

ARDELYX, INC.
Form 424B5
August 10, 2018

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PROSPECTUS SUPPLEMENT

Up to \$50,000,000

Common Stock

We have entered into a sales agreement with Leerink Partners LLC, or Leerink, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer and sell shares of our common stock, \$0.0001 par value per share, having an aggregate offering price of up to \$50,000,000 from time to time through Leerink, acting as agent.

Our common stock is listed on The Nasdaq Global Market under the symbol "ARDX." On August 7, 2018, the last reported sale price of our common stock on The Nasdaq Global Market was \$4.20 per share.

Sales of our common stock, if any, under this prospectus supplement may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The Nasdaq Global Market or any other existing trading market for our common stock. Leerink will act as sales agent on a best efforts basis and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Leerink and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Leerink will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. In connection with the sale of our common stock on our behalf, Leerink will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Leerink will be deemed to be underwriting commissions or discounts.

Investing in our common stock involves a high degree of risk. Before making an investment decision, please read the information under the heading "Risk Factors" beginning on page S-6 of this prospectus supplement 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 is truthful or complete. Any representation to the contrary is a criminal offense.

Leerink Partners

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the U.S. Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. By using a shelf registration statement, we may offer shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time under this prospectus supplement at prices and on terms to be determined by market conditions at the time of offering.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

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

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

When we refer to "Ardelyx" "we," "our," "us" and the "Company" in this prospectus, we mean Ardelyx, Inc., unless otherwise specified. When we refer to "you," we mean the holders of common stock of the Company.

Ardelyx® and our logo are some of our trademarks used in this prospectus. This prospectus also includes trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus supplement appear without the ® and symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

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MARKET, INDUSTRY AND OTHER DATA

This prospectus, including the information incorporated by reference, contains estimates, projections and other information concerning our industry, our business, and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary provides a general overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the information incorporated by reference, before deciding to invest in our common stock. Investors should carefully consider the information set forth under "Risk Factors" beginning on page S-6 and incorporated by reference to our annual report on Form 10-K, our quarterly reports on Form 10-Q and our current reports on Form 8-K that include risk factors.

Ardelyx, Inc.

Overview

We are a specialized biopharmaceutical company focused on developing first-in-class, disruptive medicines for the treatment of renal diseases. Our primary therapeutic focus is on treating people with renal diseases, which affect both the heart and the kidneys. This includes patients with end-stage renal disease, or ESRD, who suffer from elevated serum phosphorus, or hyperphosphatemia; patients with chronic kidney disease, or CKD, and/or heart failure patients with elevated serum potassium, or hyperkalemia. We have also developed a number of programs directed toward treating gastrointestinal, or GI, disorders, including the treatment of irritable bowel syndrome with constipation, or IBS-C.

Our portfolio is led by the development of tenapanor, a first-in-class inhibitor of NHE3. In our renal pipeline, tenapanor is being evaluated in a second Phase 3 trial for the treatment of hyperphosphatemia in patients with ESRD who are on dialysis. This registration trial follows a successful first Phase 3 trial completed in 2017, which achieved statistical significance for the primary endpoint. We are also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia. We believe that both tenapanor and RDX013 have the potential to provide treatment options that are differentiated significantly from binders, the current standards of care in both of these markets. We believe our small molecule approach to treating these conditions could significantly reduce the pill burden for patients, leading to higher compliance, and offer completely new mechanisms of action that interact with receptors in the gut, potentially allowing improved efficacy in some patients.

In addition to the development for renal diseases, we have developed tenapanor for the treatment of patients with IBS-C. In 2017, we completed the T3MPO program for this indication, including two Phase 3 trials, both of which achieved statistical significance for the primary endpoint, and a long-term safety extension study. We believe that data from the T3MPO program collectively demonstrated the ability of tenapanor to provide sustained relief of constipation and reduced abdominal pain with a generally favorable tolerability profile. Based on the results of the T3MPO clinical program in IBS-C, we are preparing to submit our first New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, early in the fourth quarter of 2018 for tenapanor for the treatment of IBS-C.

We believe that tenapanor for the treatment of hyperphosphatemia could represent a market opportunity of between \$500 million and \$700 million in the United States and that tenapanor for the treatment of IBS-C could represent a market opportunity of over \$500 million in the United States.

