

ARDELYX, INC.
Form 424B5
January 07, 2016
Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration Statement No. 333-205631

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated January 6, 2016.

PROSPECTUS SUPPLEMENT

(To Prospectus dated July 20, 2015)

\$75,000,000

Common Stock

We are offering up to \$75,000,000 of shares of our common stock.

Our common stock is listed on The NASDAQ Global Market under the symbol ARDX. On January 5, 2016, the last reported sale price of our common stock on The NASDAQ Global Market was \$16.46 per share.

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-11 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Per Share Total

| | | |
|---|----|----|
| Public offering price | \$ | \$ |
| Underwriting discounts and commissions(1) | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ |

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

We intend to grant the underwriters the right to purchase up to \$11,250,000 of additional shares of our common stock. The underwriters can exercise this right at any time within 30 days after the date of this prospectus supplement.

The underwriters expect to deliver the shares of common stock against payment in New York, New York on or about , 2016.

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.

Citigroup

Leerink Partners

Wedbush PacGrow

JMP Securities

Cantor Fitzgerald & Co.

Ladenburg Thalmann

The date of this prospectus supplement is , 2016

Table of Contents

Table of Contents

Prospectus Supplement

| | |
|--|-------------|
| <u>ABOUT THIS PROSPECTUS SUPPLEMENT</u> | Page S-1 |
| <u>MARKET, INDUSTRY AND OTHER DATA</u> | S-2 |
| <u>PROSPECTUS SUPPLEMENT SUMMARY</u> | S-3 |
| <u>THE OFFERING</u> | S-10 |
| <u>RISK FACTORS</u> | S-11 |
| <u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u> | S-14 |
| <u>USE OF PROCEEDS</u> | S-16 |
| <u>CAPITALIZATION</u> | S-17 |
| <u>DILUTION</u> | S-19 |
| <u>PRICE RANGE OF COMMON STOCK</u> | S-21 |
| <u>DIVIDEND POLICY</u> | S-22 |
| <u>MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS</u> | S-23 |
| <u>UNDERWRITING</u> | S-27 |
| <u>LEGAL MATTERS</u> | S-33 |
| <u>EXPERTS</u> | S-33 |

Prospectus

| | |
|--|----|
| <u>ABOUT THIS PROSPECTUS</u> | 1 |
| <u>WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE</u> | 2 |
| <u>ABOUT ARDELYX</u> | 4 |
| <u>RISK FACTORS</u> | 5 |
| <u>USE OF PROCEEDS</u> | 6 |
| <u>RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS</u> | 7 |
| <u>DESCRIPTION OF CAPITAL STOCK</u> | 8 |
| <u>DESCRIPTION OF DEBT SECURITIES</u> | 13 |
| <u>DESCRIPTION OF WARRANTS</u> | 20 |
| <u>DESCRIPTION OF PURCHASE CONTRACTS</u> | 22 |
| <u>DESCRIPTION OF UNITS</u> | 23 |
| <u>GLOBAL SECURITIES</u> | 24 |
| <u>PLAN OF DISTRIBUTION</u> | 27 |
| <u>LEGAL MATTERS</u> | 29 |
| <u>EXPERTS</u> | 29 |

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

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.

We have not authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus supplement or in any free writing prospectus we have prepared. We take no responsibility for, and provide no assurance as to the reliability of, any other information that others may give you. Neither we or the underwriters are 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.

Table of Contents

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.

S-2

Table of Contents

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-11 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 clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-systemic therapeutic drugs that work exclusively in the gastrointestinal, or GI, tract to treat GI and cardio-renal diseases. We have developed a proprietary drug discovery and design platform enabling us, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing our platform, we discovered and designed our lead product candidate, tenapanor, which is currently being evaluated in two pivotal Phase 3 clinical studies in patients with constipation-predominant irritable bowel syndrome, or IBS-C. In a Phase 2b clinical study, tenapanor demonstrated the ability to improve the symptoms of IBS-C. In a separate Phase 2b clinical trial, tenapanor demonstrated the ability to lower elevated serum phosphorus levels in patients with end-stage renal disease, or ESRD. We have initiated an additional Phase 2b clinical trial to evaluate dosing regimens of tenapanor for the treatment of hyperphosphatemia in ESRD patients, and we expect to receive results from this trial in the second half of 2016. We are developing another drug candidate, RDX022, for the treatment of hyperkalemia, or elevated serum potassium, in patients with chronic kidney disease, or CKD, and in patients with heart failure, or HF. In January 2016, we announced the results of an open label clinical study evaluating the pharmacodynamic activity of RDX022 in healthy adult volunteers. The study demonstrated that RDX022 was generally well-tolerated at all doses evaluated and effectively binds to potassium in the GI tract, supporting our plans to proceed with a Phase 3 clinical program, which we currently expect to initiate in the second half of 2016. We are pursuing a 505(b)(2) regulatory pathway for RDX022. We have additional drug candidates in earlier stages of research and development focused in GI and cardio-renal diseases including RDX009, a secretagogue of glucagon-like peptide-1, or GLP-1, and glucagon-like peptide-2, or GLP-2, and RDX013, a potassium secretagogue. We currently expect to file an investigational new drug application, or IND, for RDX009 in the second half of 2016.

Our Strategy

We are a biotechnology company with a clinical pipeline of drug candidates in the fields of GI and cardio-renal diseases. We are currently advancing the clinical development of our two product candidates, tenapanor and RDX022, and we intend to use our existing cash and cash equivalents and the net proceeds from this offering to support the tenapanor and RDX022 Phase 3 clinical programs, including manufacturing of clinical trial materials, as well as to support the IND filing for RDX009 and to fund additional research and development for our earlier stage programs.

