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Ardelyx Reports Progress of Development Programs

Ardelyx announces positive results from End-of-Phase 2 meeting with the FDA; the ongoing clinical trial evaluating tenapanor for the treatment of hyperphosphatemia for ESRD patients on dialysis may serve as the first of two registration trials
Ardelyx announces positive pharmacodynamic trial results with convenient once daily dose of RDX227675 for hyperkalemia and subsequent development plans
Conference call and webcast today at 8:30am ET

FREMONT, Calif., June 22, 2016 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on gastrointestinal and cardio-renal diseases, today announced updates to two of the Company's ongoing development programs.

Ardelyx today announced that, based on the positive outcome of a recent End-of-Phase 2 (EoP2) meeting held with the U.S. Food and Drug Administration (FDA), its ongoing Phase 2b clinical trial evaluating tenapanor for the treatment of hyperphosphatemia for end-stage renal disease (ESRD) patients on dialysis, may serve as the first of two registration trials to support the filing of a new drug application (NDA). Additionally, the Company today announced the results of a pharmacodynamic (PD) study evaluating once daily (QD) dosing of its product candidate, RDX227675, for the treatment of hyperkalemia. With these positive results, Ardelyx is accelerating its plans to commence a time to onset clinical trial in patients with hyperkalemia.

The Company will be hosting a conference call and webcast today at 8:30am ET to provide a detailed update regarding these recent developments. Please call 1-877-253-8183 (US) or 973-200-3070 (International) to listen to the conference call. The conference ID number for the live call will be 34249750. Alternatively, a live webcast can be accessed by visiting the investor section of Ardelyx's website at ir.ardelyx.com. Following the webcast, an archived version of the call will be available until July 6, 2016.

Overview of Updates to Ardelyx's Development Programs

Tenapanor for the Treatment of Hyperphosphatemia for ESRD Patients on Dialysis

Ardelyx recently met with the FDA for an EoP2 meeting regarding tenapanor for the treatment of hyperphosphatemia for ESRD patients on dialysis. The FDA guided Ardelyx to use the results of the placebo-controlled randomized withdrawal portion of the trial as the primary endpoint for its ongoing clinical trial, rather than as a secondary endpoint, in order for the trial to serve as one of two well-controlled studies to support the registration of tenapanor for the treatment of hyperphosphatemia for ESRD patients on dialysis. The overall study design will not be changed, but the Company is increasing the number of patients to be enrolled in the trial from 150 to 200 to further strengthen the trial and maintain a power of 90%.

The trial is designed to include an 8-week treatment period followed by a 4-week randomized withdrawal (RW) period where patients either stay on their current dose of tenapanor or are randomized to receive placebo. The primary endpoint will now assess the difference in the change, between a pool of subjects that respond to tenapanor during the initial 8 weeks of the trial and those on placebo from the end of the 8-week treatment period to the end of the 4-week RW period. Responders are defined as patients that demonstrate a ≥ 1.2 mg/dL decrease in serum phosphorus from baseline during the 8-week treatment period. The primary endpoint is powered at 90% to show a ≥ 1.5 mg/dL placebo adjusted effect. The FDA has accepted the new statistical analysis plan submitted to reflect these changes. As a result of the increase in enrollment, Ardelyx now expects results from the ongoing trial to be reported in the first quarter of 2017, as compared to prior guidance of the second half of 2016.

"Tenapanor, if successfully commercialized, will provide a profound improvement in the way dialysis patients are treated. It

would be the first agent approved for patients with hyperphosphatemia that is not a phosphate binder, and, as a consequence, results in a dramatically lower pill burden and overall mass required, as well as eliminating the need to be taken with all three meals and snacks," commented Mike Raab, President and Chief Executive Officer of Ardelyx. "We are extremely pleased with the outcome of our EoP2 meeting with the FDA and fully support the Agency's suggested changes to our ongoing Phase 2b clinical trial's primary endpoint and statistical analysis plan."