Corporate Information

We were founded in October 2007 as a Delaware corporation under the name Nteryx, Inc. We changed our name to Ardelyx, Inc. in June 2008. Our principal executive offices are located at 34175 Ardenwood Blvd., Suite 200, Fremont, CA 94555, and our telephone number is (510) 745-1700. Our website address is www.ardelyx.com. The information on, or that can be accessed through, our

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website is not part of this prospectus. We have included our website address as an inactive textual reference only.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering of common stock (December 31, 2019), (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (4) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$50,000,000.
Common stock to be outstanding after this offering	Up to 73,958,512 shares (as more fully described in the notes following this table), assuming sales of 11,904,761 shares of our common stock in this offering at an offering price of \$4.20 per share, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 7, 2018. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	"At the market offering" that may be made from time to time through our sales agent, Leerink Partners LLC. See "Plan of Distribution" on page S-12.
Use of Proceeds	We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, among other things, increasing our working capital and funding research and development, and capital expenditures. See "Use of Proceeds" on page S-9.
Risk Factors	You should read the "Risk Factors" section of this prospectus and in the documents incorporated by reference in this prospectus for a discussion of factors to consider before deciding to purchase shares of our common stock.
Symbol on The Nasdaq Global Market	"ARDX"

The number of shares of common stock to be outstanding after this offering is based on 62,053,751 shares of common stock outstanding as of June 30, 2018, and excludes, in each case as of June 30, 2018:

5,098,029 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$9.09 per share;

2,172,899 shares of common stock issuable upon the exercise of outstanding warrants having an exercise price of \$13.91 per share;

611,445 shares of common stock issuable upon the settlement of outstanding restricted stock units;

1,796,753 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan;

110,088 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan; and

1,000,000 shares of common stock reserved for issuance pursuant to future awards under our 2016 Employment Commencement Inducement Plan.

Unless otherwise stated, all information contained in this prospectus supplement reflects an assumed public offering price of \$4.20 per share, which was the last reported sale price of our common stock on The Nasdaq Global Market on August 7, 2018.

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RISK FACTORS

You should consider carefully the risks described below and discussed under the section captioned "Risk Factors" contained in our quarterly report for the quarterly period ended September 30, 2017, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, each of which is incorporated by reference in this prospectus in their entirety, together with other information in this prospectus, and the information and documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose 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.

Additional Risks Relating to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used for general corporate purposes, which may include, among other things, increasing our working capital and funding research and development, and capital expenditures. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

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

The price per share of our common stock being offered may be higher than the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 11,904,761 shares are sold at a price of \$4.20 per share, the last reported sale price of our common stock on The Nasdaq Global Market on August 7, 2018, for aggregate proceeds of \$50,000,000 in this offering, and after deducting commissions and estimated aggregate offering expenses payable by us, you will suffer immediate and substantial dilution of \$1.34 per share, representing the difference between the as adjusted net tangible book value per share of our common stock as of June 30, 2018 after giving effect to this offering and the assumed offering price. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

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

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering. As of June 30, 2018, 8,616,315 shares of common stock are either subject to outstanding options or restricted stock unit awards, or reserved for future issuance under our equity incentive plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules. An additional 2,172,899 shares of common stock that are subject to outstanding warrants are eligible for sale in the public market.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering, contain forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

our expectation regarding the timing of our filing of a New Drug Application with the U.S. Food and Drug Administration requesting approval to market tenapanor for patients with irritable bowel syndrome with constipation, or IBS-C;

our expectation regarding the timing of receipt of results from our second Phase 3 clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in patients with end-stage renal disease, or ESRD, on dialysis;

our expectations regarding our plans for and our participation in the commercialization of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, including our expectations regarding our plans to build our own sales and marketing organization to market and sell tenapanor for such indication;

our plans to seek one or more collaboration partners to commercialize tenapanor for IBS-C;

our expectations regarding the potential market size and the size of the patient populations for our product candidates;

our plans with respect to our pre-clinical programs;

our ability to identify and validate targets and novel drug candidates using our proprietary drug discovery and design platform including the Ardelyx Primary Enterocyte and Colonocyte Culture System;

the implementation of our business model and strategic plans for our business, product candidates and technology;

estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;

our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012;

our financial performance; and

developments and projections relating to our competitors and our industry.

