engage in passive market making and, if commenced, may end passive market making activities at any time.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters, selling group members (if any) or their affiliates. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in a wide range of activities for their own accounts and the accounts of customers, which may include, among other things, corporate finance, mergers and acquisitions, merchant banking, equity and fixed income sales, trading and research, derivatives, foreign exchange, futures, asset management, custody, clearance and securities lending. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of its business, the underwriters and their respective affiliates may, directly or indirectly, hold long or short positions, trade and otherwise conduct such activities in or with respect to debt or equity securities and/or bank debt of, and/or derivative products. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Stamp Taxes

If you purchase shares of common stock offered in this prospectus supplement, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus supplement.

NOTICE TO INVESTORS

Canada

This prospectus supplement constitutes an “exempt offering document” as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the common stock. No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this prospectus supplement or on the merits of the common stock and any representation to the contrary is an offence.

Canadian investors are advised that this prospectus supplement has been prepared in reliance on section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (“NI 33-105”). Pursuant to section 3A.3 of NI 33-105, this prospectus supplement is exempt from the requirement that the company and the underwriter(s) provide investors with certain conflicts of interest disclosure pertaining to “connected issuer” and/or “related issuer” relationships that may exist between the company and the underwriter(s) as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the common stock in Canada is being made on a private placement basis only and is exempt from the requirement that the company prepares and files a prospectus under applicable Canadian securities laws. Any resale of the common stock acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, pursuant to a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the common stock will be deemed to have represented to the company and the underwriter(s) that the investor (i) is purchasing the common stock as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an “accredited investor” as such term is defined in section 1.1 of National Instrument 45-106

Prospectus Exemptions (“NI 45-106”) or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a “permitted client” as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this prospectus supplement does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the common stock and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the common stock or with respect to the eligibility of the common stock for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum (such as this prospectus supplement), including where the distribution involves an “eligible foreign security” as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a “misrepresentation” as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur Canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.*

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or

a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each Member State of the European Economic Area , no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the relevant competent authority in that Member State in accordance with the Prospectus Directive, except that an offer of such securities may be made to the public in that Member State:

to any legal entity which is a “qualified investor” as defined in the Prospectus Directive;

to fewer than 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative of the underwriters for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

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provided that no such offer of securities shall require the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer to the public” in relation to any securities in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive), and includes any relevant implementing measure in the Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

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

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

where no consideration is given for the transfer; or

where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals”, each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are

qualified investors (as defined in the Prospectus Directive) that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the “Order”, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated or caused to be communicated. Each such person is referred to herein as a “Relevant Person”.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

Any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (the “FSMA”)) may only be communicated or caused to be communicated in connection with the issue or sale of the securities in circumstances in which Section 21(1) of the FSMA does not apply. All applicable provisions of the FSMA must be complied with in respect of anything done by any person in relation to the securities in, from or otherwise involving the United Kingdom.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP. Latham & Watkins LLP is counsel to the underwriters in connection with this offering.

EXPERTS

OUM & Co. LLP, independent registered public accounting firm, has audited our consolidated financial statements as of December 31, 2017 and 2016 included in our Annual Report on Form 10-K, 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 June 14, 2017, 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>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information

contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of the prospectus supplement and before the sale of all the securities covered by this prospectus supplement (Commission File No. 001-35068):

our Annual Report on Form 10-K for the year ended December 31, 2017, which was filed on March 9, 2018;

the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 23, 2018;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, which was filed on May 10, 2018;

our Current Reports on Form 8-K, which were filed on March 27, 2018, April 12, 2018, June 15, 2018 and July 2, 2018; 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.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Requests should be directed to: AcelRx Pharmaceuticals, Inc., Attn: Secretary, 351 Galveston Drive, Redwood City, CA 94063, telephone: (650) 216-3500.

Prospectus

\$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 "ACELRX." On May 31, 2017, the last reported sale price of our common stock was \$2.50 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 4 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 June 14, 2017.

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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 the treatment of acute pain. Our lead product candidate, DSUVIA™ (known as ARX-04 outside of the United States), and our follow-on product candidate, ZALVISO®, utilize sublingual sufentanil, delivered via a non-invasive route of sublingual administration. We anticipate developing a distribution capability and commercial organization to market and sell DSUVIA in the United States by ourselves, and potentially, in certain European Economic Area, or EEA, countries with strategic partners. In geographies where we decide not to commercialize ourselves, we may seek to out-license commercialization rights. We intend to seek regulatory approval for ZALVISO in the United States and, if successful, potentially promote ZALVISO as a follow-on product to DSUVIA, either by ourselves or with strategic partners.

We have chosen sufentanil as the therapeutic ingredient for our current product candidates. Opioids have been utilized for pain relief for centuries and are the standard-of-care for the treatment of moderate-to-severe acute pain. Sufentanil is available as an injectable in several markets around the world and is used by anesthesiologists for induction of sedation or as an epidural; however, the injectable formulation is not suitable for the treatment of acute pain. We have created a proprietary sublingual (under the tongue) tablet formulation of sufentanil intended for the treatment of moderate-to-severe acute pain. The sublingual formulation retains the therapeutic value of sufentanil and novel delivery devices provide a non-invasive route of administration. Sufentanil is highly lipophilic which provides for rapid absorption in the mucosal tissue, or fatty cells, found under the tongue, and for rapid transit across the blood-brain barrier to reach the mu-opioid receptors in the brain. The sublingual route of delivery used by DSUVIA and ZALVISO provides a recognized onset of analgesia. The sublingual delivery system also eliminates the risk of intravenous, or IV, complications, such as catheter-related infections. In addition, because patients do not require

direct connection to an IV infusion pump, or IV line, DSUVIA and ZALVISO may allow for ease of patient mobility.

Corporate 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. We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.accelrx.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC.