We expect to use our proprietary drug discovery and design platform to discover new minimally-systemic drug candidates that prevent and treat important diseases in these same therapeutic areas of GI and cardio-renal diseases. To date, all of our drug candidates have resulted from research completed by the Company.

If our drug candidates are approved for marketing by the FDA, we expect to participate in the commercialization of our products with our own specialty-based sales force, initially targeting

S-3

Table of Contents

gastroenterologists and nephrologists. Our executive management team, and in particular our President and Chief Executive Officer, Michael Raab, has extensive experience in developing and commercializing therapeutic drugs for the CKD and ESRD markets, and we expect to leverage this expertise in a manner that will allow us to create and retain significant value from our marketed products.

Our Pipeline

Tenapanor is a minimally-absorbed, small molecule that acts locally in the GI tract to inhibit the sodium transporter NHE3 and reduce sodium and phosphorus uptake from the gut. In human studies of orally-administered tenapanor, the drug was detected in the blood in only 0.7% of more than 3,000 collected serum samples, and even in those, at very low levels (< 1.5 ng/mL). We have evaluated tenapanor in fourteen human clinical studies in over 1,000 individuals to date.

In October 2014, we announced results from a Phase 2b clinical trial evaluating tenapanor in IBS-C patients. At the 50 mg twice daily dose of tenapanor, the trial met its primary efficacy endpoint of an increase in the complete spontaneous bowel movement, or CSBM, responder rate. Most secondary endpoints, including abdominal pain, the overall responder rate and other abdominal and IBS-C symptoms, demonstrated statistically significant and clinically meaningful improvements. At the 50 mg twice daily dose, 26.4% more patients receiving tenapanor than placebo achieved the overall responder rate indicating a significant response during 6 out of 12 weeks of treatment. In this trial, tenapanor was well-tolerated and caused diarrhea in 11.2% more patients than placebo at the 50 mg twice daily dose.

In the fourth quarter of 2015, we initiated two pivotal Phase 3, randomized, placebo-controlled clinical trials evaluating tenapanor in IBS-C patients. We expect to enroll approximately 600 patients in each trial and anticipate full enrollment in each of these trials to require approximately 12 months. The primary endpoint in

Table of Contents

each of the trials is the 6 of 12 week overall responder rate. An overall responder is defined as a weekly responder for 6 of 12 weeks where both an abdominal pain response and a CSBM response criteria are met during the same week. An abdominal pain responder is defined as a patient with a 30% or greater reduction in average weekly worst abdominal pain compared to baseline during the week, and a CSBM responder is defined as a patient who has an increase of one or more in average weekly CSBMs compared to baseline during the week. We are also evaluating other endpoints in these studies, including CSBM and abdominal pain responder rates for 6 of 12 weeks as well as for 9 of 12 weeks, abdominal symptoms and other clinically relevant endpoints.

In February 2015, we announced results from a Phase 2b clinical trial evaluating tenapanor for the control of hyperphosphatemia in ESRD patients. In the trial, there was a statistically significant dose-related decrease in serum phosphorus levels for tenapanor-treated patients compared to patients receiving placebo ($p=0.012$). It was noted, however, that the rate of diarrhea and the rate of discontinuations due to diarrhea were higher than expected in the 30mg once daily and 30mg twice daily dose groups.

In December 2015, we initiated a Phase 2b clinical trial to evaluate the optimal dosing regimen for tenapanor for the treatment of hyperphosphatemia in ESRD patients, and we expect to receive results from this trial in the second half of 2016.

We are also developing RDX022 for the treatment of hyperkalemia in CKD patients, with or without HF. RDX022 is our proprietary oral, non-absorbed potassium-binder. It based on polystyrene sulfonate, a well-known and well-characterized polymer. We have made numerous improvements to the polymer by engineering into RDX022 several key physical and chemical modifications in an effort to improve various properties. We have filed a patent application covering the composition of matter for these modifications.

In January 2016, we announced results from an open-label pharmacodynamic study of RDX022 in healthy adult volunteers. The study consisted of a two-day treatment-free baseline period and a four-day treatment period. The study included four cohorts, and in each cohort 12 subjects received RDX022 and three subjects received a similar dose of sodium polystyrene sulfonate, or SPS for a total of 60 subjects. RDX022 was administered at 4.6 g BID (9.2 g/day), 6.9 g BID (13.8 g/day), 4.6 g TID (13.8 g/day) and 9.2 g TID (27.5 g/day), and resulted in a mean increase of fecal potassium from baseline of 888 mg/day, 1,791 mg/day, 1,408 mg/day, and 1,670 mg/day, respectively. RDX022 was generally well-tolerated at all doses and demonstrated comparable results to those observed with SPS. Other fecal electrolytes were monitored during the study and no unexpected changes were observed; in particular, fecal magnesium remained unchanged from baseline.

Sodium is currently used as a counter-ion in SPS products marketed in the United States and certain other products under development. We formulated RDX022 with a calcium counter-ion, rather than a sodium counter-ion, as adding sodium to the daily intake of the target patient population runs counter to best clinical practice. In patients with CKD and/or HF, the standard of care is a low-sodium diet as sodium can contribute to fluid overload and edema, a common experience for these patients. In addition, excess sodium diminishes the beneficial effects of blood pressure drugs that inhibit the renin-angiotensin-aldosterone system, or RAAS. We have also improved both the physical properties of polystyrene sulfonate and the formulation in a manner that we expect may lead to improved patient adherence and compliance. Notably, in a single center, randomized, crossover study to evaluate various oral formulations of RDX022 in healthy subjects, RDX022 consistently outperformed SPS in all aspects of the taste assessments, including mouth feel, texture and flavor.