You should read this prospectus and the documents incorporated by reference herein completely and with the understanding that our actual results may differ materially from what we expect as expressed or implied by our forward-looking statements. In light of the significant risks and uncertainties to which our forward-looking statements are subject, you should not place undue reliance on or regard these statements as a

representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. We discuss many of these risks in

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greater detail in the documents incorporated by reference herein, including under the heading "Risk Factors." These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus and the documents incorporated by reference herein and therein, regardless of the time of delivery of this prospectus or any sale of our common stock and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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USE OF PROCEEDS

The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Leerink as a source of financing. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, development of tenapanor, including clinical programs and manufacturing scale up, process validation and other pre-commercial activities, increasing our working capital and funding research and development and capital expenditures.

The amounts and timing of our actual expenditures will depend on numerous factors, including our clinical and pre-commercial activities with respect to tenapanor for the treatment of hyperphosphatemia in end-stage renal disease on dialysis, our manufacturing efforts for tenapanor, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in interest-bearing investment-grade, securities, certificates of deposit or government securities.

Table of Contents**DILUTION**

Our historical net tangible book value as of June 30, 2018 was approximately \$163.4 million, or \$2.63 per share. Our net tangible book value represents total tangible assets less total liabilities and convertible preferred stock, all divided by the number of shares of common stock outstanding on June 30, 2018. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering.

After giving effect to the sale of our common stock in the aggregate amount of \$50.0 million in this offering at an assumed offering price of \$4.20, the last reported sale price of our common stock on The Nasdaq Global Market on August 7, 2018, and after deducting commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2018 would have been approximately \$211.7 million, or \$2.86 per share. This represents an immediate increase in net tangible book value of \$0.23 per share to existing stockholders and immediate dilution in net tangible book value of \$1.34 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$ 4.20
Net tangible book value per share as of June 30, 2018	\$ 2.63
Increase per share attributable to new investors	\$ 0.23
As adjusted net tangible book value per share after this offering	\$ 2.86
Dilution per share to new investors	\$ 1.34

The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$4.20 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would cause our as adjusted net tangible book value per share after the offering to be \$3.02 per share and would increase the dilution in net tangible book value per share to new investors to \$2.18 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$4.20 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would cause our as adjusted net tangible book value per share after the offering to be \$2.70 per share and would decrease the dilution in net tangible book value per share to new investors to \$0.50 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

To the extent that outstanding options are exercised or outstanding restricted stock awards vest, investors purchasing our common stock in this offering will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

The above discussion and table are based on 62,053,751 shares of common stock outstanding as of June 30, 2018, and excludes, in each case as of June 30, 2018:

5,098,029 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$9.09 per share;

2,172,899 shares of common stock issuable upon the exercise of outstanding warrants having an exercise price of \$13.91 per share;

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611,445 shares of common stock issuable upon the settlement of outstanding restricted stock units;

1,796,753 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan;

110,088 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan; and

1,000,000 shares of common stock reserved for issuance pursuant to future awards under our 2016 Employment Commencement Inducement Plan.

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PLAN OF DISTRIBUTION

We have entered into a sales agreement with Leerink Partners LLC, or Leerink, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$50,000,000 from time to time through Leerink acting as agent. The sales agreement will be filed as an exhibit to a Current Report on Form 8-K and is incorporated herein by reference.

Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Leerink may sell our common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act, including sales made directly on The Nasdaq Global Market on any other existing trading market for our common stock. We may instruct Leerink not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Leerink may suspend the offering of common stock upon notice and subject to other conditions.

We will pay Leerink commissions, in cash, for its services in acting as agent in the sale of our common stock. Leerink will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Leerink for certain specified expenses, including the fees and disbursements of its legal counsel, in an amount not to exceed \$50,000. We estimate that the total expenses for the offering, excluding discounts and commissions payable to Leerink under the terms of the sales agreement, will be approximately \$205,000.

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

Leerink will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the common stock shares under the terms and subject to the conditions set forth in the sales agreement. In connection with the sale of the common stock on our behalf, Leerink will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Leerink will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Leerink against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the termination of the sales agreement as permitted therein. We and Leerink may each terminate the sales agreement at any time upon ten days' prior notice.

Leerink and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Leerink will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

This prospectus in electronic format may be made available on a website maintained by Leerink and Leerink may distribute this prospectus electronically.