RDX227675 for the Treatment of Hyperkalemia

Separately, Ardelyx also announced today that it has received positive results from its QD dosing arm of the RDX227675 PD study in healthy adult volunteers. Ardelyx previously announced positive results in January 2016 from its PD trial evaluating twice daily (BID) and three times daily (TID) doses of RDX227675 in 60 healthy adult volunteers. The BID and TID doses successfully demonstrated the ability of RDX227675 to bind potassium in the gastrointestinal tract and RDX227675 was generally well-tolerated at all doses administered up to 27.5 g/day. Results from the new cohort, which evaluated the QD administration of RDX227675, demonstrated that a 13.8 g dose exhibited similar stool and urine potassium results to the previously-reported BID and TID dosing with the same total daily dose of 13.8 g (maximum mean increases in stool potassium of about 1,500 mg/day, with decreases in urinary potassium of about 900 mg/day). RDX227675 delivered once daily also was well-tolerated in these individuals. Based on these data, the Company has determined that once or twice daily dosing will be the most appropriate dosing regimens for further development and evaluation in the treatment of hyperkalemia in its upcoming trials.

"Treatment of hyperkalemia is an important and emerging market," said Paul Korner, MD, Executive Vice President and Chief Medical Officer. "As a result of hyperkalemia, many physicians opt to lower the dose of, or discontinue, potentially life-saving drugs such as ACE inhibitors that, as a side-effect, tend to increase serum potassium, rather than risk the potential dangers of this side effect in their CKD or heart failure patients. In addition, the RDX227675 formulation does not contain sodium or sorbitol, has significantly improved palatability, and with a convenient once or twice daily dosing, has the potential to provide significant benefits to patients with hyperkalemia."

Following these encouraging results, Ardelyx will now accelerate the commencement of a previously planned Phase 2b trial designed to evaluate the rate of onset of action of RDX227675 along with safety and efficacy in patients with chronic kidney disease (CKD) with or without heart failure (HF), one of the target patient populations for RDX227675. This study is in accordance with FDA's request to evaluate onset of action of RDX227675 and is in-line with the Company's strategy to develop a robust package insert for prescribers that includes competitive clinical data similar to those of existing potassium binders. Ardelyx expects to commence this Phase 2b clinical trial in the fourth quarter of 2016, with a target enrollment of approximately 60 patients. Results from this trial are expected to be available in the first half of 2017. The Phase 2b clinical trial will not affect the expected timing or design of the previously announced Phase 3 clinical trial for RDX227675, which is still on track to initiate in the fourth quarter of 2016.

"We have been unwavering in our focus to provide hyperkalemia patients with an efficacious product that is highly palatable and convenient as we understand that daily administration of multiple grams of any agent is not trivial," added Dr. Korner.

About Tenapanor

Tenapanor is a minimally-systemic small molecule that acts locally in the gastrointestinal (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). The Company has evaluated tenapanor in 18 human clinical trials in over 1,500 individuals, to date. The Company is currently evaluating tenapanor in two different programs:

- Irritable Bowel Syndrome with Constipation (IBS-C): In the fourth quarter of 2015, the Company initiated two pivotal Phase 3 clinical trials (T3MPO-1 and T3MPO-2) evaluating tenapanor in patients with IBS-C, and currently expects results from those trials in 2017. In a Phase 2b clinical trial evaluating a 50 mg dose of tenapanor BID, the study met its primary endpoint of an increase in the complete spontaneous bowel movement (CSBM) responder rate, demonstrating its ability to improve symptoms of IBS-C. Most secondary endpoints, including abdominal pain, the overall responder rate, and other abdominal and IBS-C symptoms, demonstrated statistically significant and clinically meaningful improvements when compared to placebo, as well. 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 compared to other forms of IBS, the Company believes that about 1.4% of the U.S. population, or approximately 4.4 million individuals, suffer from IBS-C, with approximately 1.0 million of those patients being diagnosed. Additionally, the Company estimates that there are about 6.6 million IBS-C patients in Europe and about 3.4 million in Japan.
- Hyperphosphatemia in ESRD patients on dialysis: In the fourth quarter 2015, the Company initiated a Phase 2b clinical trial to evaluate the optimal dosing regimen of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis. Pending positive data, the clinical trial may be considered the first of two registration trials to support the filing of a new drug application (NDA) for tenapanor in this indication. The Company currently expects to