We currently expect to initiate a Phase 3 clinical trial for RDX022 in the second half of 2016. The Phase 3 clinical trial will enroll patients with CKD, with or without HF, who are taking RAAS inhibitors and are diagnosed with hyperkalemia, a common side effect that occurs in patients taking RAAS inhibitors. Based on discussions with the

FDA, we believe we will be able to submit an application for RDX022 under the 505(b)(2) regulatory pathway.

S-5

Table of Contents

Other product candidates in our pipeline include the following:

RDX009 Program: Our focus is the discovery and development of minimally-absorbed TGR5 agonists that stimulate GLP-1 and GLP-2 secretion for various indications. We are evaluating RDX009 in animal models for its effect in multiple indications. In December 2015, we declared a development candidate for RDX009 and currently expect to file an IND for RDX009 in the second half of 2016.

RDX013 Program: We are continuing to research RDX013, a small molecule drug candidate for hyperkalemia. This agent, a potential potassium secretagogue, is intended to enhance potassium secretion or prevent potassium absorption with a much lower pill burden than potassium binders and may provide significant advantages as a stand-alone agent or used in combination with potassium binders, including RDX022.

NHE3 and Hyperphosphatemia Program: We intend to leverage our knowledge of NHE3 inhibitors and their effect on phosphate management as we seek to further understand tenapanor's phosphate lowering mechanism of action. We also intend to evaluate new indications for tenapanor and other NHE3 inhibitors in order to exploit the unique capabilities and tools we have developed to modulate ion transport channels located on mucosal surfaces.

Our Proprietary Drug Discovery and Design Platform

Our platform, comprised of proprietary know-how and drug discovery and design tools, provides us with a competitive advantage in drug development. This platform enables us, in a rapid and cost-efficient manner, to discover and design novel drug candidates that work exclusively in the GI tract to treat GI and cardio-renal diseases. By targeting receptors and transporters localized in the GI tract, we can modulate important functions of the gut, such as absorption of specific nutrients and minerals, or the gut's various hormonal functions, to treat and prevent diseases while avoiding systemic toxicities.

The pillars of our drug discovery and design platform include the following:

Medicinal Chemistry to develop minimally-systemic products: our medicinal chemistry team has developed the tools, expertise and approach to ensure that our small molecule drug candidates are potent, have appropriate drug properties, are able to be readily manufactured, and are minimally-systemic, a property that we believe is not generally targeted for most other drug programs;

***In vivo* pharmacology:** Our *in vivo* pharmacology group has developed animal models and expertise in-house that allow it to rapidly assess the minimally-systemic nature of our drug candidates as well as test the hypotheses that our drug candidates can treat and prevent diseases and conditions in our targeted therapeutic fields;

GI Informatics: With genetic and proteomic informatics tools, we have identified over 3,800 human GI tract-specific RNA transcripts and proteins on the inner surface of the gut, many of which we believe may be drug targets. We intend to become leading experts in human and rodent gut physiology and the molecular pathways that lead to disease in our targeted therapeutic areas;

***In vitro* expertise:** We have developed a cell-culture system that simulates gut tissue. We call this component of our discovery platform Ardelyx Primary Enterocyte and Colonocyte Culture System, or APECCS. APECCS involves the biopsy of various segments of the gut and the growth of those cells under proprietary conditions to maintain, to the extent possible, the integrity and functionality of the various cell types and substructures. We have developed this into a miniaturized format that allows us to utilize it for cell based drug screening. In addition to using APECCS in the design of our small molecule drug candidates, we use the APECCS technology to measure epithelial transport of ions and nutrients and to screen compounds to identify potential disease modulators such as inhibitors or activators using phenotypic screening. APECCS has the potential to allow us to identify novel targets, mechanisms of action and physiology as well as provide us an early understanding of how identified

Table of Contents

compounds may interact with specific gut tissues. In addition, we believe that APECCS may also provide us with a clear path to translate cell-based observations into *in vivo* rodent models and ultimately into human clinical studies.

Our Markets

Constipation-Predominant Irritable Bowel Syndrome, or IBS-C

IBS-C is a GI disorder in which abdominal pain or discomfort is associated with constipation, which significantly affects the health and quality of life of affected patients. It is unknown what causes IBS-C. There is no specific test or biomarker for IBS-C and therefore its presence is diagnosed by symptoms and by eliminating other disorders. IBS-C is very similar to chronic constipation but it is clinically distinguished by a significant pain component.

Numerous treatments exist for the constipation component of IBS-C, many of which are over-the-counter. We are aware of two prescription products marketed for IBS-C, Linzess (linaclotide) marketed by Ironwood Pharmaceuticals and Allergan and Amitiza (lubiprostone) marketed by Sucampo and Takeda. In Phase 3 clinical trials of Linzess in IBS-C patients, up to 20% more patients receiving Linzess than placebo reached the primary endpoint, overall responder rate, indicating a significant response during 6 out of 12 weeks of treatment. In these studies, Linzess caused diarrhea in up to 17% more patients than placebo.

We believe that tenapanor may offer a significant benefit over currently marketed drugs like Amitiza and Linzess, due in part to the potential to adjust the dose and/or dose frequency of tenapanor in order to optimize its efficacy and minimize diarrhea. The data we have generated in both animal and human studies have suggested that the effect of tenapanor for the treatment of IBS-C can be modulated by adjusting its dose and dose frequency.

