Ardelyx Presents New Preclinical Data Demonstrating Synergy between Tenapanor and Sevelamer When Dosed in Combination for Elevated Serum Phosphorus

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Company Plans to Commence a Phase 2/3 Clinical Study Evaluating Tenapanor in Combination with Phosphate Binders

FREMONT, Calif., Oct. 26, 2018 /PRNewswire/ -- Ardelyx, Inc. (Nasdaq: ARDX), today announced the presentation of preclinical data suggesting therapeutic synergy of tenapanor in combination with sevelamer, the current standard-of-care phosphate binder treatment for hyperphosphatemia, or elevated serum phosphorus. The data, showing that the combination meaningfully reduced serum phosphorus, were presented today in a poster titled "Combination treatment with tenapanor and sevelamer synergistically reduces urinary phosphorus excretion in rats," at the American Society of Nephrology (ASN) Annual Meeting. Tenapanor, Ardelyx's lead product candidate, is a sodium/hydrogen exchanger 3 (NHE3) inhibitor that is currently being evaluated as a monotherapy in a second, Phase 3 registration trial, the PHREEDOM trial, for the treatment of hyperphosphatemia in patients with end-stage renal disease (ESRD) who are on dialysis. Data from that study are anticipated in 2019.

The preclinical data presented today support Ardelyx's plans to evaluate tenapanor in combination with phosphate binders in a planned Phase 2/3 clinical trial. During the treatment period of the planned Phase 2/3 combination trial, patients will remain on their binders with either tenapanor or a placebo added to their treatment regimen.

"If we are able to replicate what we've seen in these preclinical studies in our planned human studies, we believe tenapanor could be used as an add-on to current binder therapy," said David P. Rosenbaum, chief development officer of Ardelyx. "Most dialysis patients have phosphate levels that are significantly higher than normal, but to date, the only options for treatment have been to add more phosphate binders, which all have similar mechanisms of binding to dietary phosphate in the gastrointestinal tract. Given the uniquely different mechanism of tenapanor and its potential synergy with phosphate binders, we could imagine nephrologists adding tenapanor to the phosphate binder regimen of their patients, potentially improving phosphate management and reducing the pill burden of phosphate binders. We are excited to see if this effect is supported by our planned human study."

In preclinical models, sevelamer was administered at three dose levels with either tenapanor or placebo added twice daily for 11 days. Two additional groups received either tenapanor or placebo alone. Results showed that in combination with tenapanor, sevelamer dose-dependently decreased urinary phosphorus excretion and reduced renal phosphorus clearance, resulting in a treatment effect that was greater than either tenapanor or the equivalent dose of sevelamer administered alone across all sevelamer dose levels, or the expected additive reduction of the two treatments combined. Treatment with tenapanor significantly decreased urinary sodium excretion versus placebo, both when administered alone and when co-administered with all doses of sevelamer. In addition, treatment with tenapanor alone significantly reduced renal sodium clearance versus placebo, a reduction that was not significantly affected by combination treatment with sevelamer at the two lower doses. Notably, the combination effect of tenapanor and sevelamer on urinary phosphorus excretion was synergistic, with the strongest synergy at the lowest and most clinically relevant sevelamer dose.

About Ardelyx, Inc.
Ardelyx is focused on enhancing the way people with cardiorenal diseases are treated by developing first-in-class medicines. Ardelyx's cardiorenal pipeline includes the Phase 3 development of tenapanor for the treatment of hyperphosphatemia in people with end-stage renal disease who are on dialysis and RDX013, a potassium secretagogue program for the potential treatment of high potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease. In addition, Ardelyx has completed Phase 3 development of tenapanor for the treatment of irritable bowel syndrome with constipation (IBS-C) and submitted a New Drug Application to the U.S. Food and Drug Administration seeking U.S. marketing approval for this indication. To efficiently bring its treatments to market, Ardelyx is pursuing strategic collaborations for tenapanor for IBS-C and hyperphosphatemia in certain territories. Ardelyx has established agreements with Kyowa Hakko Kirin in Japan, Fosun Pharma in China and Knight Therapeutics in Canada. For more information, please visit http://www.ardelyx.com/ and connect with us on Twitter @Ardelyx.

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 Ardelyx's product candidates in treating the diseases and conditions for which they are being developed, the potential for the use of tenapanor in combination with phosphate binders as adjunctive therapy for the treatment of hyperphosphatemia, and Ardelyx's expected timing for receipt of data from its ongoing Phase 3 clinical trial of tenapanor for the treatment of hyperphosphatemia in ESRD patients. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of Ardelyx's product candidates 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 the clinical development process, including the regulatory approval process. 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 August 7, 2018, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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Monique Allaire, THRUST Strategic Communications, 781-631-0759, monique@thrustsc.com