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, research and development expenses, general and administrative expenses, for making scheduled payments under our debt facility and capital expenditures. See “Use of Proceeds” in this prospectus.

NASDAQ Global Market Listing

Our common stock is listed on the NASDAQ Global Market under the symbol “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 occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled “Special Note Regarding Forward-Looking Statements.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

our ability to obtain, without delays, and maintain regulatory approval of DSUVIA™ (sufentanil sublingual tablet, 30 mcg), formerly known as ARX-04 in the United States, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

our ability to obtain, without delays, and maintain regulatory approval of ARX-04 (sufentanil sublingual tablet, 30 mcg) in the European Union, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

the success, cost and timing of our product development activities and clinical trials, including the additional clinical study, IAP312, for ZALVISO[®] (sufentanil sublingual tablet system);

our ability to successfully execute the pathway towards a resubmission of the ZALVISO New Drug Application, or NDA, including our ability to satisfactorily conduct the clinical study, IAP312, requested by the U.S. Food and Drug Administration, or FDA, and any additional studies or activities that may be required by the FDA in order to resubmit the ZALVISO NDA, and subsequently obtain, without further delays, and maintain regulatory approval of ZALVISO in the United States and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

our ability to manufacture and supply ZALVISO to Grünenthal GmbH, or Grünenthal, in accordance with their forecast and the Manufacture and Supply Agreement with Grünenthal;

the outcome of any potential FDA Advisory Committee meetings held for any of our product candidates, including the anticipated joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee to obtain committee input on the safety and efficacy of DSUVIA;

the status of the Collaboration and License Agreement with Grünenthal or any other future potential collaborations, including potential milestones and royalty payments under the Grünenthal agreement and obligations under the Purchase and Sale Agreement with PDL BioPharma, Inc., or PDL;

our plans to research, develop and commercialize our product candidates;

our ability to attract additional collaborators with development, regulatory and commercialization expertise;

our ability to successfully retain our key scientific, engineering, medical or management personnel and hire new personnel as needed;

the size and growth potential of the markets for our product candidates, and our ability to serve those markets;

our ability to successfully commercialize our product candidates;

the rate and degree of market acceptance of our product candidates;

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;

our ability to manufacture and supply DSUVIA, if approved, in support of any potential U.S. commercial launch;

our ability to obtain adequate government or third-party payor reimbursement;

regulatory developments in the United States and foreign countries;

the performance of our third party suppliers and manufacturers;

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 our product candidates.

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

USE OF PROCEEDS

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, research and development expenses, general and administrative expenses, for making scheduled payments under our debt facility and capital expenses, or any other purpose we describe in the applicable prospectus supplement.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges for each of the periods in the table below and, accordingly, we have not included a ratio of earnings to fixed charges for these periods. The table below sets forth our deficiency of earnings to cover fixed charges on a historical basis for the periods indicated (in millions). This table is qualified by the more detailed information appearing in the computation table found in Exhibit 12.1 to the registration statement of which this prospectus is a part.

| | Three Months Ended March 31, | Years Ended December 31, | | | | |
|---|---|---------------------------------|-------------|-------------|-------------|-------------|
| | | 2016 | 2015 | 2014 | 2013 | 2012 |
| | 2017 | | | | | |
| Deficiency of Earnings to Cover Fixed Charges | \$(15,551) | \$(43,191) | \$(23,639) | \$(33,353) | \$(23,426) | \$(33,363) |

Earnings consist of pre-tax loss from continuing operations and fixed charges. Fixed charges consist of the sum of (i) interest expense, (ii) non-cash interest expense on liability related to future sale of royalties, (iii) amortized premiums, debt discounts and capitalized interest related to indebtedness, and (iv) an estimate of the interest within rental expense that is considered by us to be a reasonable approximation of the interest factor, which is zero.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 100,000,000 shares of common stock, \$0.001 par value, and 10,000,000 shares of preferred stock, \$0.001 par value. A description of 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 amended and restated 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 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 amended and restated 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 amended and restated 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 amended and restated certificate of incorporation and amended and restated 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 amended and restated certificate of incorporation 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 amended and restated 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 amended and restated 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.

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 250 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 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 depositary for such global security or securities;

if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;

if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;

additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;

additions to or changes in the Events of Default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;

additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;

additions to or changes in the provisions relating to satisfaction and discharge of the indenture;

additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

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 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 a 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 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 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 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, depository 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 depository on behalf of other financial institutions that participate in the depository’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 depository or its participants. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository 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 depository 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 depository’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 depository 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 depository'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 depository. 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 depository. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depository 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 depository, its nominee or a successor depository, 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 depositary'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 depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

the depositary 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 depositary'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 depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary 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 depositary, 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 as of December 31, 2016 and 2015 and for each of the two years in the period ended December 31, 2016 included in our Annual Report on Form 10-K, 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 report, given on their authority as experts in accounting and auditing.

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements for the period ended December 31, 2014 included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement of which this prospectus supplement and the accompanying prospectus form a part. Such financial statements are incorporated by reference in reliance on Ernst & Young 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>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

our Annual Report on Form 10-K for the year ended December 31, 2016, which was filed on March 3, 2017;
the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016 from our definitive proxy statement relating to our 2017 annual meeting of stockholders, which was filed on April 28, 2017;
our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, which was filed on May 8, 2017;
our Current Reports on Form 8-K which were filed on January 9, 2017, February 9, 2017, February 16, 2017, March 7, 2017, March 10, 2017, May 10, 2017 and June 5, 2017; and
the description of our common stock in our registration statement on Form 8-A filed with the SEC on February 1, 2011.

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

(650) 216-3500

Attn: Secretary

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Shares

Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Cantor

Lead Manager

H.C. Wainwright & Co.

, 2018