Based on reports in the literature regarding the prevalence of IBS in the U.S. population and the percentage of individuals who have IBS-C as opposed to other forms of IBS, we estimate that approximately 1.4% of the U.S. population has IBS-C, or about 4.4 million individuals, and that approximately 1.0 million of those patients have been diagnosed with IBS-C. Additionally, we estimate there are about 6.6 million IBS-C patients in Europe and about 3.4 million in Japan.

Hyperphosphatemia

CKD is the progressive deterioration of renal function that can occur over several months or years. The symptoms of worsening kidney function are nonspecific, and can include having less energy, reduced appetite, dry itchy skin, swollen feet and ankles, or generally just not feeling well. If the deterioration continues and is not halted by either changes in lifestyle or with the assistance of pharmacological intervention, the disease will likely cause significant cardiovascular morbidity, and can progress to ESRD, the final stage of CKD, where kidney function will be lost entirely.

Current management of ESRD includes hemodialysis, and peritoneal dialysis as a means to filter toxins from the blood once kidneys have failed. Unless this intervention occurs, kidney failure results in the accumulation of waste products that may ultimately cause death. Hemodialysis, the most common form of dialysis, generally requires a patient to visit a dialysis center at least three times per week for a three- to five-hour session, significantly reducing quality of life.

Phosphorus, a vital element required for most cellular processes, is present in almost every food in the Western diet, and, in individuals with normal kidney function, any excess dietary phosphorus is efficiently removed by the kidney and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.6 to 3.8 mg/dL. With

kidney failure, elevated phosphorus becomes harmful and is diagnosed as

S-7

Table of Contents

hyperphosphatemia when serum phosphorus levels are greater than 5.0 mg/dL. Although patients with ESRD rely on dialysis to eliminate harmful agents, phosphorus is not readily removed by the procedure and other means of managing phosphorus levels must be employed.

In ESRD, excess levels of phosphorus have been shown to lead to an increase in cardiovascular disease risk, as well as increases in serum FGF-23, an important serum endocrine hormone that regulates phosphorus metabolism, and elevated parathyroid hormone, also known as secondary hyperparathyroidism. These endocrine changes in ESRD patients are a concern as elevated parathyroid hormone leads to the development of renal osteodystrophy, a condition of abnormal bone growth characterized by brittle bones.

Since dialysis is unable to efficiently eliminate excess phosphorus, ESRD patients are put on restrictive low phosphorus diets and are prescribed medications called phosphate binders, the only pharmacologic interventions currently marketed for the treatment of hyperphosphatemia. Binders are a collection of drugs whose function is to bind, or absorb, dietary phosphorus and are taken in conjunction with meals and snacks. They include calcium, iron or lanthanum, a rare-earth metal, which bind to and precipitate with dietary phosphate in the GI tract. The goal of these elemental phosphorus binders is for patients to eliminate the precipitated phosphorus in their stool. A limitation of this approach is the systemic excess absorption of calcium, iron or lanthanum, resulting in side effects and other unintended consequences for ESRD patients.

Safety and tolerability have been significant concerns with many approved phosphate binders. The more common side effects of approved phosphate binders include long-term vascular calcification, nausea and vomiting, diarrhea or constipation and ileus or disruption of the normal propulsive ability of the GI tract.

ESRD patients take on average 10-14 oral medications each day, and they are severely restricted in their fluid intake. In addition, to control their serum phosphorus, their phosphate binder-related pill burden is significant, typically consisting of nine or more pills a day. The amount of phosphate a binder can remove is limited by its binding capacity, and therefore, increasing the dose, and therefore the pill burden, of the binder is the only way to increase the amount of phosphate being bound and excreted. As a result, prescribed binder doses are intolerable for many patients.

According to the most recent data available from the U.S. Renal Data System, in 2013 there were 421,349 patients on hemodialysis in the United States. Additionally, according to the European ERA-EDTA Registry 2012 Annual Report and a study in 2010 by the Japanese Society for Dialysis Therapy, there were approximately 280,000 patients on hemodialysis in Europe and about 250,000 in Japan. We estimate, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are approximately 290,000, 225,000 and 220,000 ESRD patients with hyperphosphatemia in the United States, Europe and Japan, respectively.

Because many ESRD patients with hyperphosphatemia are unable to lower serum phosphorus levels to below 5.5 mg/dL with currently marketed phosphate binders, we believe there is a significant opportunity for new agents with new mechanisms, demonstrated efficacy, a strong safety profile, and significantly lower pill burden.

We believe that tenapanor, if approved, has the potential to have the lowest pill burden among any currently marketed hyperphosphatemia drugs, with milligram rather than gram quantities dosed once or twice daily. In addition, we may evaluate whether tenapanor has the potential to be used in combination with phosphate binders for those patients who cannot achieve adequate phosphate control with a single agent.

Hyperkalemia

Hyperkalemia is defined as the presence of blood potassium levels greater than 5.0mEq/L. Normal levels are 3.5 to 5.0 mEq/L. When hyperkalemia is severe, or above 7.0mEq/L, there is a significantly increased risk of death because of the potential for heart conductance problems.

S-8

Table of Contents

Hyperkalemia can be caused by a variety of sources. Kidney disease can result in the build-up of potassium in the blood. Also, certain drugs such as the common blood pressure medications known as RAAS inhibitors, or inhibitors of the renin-angiotensin-aldosterone system, can cause hyperkalemia. RAAS inhibitors, though quite effective for controlling blood pressure, are often significantly reduced in patients, such as in those with CKD and HF whose potassium levels are elevated because of the fear that elevated potassium can cause significantly worse problems than hypertension including sudden cardiac arrest in severe cases.

