Ardelyx Announces Tenapanor Reduces Pain Caused by IBS-C Through Inhibition of TRPV-1 Signaling

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Preclinical data provide new mechanistic insights linking tenapanor's analgesic action to a well-established pain pathway for the treatment of patients with IBS-C

FREMONT, Calif., Oct. 16, 2017 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX) today reported that data from preclinical studies have shown that tenapanor works to reduce abdominal pain caused by irritable bowel syndrome with constipation (IBS-C) through the inhibition of TRPV-1 dependent signaling. TRPV-1, better known as the "hot chili pepper receptor," is a well-established pain target known for transmitting painful stimuli from a variety of sources including heat, protons and inflammatory molecules. Tenapanor, Ardelyx's investigational, minimally systemic, small-molecule inhibitor of NHE3, has demonstrated statistically significant results in two positive Phase 3 studies in patients with IBS-C, and the ability to reduce abdominal pain and alleviate constipation.

The preclinical data on tenapanor's pain mechanism are being presented by investigators from the Johns Hopkins University School of Medicine in a poster session on Tuesday, October 17, 2017 at the American College of Gastroenterology (ACG) World Congress 2017. The congress is being held October 13 – 18, 2017 in Orlando, Florida.

These preclinical data were generated at Dr. Jay Pasricha's laboratory at Johns Hopkins University School of Medicine under a sponsored research agreement with Ardelyx. Using an established rodent model of IBS-like colonic hypersensitivity, the results show that tenapanor treatment reduced visceral hypersensitivity (pain in the internal organs) and normalized colonic sensory neuronal excitability and TRPV-1 currents. Treatment with tenapanor also increased stool excretion and stool water content. Tenapanor had a significantly better effect on visceral hypersensitivity than placebo or PEG, a well-known laxative not known to have an analgesic effect.

"This may be a critical aspect of tenapanor's therapeutic mechanism for IBS-C patients. This work links tenapanor's ability to improve the symptoms of visceral hypersensitivity and abdominal pain, two of the most important and burdensome symptoms for patients with IBS-C, to a well-established pain target. These experiments have demonstrated that tenapanor inhibits TRPV-1 dependent pain signaling in neurons lining the GI tract," said Jeremy Caldwell, Ph.D., chief scientific officer of Ardelyx. "Based on this research, tenapanor influences TRPV-1 indirectly, which we plan to further investigate to fully elucidate this first-in-class mechanism of action. To the best of our knowledge, tenapanor is the only potential treatment option for IBS-C that has shown the ability to reduce abdominal pain through inhibition of TRPV-1 signaling, representing a completely novel therapeutic option for these patients."

"The findings related to tenapanor's mechanism of action further support the positive Phase 3 IBS-C results that we have reported throughout 2017, including the exciting data from our second IBS-C Phase 3 study, T3PMO-2, which we reported last week," said David Rosenbaum, Ph.D., chief development officer of Ardelyx. "Our T3MPO program is nearing completion, and we are moving forward to submit our first New Drug Application to the U.S. Food and Drug Administration for this indication in the second half of 2018. With the combination of tenapanor's first-in-class mechanism and its demonstrated ability to reduce pain and alleviate constipation, we believe tenapanor represents a significant new treatment approach for physicians and patients."

In addition to the poster session, Bill Chey, M.D., a principal investigator in the T3MPO clinical program, will present detailed data from Ardelyx's first, positive Phase 3 study, T3MPO-1, evaluating tenapanor for the treatment of people with IBS-C, which were originally announced in May 2017. The data will be presented in an oral session at the meeting on Tuesday, October 17, 2017 at 2:40 p.m.

About Tenapanor
Tenapanor, invented and developed by scientists at Ardelyx, is a first-in-class, proprietary, minimally absorbed, oral, experimental medication in late-stage clinical development. It has a unique mechanism of action that, in IBS-C, acts by inhibiting, or blocking, the NHE3 transporter in the gastrointestinal (GI) tract to reduce the absorption of dietary sodium. Blocking NHE3 results in an increase in the amount of sodium in the gut. This increased sodium in the gut leads to an increase of fluid in the gut, loosening stool and helping to relieve constipation. We have also seen a desired benefit in the abdominal pain component of IBS-C in our studies to-date.

Tenapanor is also in Phase 3 development for the treatment of hyperphosphatemia in patients with end-stage renal disease who are on dialysis. In hyperphosphatemia, tenapanor blocks the NHE3 sodium transporter in the GI tract, reducing the absorption of dietary sodium and resulting in increased protons within the cells. The increase in protons causes a preferential reduction in phosphate uptake by tightening junctions or pores that regulate phosphate absorption in the GI tract. We have not observed this impact on other ions, nutrients or macromolecules in our clinical trials, suggesting that this effect is preferential for phosphate.

About IBS-C
Irritable bowel syndrome with constipation, or IBS-C, is a gastrointestinal disorder characterized by significant abdominal pain and constipation. Ardelyx estimates that approximately 11 million people in the United States suffer from IBS-C. This condition significantly impacts the health and quality of life of affected patients. The cause of IBS-C is unknown.

About Ardelyx, Inc.
Ardelyx is focused on enhancing the way patients with cardiorenal and gastrointestinal (GI) diseases are treated by using the gut as the gateway to delivering medicines that matter. The company has established unique cardiorenal and GI business portfolios aimed at bringing new, effective medicines with distinct safety and dosing advantages to underserved patients. Ardelyx's cardiorenal portfolio includes the Phase 3 development of tenapanor for the treatment of hyperphosphatemia in people with end-stage renal disease who are on dialysis and the Phase 3 development of RDX7675 for the treatment of people with hyperkalemia. The company's GI portfolio includes the Phase 3 development of tenapanor for the treatment of people with irritable bowel syndrome with constipation (IBS-C), and RDX8940, the company's TGR5 agonist. 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 tenapanor in treating patients with IBS-C, including tenapanor's ability to reduce pain in IBS-C patients by inhibiting TRPV-1 signaling; and Ardelyx's expectations regarding the timing of the completion of its T3MPO program and the timing of its submission of an NDA for tenapanor for the treatment of IBS-C 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 research and 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 9, 2017, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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