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LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Latham & Watkins LLP, Menlo Park, California. Leerink Partners LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our 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 MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus forms a part. The rules and regulations of the SEC allow us to omit from this prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC under the Exchange Act. You may read and copy this information from the Public Reference Room of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with them which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act between the date of this prospectus and the termination of this offering, provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K:

our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 14, 2018;

the information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 26, 2018;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018 and June 30, 2018, filed with the SEC on May 8, 2018 and August 7, 2018, respectively;

our Current Reports on Form 8-K filed with the SEC on February 12, 2018, May 21, 2018, May 29, 2018, June 14, 2018 and July 9, 2018; and

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the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on June 9, 2014, including any amendments or reports filed for the purpose of updating such description.

These documents may also be accessed on our website at www.ardelyx.com. Except as otherwise specifically incorporated by reference in this prospectus, information contained in, or accessible through, our website is not a part of this prospectus.

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 by writing or telephoning us at the following address:

Ardelyx, Inc.
34175 Ardenwood Blvd., Suite 200
Fremont, CA 94555
(510) 745-1700
Attention: General Counsel

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PROSPECTUS

\$250,000,000

**Common Stock, Preferred Stock, Debt Securities,
Warrants, Purchase Contracts, Units**

We may offer and sell up to \$250,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on The NASDAQ Global Market under the symbol "ARDX." On April 21, 2017, the last reported sale price of our common stock on The NASDAQ Global Market was \$12.50 per share.

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

The date of this prospectus is May 4, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$250,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading "Where You Can Find More Information; Incorporation by Reference."

Neither we nor any underwriter has authorized any other person to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe 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 this prospectus, 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.

When we refer to "Ardelyx," "we," "our," "us" and the "Company" in this prospectus, we mean Ardelyx, Inc., unless otherwise specified. When we refer to "you," we mean the holders of the applicable series of securities.

Ardelyx® and our logo are some of our trademarks used in this prospectus. This prospectus also includes trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus appear without the ® and symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

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WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Section of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our website address is www.ardelyx.com. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus. We have included our website address as an inactive textual reference only.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including any Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on February 17, 2017;

our Current Reports on Form 8-K filed with the SEC on February 15, 2017, March 9, 2017 and March 21, 2017; and

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the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on June 9, 2014, including any amendments or reports filed for the purpose of updating such description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Ardelyx, Inc.
34175 Ardenwood Blvd., Suite 200
Fremont, CA 94555
(510)745-1700
Attention: General Counsel

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

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ABOUT ARDELYX

We are a clinical-stage biopharmaceutical company focused on enhancing the way patients with cardiorenal and gastrointestinal, or GI, diseases are treated by using the gut as the gateway to delivering medicines that matter. We have pioneered the development of small molecule therapeutics that act predominantly in the GI tract, thereby avoiding potentially negative side effects on the rest of the body.

We were founded in October 2007 as a Delaware corporation under the name Nteryx, Inc. Our principal executive offices are located at 34175 Ardenwood Blvd., Suite 200, Fremont, CA 94555, and our telephone number is (510) 745-1700. Our website address is www.ardelyx.com. The information on, or that can be accessed through, our website is not part of this prospectus. We have included our website address as an inactive textual reference only. References in this prospectus to "we," "us," "our," "our company" or "Ardelyx" refer to Ardelyx, Inc.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering of common stock (December 31, 2019), (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.0 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (4) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

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Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS**

The following table sets forth our ratio of earnings to fixed charges for the periods indicated (in thousands). The ratio of earnings to fixed charges is computed by dividing fixed charges into earnings before income taxes plus fixed charges. Fixed charges consist of interest expense and that portion of rental expense deemed representative of interest. We do not have any shares of preferred stock outstanding, so our ratio of earnings to fixed charges and preferred stock dividends for any given period is equivalent to our ratio of earnings to fixed charges. Our earnings have been inadequate to cover fixed charges and preference dividends. The following table sets forth the dollar amount of the deficiency to cover fixed charges for each of the years ended December 31, 2016, 2015, 2014, 2013 and 2012. We have derived the deficiency of earnings to cover fixed charges from our historical financial statements. The following should be read in conjunction with our financial statements, including the notes thereto, and the other financial information included or incorporated by reference herein. See Exhibit 12.1 hereto for additional detail regarding the computation of the deficiency of earnings to cover fixed charges.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
Deficiency of earnings available to cover fixed charges	\$ (112,387)	\$ (29,650)	\$ (3,147)	\$ (6,423)	\$ (9,785)

For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments.