According to a retrospective observational study of a national cohort of 246,000 veterans cared for in the Veterans Health Administration, about 21% and 42% of patients with CKD Stage 3b and Stage 4, respectively, had a hyperkalemic event during a 12-month period, suggesting that hyperkalemia affects about 900,000 individuals with CKD Stage 3b or Stage 4 in the United States. According to the United States Renal Data System 2014 Atlas of CKD & ESRD, over 50% of CKD Stage 3b and Stage 4 patients are prescribed RAAS inhibitors because of their efficacy in controlling hypertension and success in slowing the clinical course of CKD. Additionally, according to the American Heart Association, 5.7 million Americans are living today with heart failure. Our proprietary research suggests that up to 16%, or approximately 900,000, of these patients had hyperkalemia during a 12-month period. Over half of heart failure patients are prescribed RAAS inhibitors.

Despite the success of RAAS inhibitors in both of these populations, several published guidelines have suggested that physicians should reduce and possibly discontinue RAAS inhibitors in order to manage the risk of hyperkalemia in CKD and heart failure patients. The alternative medications used to control hypertension, including diuretics and calcium channel blockers, are significantly less effective than RAAS inhibitors, particularly in patients with failing kidneys and severe hypertension. According to the publication Market Dynamix: Hyperkalemia recently released by Spherix Global Insights, U.S. cardiologists reported that of the patients who would benefit from RAAS inhibition, up to 38% of patients with heart failure and up to 55% of patients with both heart failure and CKD are being administered a sub-optimal dose or none at all, and nephrologists reported that at least one-third of patients who would benefit from RAAS inhibition receive a sub-optimal dose or none at all. We believe there is a strong medical need for new medications that control hyperkalemia in order to allow for continued use of RAAS inhibitors to control hypertension in these patient populations.

An additional market not currently addressed by any product on the market is hyperkalemia in ESRD patients. Our proprietary research suggests that up to 48% of patients on dialysis have at least one intervention for hyperkalemia during a 12-month period despite being dialyzed, resulting in a 7% mortality rate. This suggests up to 200,000 patients with ESRD that could benefit from an agent that treats hyperkalemia.

Corporate Information

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.

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.

S-9

Table of Contents

THE OFFERING

| | |
|---|---|
| Issuer | Ardelyx, Inc. |
| Common stock we are offering | shares |
| Common stock to be outstanding after the offering | shares |
| Option to purchase additional shares | We intend to grant the underwriters a 30-day option to purchase up to an additional shares of our common stock. |
| Use of proceeds | We currently expect to use our existing cash and cash equivalents and the net proceeds from this offering to support the tenapanor and RDX022 Phase 3 clinical programs, including manufacturing of clinical trial materials, as well as to support the IND filing for RDX009 and to fund additional research and development for our earlier stage programs. See Use of Proceeds on page S-16. |
| 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 25,954,941 shares of common stock outstanding as of September 30, 2015, and excludes the following, in each case as of such date:

1,253,105 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$9.50 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;

1,682,346 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; and

347,074 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.

Unless otherwise stated, all information contained in this prospectus supplement reflects an assumed public offering price of \$16.46 per share, which was the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016.

S-10

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. 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, 2015, 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. We expect to use our existing cash and cash equivalents and the net proceeds from this offering to support the tenapanor and RDX022 Phase 3 clinical programs, including manufacturing of clinical trial materials, as well as to support the IND filing for RDX009 and to fund additional research and development for our earlier stage programs. However, 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 is higher than the net tangible book value per share of our common stock outstanding prior to this offering. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of \$10.07 per share, based on an assumed public offering price of \$16.46 per share, which was the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, and our as-adjusted net tangible book value as of September 30, 2015 after giving effect to this offering. For information on how the foregoing amounts were calculated, see Dilution.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

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 September 30, 2015, approximately

S-11

Table of Contents

3.3 million shares of common stock that are either subject to outstanding options, 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. Additionally, as of September 30, 2015, approximately 2.2 million shares of common stock that are subject to outstanding warrants are eligible for sale in the public market.

Our stock price may be volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

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

results from, or any delays in, clinical trial programs relating to our product candidates, including the ongoing and planned clinical trials for tenapanor and RDX022;

our ability to commercialize or obtain regulatory approval for our product candidates, or delays in commercializing or obtaining regulatory approval;

announcements of regulatory approval or a complete response letter to tenapanor or RDX022, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;

announcements relating to future collaboration partnerships;

announcements of therapeutic innovations or new products by us or our competitors;

adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;

changes or developments in laws or regulations applicable to our product candidates;

the success of our testing and clinical trials;

the success of our efforts to acquire or license or discover additional product candidates;

any intellectual property infringement actions in which we may become involved;

announcements concerning our competitors or the pharmaceutical industry in general;

achievement of expected product sales and profitability;

manufacture, supply or distribution shortages;

actual or anticipated fluctuations in our operating results;

FDA or other U.S. or foreign regulatory actions affecting us or our industry or other healthcare reform measures in the United States and applicable foreign jurisdictions;

changes in financial estimates or recommendations by securities analysts;

trading volume of our common stock;

sales of our common stock by us, our executive officers and directors or our stockholders in the future;

general economic and market conditions and overall fluctuations in the United States equity markets; and

the loss of any of our key scientific or management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that

Table of Contents

stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

If securities or industry analysts cease to publish research, or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Table of Contents

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, estimate, expect, goal, intend, may, objective, plan, predict, potential, positioned, seek, should, 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:

the timing of the receipt of results for a Phase 2b clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients;

the timing of the initiation of a Phase 3 clinical program for RDX022;

our expectation regarding the availability of the 505(b)(2) regulatory pathway for RDX022;

the timing of the filing of an IND for RDX009;

our expectations regarding our plans for and our participation in the commercialization of our product candidates;

our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;

our plans with respect to our pre-clinical program;

our ability to identify and validate targets and novel drug candidates using our proprietary drug discovery and design platform including APECCS;

our ability to develop, acquire and advance product candidates into, and successfully complete, clinical trials;

the timing or likelihood of regulatory filings, approvals and commercialization for our product candidates, including tenapanor and RDX022;

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 JOBS Act;

our use of proceeds from this offering;

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 greater detail in the documents incorporated by reference herein, including

Table of Contents

under the heading Risk Factors. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus 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.

