Ardelyx's Pivotal Phase 3 Study of Tenapanor for IBS-C Hits Primary and All Secondary Endpoints to Support NDA Submission in 2018

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Six of 12-week combined responder rate shows clear benefit in treated patients with consistent response throughout 26 weeks
Best-in-class, nine of 12-week combined responder rate demonstrates ability to normalize patients' bowel function
Conference call to be held today at 4:30 p.m. ET

FREMONT, Calif., Oct. 11, 2017 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX) today reported positive results from T3MPO-2, its second Phase 3 study of tenapanor for irritable bowel syndrome with constipation (IBS-C). The study hit statistical significance for the primary endpoint and all secondary endpoints evaluated for the topline results and demonstrated the ability to normalize bowel movements. The primary endpoint, the combined responder rate for six of 12 weeks, showed that a greater proportion of tenapanor-treated patients compared to placebo-treated patients (36.5% vs. 23.7%, p<0.001) had at least a 30 percent reduction in abdominal pain and an increase of one or more complete spontaneous bowel movements (CSBM) in the same week for at least six of the 12 weeks of the treatment period. In addition, tenapanor achieved statistical significance for the CSBM and abdominal pain responder rates in the six of 12 and nine of 12-treatment weeks, with a consistent response across the 26 weeks of the study. Tenapanor was well-tolerated in treated patients.

"These results are a game-changer for patients with IBS-C, their treating physicians and for Ardelyx as a company," said Mike Raab, president and chief executive officer of Ardelyx. "They demonstrate the significant benefit tenapanor can have for patients with IBS-C, importantly, leading to a normalization of bowel movements for many patients. These results show that tenapanor has significant potential in the market and bolsters our commitment to identify the ideal collaboration partner to help ensure that we reach the most patients possible who would benefit from therapy."

"IBS-C is a highly burdensome and difficult-to-treat condition affecting more than 11 million people in the United States, and often preventing them from engaging in day-to-day activities, such as going to work, exercising and even meeting socially with family and friends," said William Chey, M.D., University of Michigan. "Based on tenapanor's unique mechanism of action, which relies upon the inhibition of sodium absorption, and the exciting data reported today, tenapanor has the potential to be an important advancement and a new treatment option for patients suffering from IBS-C."

T3MPO-2 Trial Design
T3MPO-2 is a 26-week, double-blind, placebo-controlled, multi-center, randomized trial. The trial was conducted in a total of 593 patients meeting the ROME III criteria for the diagnosis of IBS-C. Patients were randomized one-to-one to receive either 50 mg of tenapanor (n=293) or placebo (n=300) twice-daily. The trial included a two-week screening period, during which patients with active disease, based on bowel movement frequency and abdominal pain score recorded in a daily phone diary, were randomized into the trial.

T3MPO-2 Top-line Efficacy Results
During the two-week screening period, the baseline scores were well-balanced between the tenapanor and placebo groups. The mean weekly CSBMs were 0.11 and the mean abdominal pain score was 6.26 (on a 0 - 10 scale where 0 was no pain and 10 was very severe). Key data are as follows:

Table 1

6 of 12 Treatment Week Results	Tenapanor	Placebo	P value
Combined responder (primary endpoint) (abdominal pain and CSBM responder)	36.5%	23.7%	p<0.001
CSBM responder (increase ≥ 1 CSBM from baseline)	47.4%	33.3%	p<0.001
Abdominal pain responder (≥ 30% abdominal pain reduction)	49.8%	38.3%	p=0.004

Table 2

9 of 12 Treatment Week Results	Tenapanor	Placebo	P value
Combined responder (abdominal pain and CSBM responder)	18.4%	5.3%	p<0.001
CSBM responder (increase ≥ 1 CSBM from baseline and ≥3 CSBM/week)	22.2%	6.0%	p<0.001
Abdominal pain responder (≥ 30% abdominal pain reduction)	35.8%	26.7%	p=0.015

Table 3

Durable Responder Results (9 of 12 and ≥3 of last 4 treatment weeks)	Tenapanor	Placebo	P value
Combined responder (abdominal pain and CSBM responder)	18.1%	5.0%	p<0.001
CSBM responder (increase ≥ 1 CSBM from baseline and ≥3 CSBM/week)	21.2%	5.7%	p<0.001
Abdominal pain responder (≥ 30% abdominal pain reduction)	34.8%	26.7%	p=0.028

T3MPO-2 Safety Results
Tenapanor was well-tolerated, consistent with the experience across previous clinical trials. The only adverse events observed in more than two percent of patients in the tenapanor-treated group that were also greater than placebo were diarrhea (16.0% vs. 3.7%), flatulence (3.1% vs. 1.0%), nasopharyngitis (4.4% vs. 3.7%) and abdominal distension (3.4% vs. 0.3%). The placebo adjusted discontinuation rate due to diarrhea was 5.8 percent.

Based on positive results from two positive Phase 3 trials, Ardelyx is on track to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration for tenapanor for the treatment of IBS-C in the second half of 2018. Final, detailed results from the study are expected to be presented at a medical meeting in 2018.

T3MPO-3
Patients who have completed T3MPO-1 and T3MPO-2 are eligible to enter T3MPO-3, Ardelyx's open-label, long-term safety trial where patients can continue to receive tenapanor for up to one year. T3MPO-3 is fully enrolled and expected to conclude in late 2017. The results of the trial will be included in the NDA submission for tenapanor for the treatment of patients with IBS-C.

T3MPO-2 Primary and Secondary Endpoint Definitions

Primary Endpoint:

- Combined responder rate (6/12 week): A six of 12-week combined responder is a CSBM responder and an abdominal pain responder during the same week for six of 12 weeks.

Secondary Endpoints:

- CSBM responder rate (6/12 week): A six of 12-week CSBM responder is a patient that has an increase of at least one CSBM from baseline during a week for six of 12 weeks.
- Abdominal pain responder rate (6/12 week): A six of 12-week abdominal pain responder is a patient that has at least a 30 percent decrease in abdominal pain from baseline during a week for six of 12 weeks.
- Combined responder rate (9/12 week): A nine of 12-week combined responder is a nine of 12 week CSBM responder and an abdominal pain responder during the same week for nine of 12 weeks.
- CSBM responder rate (9/12 week): A nine of 12-week CSBM responder is a patient that has an increase of at least one CSBM from baseline and at least three CSBMs during a week for nine of 12 weeks. Normal bowel function is characterized by at least three bowel movements a week up to three bowel movements a day.
- Abdominal pain responder rate (9/12 week): A nine of 12-week abdominal pain responder is a patient that has at least a 30 percent decrease in abdominal pain from baseline during a week for nine of 12 weeks.
- Durable responder rates (9/12 week): All three durable responder endpoints – combined responder rate, CSBM responder rate and abdominal pain responder rate – are identical to the nine of 12-week responder endpoints, except the response must also occur in three of the last four treatment period weeks.

Conference Call Information
The company will host a conference call today, October 11, 2017 at 4:30 p.m. ET to discuss the T3MPO-2 results. To participate in the conference call, please dial (855) 296-9612 (toll-free) or (920) 663-6277 (toll) and reference call ID number 98932908. A webcast of the call and reference slides that will be used during the call, can be accessed by visiting the Investor page of the company's website www.ardelyx.com, and will be available on the website for 60 days following the call.

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 a late-stage company 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; Ardelyx's expectations regarding the timing for the completion of T3MPO-3; Ardelyx's expectations regarding the filing of an NDA for tenapanor for the treatment of IBS-C; and Ardelyx's ability to establish collaboration partnerships in the future. 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. 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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SOURCE Ardelyx

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