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DESCRIPTION OF CAPITAL STOCK

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, our investor rights agreement and registration rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws, amended and restated investor rights agreement, and registration rights agreement, copies of which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part.

General

Our amended and restated certificate of incorporation authorizes 300,000,000 shares of common stock, \$0.0001 par value per share, and 5,000,000 shares of preferred stock, \$0.0001 par value per share.

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. 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. In addition, the affirmative vote of holders of 66²/₃% of the voting power of all of the then outstanding voting stock will be required to take certain actions, including amending certain provisions of our amended and restated certificate of incorporation, such as the provisions relating to amending our amended and restated bylaws, the classified board and director liability.

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 legally available funds.

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 in this offering will be, fully paid and nonassessable.

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Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Registration Rights

Based on the number of shares outstanding as of December 31, 2016, under our amended and restated investor rights agreement, the holders of approximately 5.6 million shares of common stock, or their transferees have the right to require us to register their shares under the Securities Act of 1933, as amended, or the Securities Act, so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Based on the number of shares outstanding as of December 31, 2016, the holders of approximately 5.6 million shares of our common stock, or their transferees, will be entitled to certain demand registration rights. The holders of at least 25% of these shares can, on not more than two occasions, request that we register all or a portion of their shares.

Piggyback Registration Rights

Based on the number of shares outstanding as of December 31, 2016, in the event that we determine to register any of our securities under the Securities Act (subject to certain exceptions), either for our own account or for the account of other security holders, the holders of approximately 5.6 million shares of our common stock, or their transferees, will be entitled to certain "piggyback" registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to employee benefit plans, the offer and sale of debt securities, or corporate reorganizations or certain other transactions, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. In an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include.

Form S-3 Registration Rights

Based on the number of shares outstanding as of December 31, 2016, the holders of approximately 5.6 million shares of our common stock, or their transferees, are entitled to certain Form S-3 registration rights. The holders of these shares can make a written request that we register their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least \$1.0 million. These stockholders may make an unlimited number of requests for registration on Form S-3. In addition, to fulfill our obligation to file a Form S-3 registration statement on behalf of the holders of 22,016,121 million shares of our common stock,

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including shares issuable upon exercise of warrants, on July 13, 2015 and August 11, 2016, we filed registration statements on Form S-3 (File Nos. 333-205630 and 333-213085) for the resale of an aggregate of 22,016,121 shares of our common stock.

Expenses of Registration

We will pay the registration expenses of the holders of the shares registered pursuant to the demand, piggyback and Form S-3 registration rights described above including reasonable fees (up to a maximum of \$35,000) for one counsel for the selling shareholders.

Expiration of Registration Rights

The demand, piggyback and Form S-3 registration rights described above (other than with respect to the Form S-3 registration statements filed on July 13, 2015 and August 11, 2016) will expire, with respect to any particular stockholder, upon the earlier of five years after the consummation of our initial public offering in June 2014 or when that stockholder can sell all of its shares under Rule 144 of the Securities Act during any 90 day period.

Anti-Takeover Effects of Provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws and Delaware Law

Some provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person 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 a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

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Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Special Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, Chief Executive Officer or President, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors; Filling Vacancies

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders, 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. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. Our amended and restated certificate of incorporation provides for the removal of any of our directors only for cause and requires at least a 66²/₃% stockholder vote. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by a resolution of the board of directors unless the board of directors determines that such vacancies shall be filled by the stockholders. This system of electing and removing directors and filling vacancies may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty, or other wrongdoing by, any of our directors, officers, employees or stockholders; any action asserting a claim against us or any of our directors, officers or employees arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; or any action asserting a claim against us or any of our directors, officers or employees that is governed by the internal affairs doctrine. Although our amended and restated certificate of incorporation contains the choice of forum provision described above, it is possible that a

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court could find that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least 66²/₃% of the voting power of our then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Limitations of Liability and Indemnification Matters

Our amended and restated certificate of incorporation contains provisions that limit the liability of our directors for monetary damages for breach of fiduciary duty as a director to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

any breach of the director's duty of loyalty to us or our stockholders;

any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or

any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage.