S-15

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of 4,556,501 shares of common stock in this offering will be approximately \$69.8 million, based on an assumed public offering price of \$16.46 per share, which was the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase an additional 683,475 shares in full, we estimate that net proceeds will be approximately \$80.4 million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A \$1.00 increase (decrease) in the assumed public offering price of \$16.46 per share, which was the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, would increase (decrease) the net proceeds to us by approximately \$4.3 million, assuming that the number of shares offered by us without the exercise of the underwriters' option to purchase additional shares (based on the assumed public offering price of \$16.46 per share) remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$15.5 million, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We currently expect to use our existing cash and cash equivalents of approximately \$105 million as of December 31, 2015 and the net proceeds from this offering to support the tenapanor and RDX022 Phase 3 clinical programs, including manufacturing of clinical trial materials, as well as to support the IND filing for RDX009 and to fund additional research and development for our earlier stage programs.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts with respect to tenapanor and RDX022, 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**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2015:

on an actual basis; and

on an as adjusted basis to give effect to the issuance and sale by us of 4,556,501 shares of our common stock in this offering at \$16.46, the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes incorporated by reference in this prospectus. For more details on how you can obtain our SEC reports and other information, you should read the section of the prospectus entitled **Where You Can Find More Information**.

| | As of September 30, 2015 | |
|---|--|-----------------------|
| | Actual | As Adjusted(1) |
| | (in thousands, except share and per share data) | |
| Cash and cash equivalents | \$ 129,047 | \$ 198,848 |
| Stockholders' equity: | | |
| Preferred stock \$0.0001 par value 5,000,000 shares authorized, Actual as adjusted and pro forma as adjusted; no shares issued or outstanding, actual as adjusted and pro forma as adjusted | | |
| Common stock \$0.0001 par value authorized, 300,000,000 actual and as adjusted; issued and outstanding, 25,954,941 actual and 30,511,442 as adjusted | 3 | 3 |
| Additional paid-in capital | 209,615 | 279,416 |
| Accumulated deficit | (84,488) | (84,488) |
| Total stockholders' equity | 125,130 | 194,931 |
| Total capitalization | \$ 125,130 | \$ 194,931 |

(1) A \$1.00 increase (decrease) in the assumed public offering price of \$16.46 per share, which is the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, would increase (decrease) the as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately \$4.3 million, assuming that the number of shares offered by us (based on the assumed public offering price of \$16.46 per share) remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A 1,000,000 share increase (decrease) in the number of shares offered by us would increase (decrease) the as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total

stockholders' equity and total capitalization by approximately \$15.5 million, assuming that the assumed public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

The outstanding share information in the table above excludes the following, in each case as of September 30, 2015:

1,253,105 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$9.50 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;

1,682,346 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; and

Table of Contents

347,074 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.

S-18

Table of Contents**DILUTION**

If you invest in our common stock in this offering, your interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock in this offering and the net tangible book value per share of our common stock after this offering. As of September 30, 2015, we had a historical net tangible book value of \$125.1 million, or \$4.82 per share of common stock. 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 September 30, 2015.

After giving effect to the sale of 4,556,501 shares of common stock in this offering at an assumed price of \$16.46 per share, the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value at September 30, 2015 would have been approximately \$194.9 million, or \$6.39 per share. This represents an immediate increase in as adjusted net tangible book value of \$1.57 per share to existing stockholders and an immediate dilution of \$10.07 per share to new investors. The following table illustrates this per share dilution:

| | |
|--|----------|
| Assumed public offering price per share | \$ 16.46 |
| Net tangible book value per share as of September 30, 2015 | \$ 4.82 |
| Increase per share attributable to new investors | \$ 1.57 |
| As adjusted net tangible book value per share as of September 30, 2015, after giving effect to this offering | \$ 6.39 |
| Dilution per share to new investors purchasing our common stock in this offering | \$10.07 |

If the underwriters fully exercise their option to purchase additional shares, as adjusted net tangible book value after this offering would increase to approximately \$6.59 per share, and there would be an immediate dilution of approximately \$9.87 per share to new investors.

A \$1.00 increase (decrease) in the assumed public offering price of \$16.46 per share, the last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016, would increase (decrease) the as adjusted net tangible book value by approximately \$4.3 million, or approximately \$0.14 per share, and increase (decrease) the dilution per share to new investors by approximately \$0.86 per share, assuming that the number of shares offered by us (based on the assumed public offering price of \$16.46 per share) remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) the as adjusted net tangible book value by approximately \$15.5 million, or \$0.29 and \$(0.31) per share, and would increase (decrease) the dilution per share to new investors by approximately \$0.29 and \$(0.31) per share, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

To the extent that outstanding options or warrants are exercised, 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.

S-19

Table of Contents

The number of shares of common stock to be outstanding after this offering is based on 25,954,941 shares of common stock outstanding as of September 30, 2015, and excludes the following, in each case as of such date:

1,253,105 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of \$9.50 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;

1,682,346 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; and

347,074 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.