announce results from this ongoing trial in the first quarter of 2017. Results from an earlier Phase 2b clinical trial in this indication were announced in 2015. In that study, 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 for patients that were treated with tenapanor, based on previous clinical trials. Higher discontinuations rates due to diarrhea were observed primarily in the 30 mg QD and 30 mg BID dose groups. The ongoing registration clinical trial has a down-titration arm to optimize tolerance while retaining efficacy. The overall safety profile of the previously completed Phase 2b trial remained consistent with that observed in previous tenapanor trials. The Company estimates, based on phosphate binder utilization, that there are approximately 290,000, 225,000, and 220,000 ESRD patients with hyperphosphatemia in the United States, Europe, and Japan, respectively.

About RDX227675

RDX227675 is Ardelyx's proprietary oral, non-absorbed, potassium-binding polymer based on sodium polystyrene sulfonate (SPS), a well-known and well-characterized polymer, also known as Kayexalate®. Ardelyx has made numerous improvements to the polymer by engineering into RDX227675 several key physical and chemical modifications in an effort to improve various properties. In a separate single center, randomized, crossover study to evaluate various oral formulations of RDX227675 in healthy adult volunteers, RDX227675 consistently outperformed SPS in all aspects of the taste assessments, including mouth feel, texture, and flavor. A human adult pharmacodynamic study has shown that 13.8 g of RDX227675, whether delivered once, twice or three times daily, results in a similar increase of stool potassium of about 1,500 mg/day, with decrease in urinary potassium of about 900 mg/day. The Company expects to begin a Phase 2b trial designed to evaluate the rate of onset of action and a Phase 3 clinical program with RDX227675 in fourth quarter 2016. The Company believes that hyperkalemia (HK) affects about 900,000 individuals with Stage 3b or Stage 4 CKD in the United States as well as approximately 900,000 patients with HF and up to 200,000 ESRD patients on dialysis in the United States. Ardelyx has filed a patent application covering the composition of matter of RDX227675.

About Ardelyx, Inc.

Ardelyx is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of innovative, minimally-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat gastrointestinal and cardio-renal diseases. Ardelyx has developed a proprietary drug discovery and design platform enabling it, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing this platform, Ardelyx has discovered and designed tenapanor, which it is evaluating for the treatment of IBS-C and management of hyperphosphatemia in patients with ESRD on dialysis. In addition to tenapanor, Ardelyx is developing RDX227675, a non-absorbed polymer for the treatment of hyperkalemia, or high potassium, a problem prevalent in patients with kidney and heart disease. Ardelyx is also advancing several research programs focused in gastrointestinal and cardio-renal diseases. Ardelyx is located in Fremont, California. For more information, please visit Ardelyx's website at www.ardelyx.com.

Forward Looking Statements

To the extent that statements contained in this press release are not descriptions of historical facts regarding Ardelyx, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor of the Private Securities Reform Act of 1995, including the potential for tenapanor in treating IBS-C patients, the expected timing for the receipt of the results from Ardelyx's two ongoing Phase 3 clinical trials evaluating tenapanor for the treatment of IBS-C, the potential for tenapanor in treating hyperphosphatemia in ESRD patients on dialysis, the expected timing of the results of the ongoing clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, the potential for the ongoing clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis to serve as the first of two well-controlled clinical trials to support registration, the potential for RDX227675 in treating hyperkalemia in CKD patients, the expected timing of the initiation of the Phase 2b and Phase 3 clinical trials evaluating RDX227675 in treating hyperkalemia in CKD patients and the expected timing of the results of the Phase 2b trial, and the potential of Ardelyx's drug discovery and design platform. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of tenapanor, RDX227675, or Ardelyx's future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in research and the clinical development process and the uncertainties in the manufacture of clinical trial material, including process development, scale up and tech transfer of manufacturing processes. Ardelyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Ardelyx's business in general, please refer to Ardelyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 9, 2016, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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