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The NASDAQ Global Market Listing

Our common stock is listed on The NASDAQ Global Market under the symbol "ARDX."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

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DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a third party to be identified therein. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, "Ardelyx," "we," "our" or "us" refer to Ardelyx, Inc. excluding our subsidiaries, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

the title and ranking of the debt securities (including the terms of any subordination provisions);

the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;

any limit on the aggregate principal amount of the debt securities;

the date or dates on which the principal of the securities of the series is payable;

the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;

the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for

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registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;

the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;

if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;

the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;

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any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and

whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Global Debt Securities and Book-Entry System" below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see "Global Securities."

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have

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a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a "successor person") unless:

we are the surviving corporation or the successor person (if other than Ardelyx) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

"Event of Default" means with respect to any series of debt securities, any of the following:

default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

default in the payment of principal of any security of that series at its maturity;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Ardelyx and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Ardelyx; and

any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of

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that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, 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. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and

the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

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Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets";

to provide for uncertificated securities in addition to or in place of certificated securities;

to add guarantees with respect to debt securities of any series or secure debt securities of any series;

to surrender any of our rights or powers under the indenture;

to add covenants or events of default for the benefit of the holders of debt securities of any series;

to comply with the applicable procedures of the applicable depository;

to make any change that does not adversely affect the rights of any holder of debt securities;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

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reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on

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those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the beneficial owners of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

we may omit to comply with the covenant described under the heading "Consolidation, Merger and Sale of Assets" and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series ("covenant defeasance").

The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient

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in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the beneficial owners of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect of or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability.

This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

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DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;

the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;

the terms of any rights to redeem or call the warrants;

the date on which the right to exercise the warrants will commence and the date on which the right will expire;

United States Federal income tax consequences applicable to the warrants; and

any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled to:

vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of Ardelyx.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify

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in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office

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of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

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DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts for the purchase or sale of:

debt or equity securities issued by us, a basket of such securities, an index or indices of such securities or any combination of the above as specified in the applicable prospectus supplement;

currencies; or

commodities.

Each purchase contract will entitle the holder thereof to purchase or sell, and obligate us to sell or purchase, on specified dates, such securities, currencies or commodities at a specified purchase price, which may be based on a formula, all as set forth in the applicable prospectus supplement. We may, however, satisfy our obligations, if any, with respect to any purchase contract by delivering the cash value of such purchase contract or the cash value of the property otherwise deliverable or, in the case of purchase contracts on underlying currencies, by delivering the underlying currencies, as set forth in the applicable prospectus supplement. The applicable prospectus supplement will also specify the methods by which the holders may purchase or sell such securities, currencies or commodities and any acceleration, cancellation or termination provisions or other provisions relating to the settlement of a purchase contract.

The purchase contracts may require us to make periodic payments to the holders thereof or vice versa, which payments may be deferred to the extent set forth in the applicable prospectus supplement, and those payments may be unsecured or prefunded on some basis. The purchase contracts may require the holders thereof to secure their obligations in a specified manner to be described in the applicable prospectus supplement. Alternatively, purchase contracts may require holders to satisfy their obligations thereunder when the purchase contracts are issued. Our obligation to settle such pre-paid purchase contracts on the relevant settlement date may constitute indebtedness. Accordingly, pre-paid purchase contracts will be issued under the applicable indenture.

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DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

the title of the series of units;

identification and description of the separate constituent securities comprising the units;

the price or prices at which the units will be issued;

the date, if any, on and after which the constituent securities comprising the units will be separately transferable;

a discussion of certain United States federal income tax considerations applicable to the units; and

any other terms of the units and their constituent securities.

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GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in a prospectus supplement, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a "banking organization" within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and
- a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants' accounts, thereby eliminating the need for physical movement of securities certificates. "Direct participants" in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC's records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants' records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC's records reflect only the identity of the direct participants to whose accounts the securities are credited,

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which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depositary or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

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DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

We have obtained the information in this section and elsewhere in this prospectus concerning DTC and DTC's book-entry system from sources that are believed to be reliable, but we take no responsibility for the accuracy of this information.

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PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed 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.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock or preferred stock will be listed on The NASDAQ Global Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short

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positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

If indicated in the applicable prospectus supplement, underwriters or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement, pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions. Delayed delivery contracts will be subject to the condition that the purchase of the securities covered by the delayed delivery contracts will not at the time of delivery be prohibited under the laws of any jurisdiction in the United States to which the purchaser is subject. The underwriters and agents will not have any responsibility with respect to the validity or performance of these contracts.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

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LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Ardelyx, Inc. 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

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

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Up to \$50,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Leerink Partners

August 9, 2018