Table of Contents**PRICE RANGE OF COMMON STOCK**

Our common stock commenced trading on The NASDAQ Global Market under the symbol ARDX on June 19, 2014. Prior to that date, there was no public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low reported sales prices of our common stock as reported on The NASDAQ Global Market:

| | High | Low |
|---|----------|----------|
| Year ended December 31, 2014 | | |
| Second quarter (from June 19, 2014) | \$ 16.00 | \$ 14.05 |
| Third quarter | \$ 21.60 | \$ 11.37 |
| Fourth quarter | \$ 35.48 | \$ 15.10 |
| Year ended December 31, 2015 | | |
| First quarter | \$ 27.99 | \$ 13.00 |
| Second quarter | \$ 17.66 | \$ 7.95 |
| Third quarter | \$ 22.15 | \$ 15.00 |
| Fourth quarter | \$ 21.27 | \$ 15.13 |
| Year ending December 31, 2016 | | |
| First quarter (through January 5, 2016) | \$ 17.22 | \$ 16.46 |

The last reported sale price of our common stock on The NASDAQ Global Market on January 5, 2016 was \$16.46 per share. As of January 5, 2016, there were approximately 40 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Table of Contents

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

S-22

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the Code), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the IRS), in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

U.S. expatriates and former citizens or long-term residents of the United States;

persons subject to the alternative minimum tax;

persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;

banks, insurance companies, and other financial institutions;

brokers, dealers or traders in securities;

controlled foreign corporations, passive foreign investment companies, and corporations that accumulate earnings to avoid U.S. federal income tax;

partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);

tax-exempt organizations or governmental organizations;

persons deemed to sell our common stock under the constructive sale provisions of the Code; and

tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

S-23

Table of Contents

Definition of a Non-U.S. Holder

For purposes of this discussion, a **Non-U.S. Holder** is any beneficial owner of our common stock that is neither a U.S. person nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

an individual who is a citizen or resident of the United States;

a corporation created or organized under the laws of the United States, any state thereof or the District of Columbia;

an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

a trust that (1) is subject to the primary supervision of a U.S. court and all substantial decisions of which are subject to the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled **Dividend Policy**, we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under **Sale or Other Taxable Disposition**.

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

S-24

Table of Contents

Sale or Other Taxable Disposition

Subject to the discussions below under **Information Reporting and Backup Withholding** and **Additional Withholding Tax on Payments Made to Foreign Accounts**, a Non-U.S. Holder will not be subject to U.S. federal income or withholding tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);

the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or

our common stock constitutes a U.S. real property interest (**USRPI**) by reason of our status as a U.S. real property holding corporation (**USRPHC**) for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by certain U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN,

W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock

Table of Contents

conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or "FATCA") on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or a non-financial foreign entity (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain specified United States persons or United States-owned foreign entities (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock, and will apply to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2019.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Table of Contents**UNDERWRITING**

Citigroup Global Markets Inc. and Leerink Partners LLC are acting as joint book-running managers of the offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus supplement, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name.

| Underwriter | Number of Shares |
|-------------------------------|-------------------------|
| Citigroup Global Markets Inc. | |
| Leerink Partners LLC | |
| Wedbush Securities Inc. | |
| JMP Securities LLC | |
| Cantor Fitzgerald & Co. | |
| Ladenburg Thalmann & Co. Inc. | |
| Total | |

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the option to purchase additional shares described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount from the public offering price not to exceed \$ _____ per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms. If the underwriters sell more shares than the total number set forth in the table above, we intend to grant to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to _____ additional shares at the public offering price less the underwriting discount. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, and our officers, directors, and certain of our other stockholders have agreed that, subject to specified limited exceptions, for a period of 60 days from the date of this prospectus supplement, we and they will not, without the prior written consent of Citigroup and Leerink, dispose of or hedge any shares or any securities convertible into or exchangeable for our common stock. Citigroup and Leerink in their sole discretion may release any of the securities subject to these lock-up agreements at any time without notice.

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

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

| | Paid by Ardelyx | |
|-----------|------------------------|----------------------|
| | No Exercise | Full Exercise |
| Per share | \$ | \$ |
| Total | \$ | \$ |

S-27

Table of Contents

We estimate that our portion of the total expenses of this offering will be approximately \$0.7 million.

We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to \$32,500 as set forth in the underwriting agreement.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' option to purchase additional shares, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

Covered short sales are sales of shares in an amount up to the number of shares represented by the underwriters' option to purchase additional shares.

Naked short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters' option to purchase additional shares.

Covering transactions involve purchases of shares either pursuant to the underwriters' option to purchase additional shares or in the open market in order to cover short positions.

To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

To close a covered short position, the underwriters must purchase shares in the open market or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates for which they received, or may in the future receive, customary fees and commissions for these transactions.

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have engaged in, and may in the future engage in, transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or

Table of Contents

hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and

for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus supplement and the accompanying prospectus may not be made to the public in that relevant member state other than:

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

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

S-29

Table of Contents

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

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus supplement and the accompanying prospectus.

Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus supplement and the accompanying prospectus are only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus supplement, the accompanying prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

Neither this prospectus supplement, nor the accompanying prospectus nor any other offering material relating to the shares described in this prospectus supplement and the accompanying prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement, nor the accompanying prospectus nor any other offering material relating to the shares has been or will be:

released, issued, distributed or caused to be released, issued or distributed to the public in France; or

used in connection with any offer for subscription or sale of the shares to the public in France. Such offers, sales and distributions will be made in France only:

to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with

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articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code *monétaire et financier*;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code *monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

S-30

Table of Contents

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia (Corporations Act)) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission (ASIC). This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

a) you confirm and warrant that you are either:

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

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

iii) a person associated with the company under section 708(12) of the Corporations Act; or

iv) a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

b) you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus supplement and the accompanying prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including

any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

S-31

Table of Contents

Notice to Prospective Investors in Singapore

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

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

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

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$0.2 million (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

The Company has agreed to provide for indemnification of the underwriters for specified liabilities, including matters arising under the Securities Act.

Table of Contents

LEGAL MATTERS

The validity of the issuance of our common stock offered hereby will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Davis Polk & Wardwell LLP is acting as counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2014, 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.

S-33

Table of Contents

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, 2014, filed with the SEC on March 5, 2015, as amended by Amendment No. 1 on Form 10-K/A filed with the SEC on March 11, 2015;

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 24, 2015;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015, June 30, 2015, and September 30, 2015, filed with the SEC on May 12, 2015, August 12, 2015, and November 12, 2015, respectively; and

our Current Reports on Form 8-K filed with the SEC on April 20, 2015, June 3, 2015, June 12, 2015, July 14, 2015, September 1, 2015, October 27, 2015 (as amended by a Current Report on Form 8-K/A filed on December 16, 2015), December 15, 2015 and January 6, 2016; and

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.

S-34

Table of Contents

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

S-35

Table of Contents

PROSPECTUS

\$200,000,000

Common Stock, Preferred Stock, Debt Securities,

Warrants, Purchase Contracts, Units

We may offer and sell up to \$200,000,000 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 July 9, 2015, the last reported sale price of our common stock on The NASDAQ Global Market was \$16.46 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 July 20, 2015.

Table of Contents

TABLE OF CONTENTS

| | |
|--|----|
| <u>ABOUT THIS PROSPECTUS</u> | 1 |
| <u>WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE</u> | 2 |
| <u>ABOUT ARDELYX</u> | 4 |
| <u>RISK FACTORS</u> | 5 |
| <u>USE OF PROCEEDS</u> | 6 |
| <u>RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS</u> | 7 |
| <u>DESCRIPTION OF CAPITAL STOCK</u> | 8 |
| <u>DESCRIPTION OF DEBT SECURITIES</u> | 13 |
| <u>DESCRIPTION OF WARRANTS</u> | 20 |
| <u>DESCRIPTION OF PURCHASE CONTRACTS</u> | 22 |
| <u>DESCRIPTION OF UNITS</u> | 23 |
| <u>GLOBAL SECURITIES</u> | 24 |
| <u>PLAN OF DISTRIBUTION</u> | 27 |
| <u>LEGAL MATTERS</u> | 29 |
| <u>EXPERTS</u> | 29 |

Table of Contents

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 \$200,000,000 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.

Table of Contents

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, 2014, filed with the SEC on March 5, 2015, as amended by Amendment No. 1 on Form 10-K/A filed with the SEC on March 11, 2015;

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 24, 2015;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, filed with the SEC on May 12, 2015; and

Table of Contents

our Current Reports on Form 8-K filed with the SEC on April 20, 2015, June 3, 2015 and June 12, 2015; and

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.

Table of Contents

ABOUT ARDELYX

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-systemic therapeutic drugs that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal, GI and metabolic diseases. We have developed a proprietary drug discovery and design platform enabling us, in a rapid and cost-efficient manner, to discover and design novel drug candidates.

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.

Table of Contents

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 Quarterly Report on 10-Q and any subsequent Annual Reports on Form 10-K, 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.

Table of Contents

USE OF PROCEEDS

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

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 the three-month period ended March 31, 2015 and each of the years ended December 31, 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.

| | Three Months Ended March 31, 2015 | Year Ended December 31, | | |
|---|--|--------------------------------|-------------|-------------|
| | | 2014 | 2013 | 2012 |
| Deficiency of earnings available to cover fixed charges | \$ (3,502) | \$ (3,281) | \$ (6,705) | \$ (9,785) |

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

Table of Contents

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 66 2/3% 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.

Table of Contents

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 June 30, 2015, under our amended and restated investor rights agreement, the holders of approximately 9.7 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 June 30, 2015, the holders of approximately 9.7 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 June 30, 2015, 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 9.7 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 June 30, 2015, the holders of approximately 9.7 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 9,415,891 million shares of our common stock, including shares

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issuable upon exercise of warrants, on or prior to July 20, 2015, we filed a registration statement on Form S-3 for the resale of 9,415,891 shares of our common stock on July 13, 2015.

Table of Contents

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 statement filed on July 13, 2015) 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.

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.

Table of Contents

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 66 2/3% 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 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 66 2/3% 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

Table of Contents

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.

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.

Table of Contents

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.

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 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

Table of Contents

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;

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.

Table of Contents

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 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.

Table of Contents

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 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.

Table of Contents

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)

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 depositary;

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;

Table of Contents

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;

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 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

Table of Contents

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 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 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. (Section 10.10)

Table of Contents

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 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 of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are

Table of Contents

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.

Table of Contents

DESCRIPTION OF PURCHASE CONTRACTS

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

debt or equity securities issued by us or securities of third parties, 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.

Table of Contents

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.

Table of Contents

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

Table of Contents

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository 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 depository 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.

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.

Table of Contents

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.

Table of Contents

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 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

Table of Contents

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.

Table of Contents

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 financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2014, 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.

Table of Contents

\$75,000,000

Common Stock

Prospectus Supplement

Citigroup

Wedbush PacGrow

Cantor Fitzgerald & Co.

Leerink Partners

JMP Securities

Ladenburg Thalmann

, 2016