May 12, 2017

Ardelyx Reports Successful Phase 3 T3MPO-1 Trial of Tenapanor in Patients with IBS-C

Study achieves primary endpoint; tenapanor well-tolerated in treated patients
Company to hold conference call at 8:30 a.m. ET today

FREMONT, Calif., May 12, 2017 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a late-stage clinical company focused on enhancing the treatment of patients with cardiorenal and gastrointestinal (GI) diseases, today reported positive, topline results from the T3MPO-1 trial, the first of two Phase 3 trials evaluating tenapanor for the treatment of patients with irritable bowel syndrome with constipation (IBS-C). Tenapanor is Ardelyx's investigational, minimally systemic, small-molecule NHE3 inhibitor.

The T3MPO-1 trial achieved statistical significance for the primary endpoint and seven of eight secondary endpoints. 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 (27.0% vs 18.7%, p=0.02) 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. Tenapanor was well-tolerated, consistent with the experience across previous clinical trials.

"We're pleased to have achieved the primary endpoint in the T3MPO-1 trial," said Mike Raab, president and chief executive officer of Ardelyx. "IBS-C is an extremely difficult, life-altering condition, and despite advancements, there remains a strong need for new, innovative treatments. In this trial, tenapanor demonstrated clinical activity across a large number of study parameters and had a favorable safety profile consistent with previous clinical experience. With a differentiated mechanism of action, we believe tenapanor has the potential to augment the care of patients with IBS-C."

T3MPO-1 Trial Design

T3MPO-1 was a 12-week, double-blind, placebo-controlled, multi-center, randomized trial with a four-week, randomized withdrawal period conducted in a total of 610 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=309) or placebo (n=301) 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-1 Topline Efficacy Results

During the two-week screening period, the baseline mean weekly CSBMs were 0.2 and the mean abdominal pain score was 6.3 (on a 0 - 10 scale where 0 is no pain and 10 is 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)	27.0%	18.7%	p=0.02
CSBM responder (increase ≥ 1 CSBM from baseline)	33.9%	29.4%	p=0.27
Abdominal pain responder (≥ 30% abdominal pain reduction)	44.0%	33.1%	p=0.008

Table 2

9 of 12 Treatment Week Results	Tenapanor	Placebo	P value
Combined responder (abdominal pain and CSBM responder)	13.7%	3.3%	p < 0.001
CSBM responder (increase ≥ 1 CSBM from baseline and ≥3 CSBM/week)	16.9%	5.0%	p < 0.001

Abdominal pain responder (≥ 30% abdominal pain reduction)	30.3%	19.4%	p=0.003

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)	13.0%	3.3%	p < 0.001
CSBM responder (increase ≥ 1 CSBM from baseline and ≥3 CSBM/week)	16.0%	4.7%	p < 0.001
Abdominal pain responder (≥ 30% abdominal pain reduction)	29.3%	19.4%	p=0.006

"When we look at the totality of the topline results from T3MPO-1, we believe tenapanor has the potential to offer benefit to patients with IBS-C," said David Rosenbaum, Ph.D., chief development officer of Ardelyx. "We are encouraged that the nine of 12 week data demonstrate a durable and sustained response for constipation and abdominal pain, as well as a normalization of bowel movement frequency, for many patients. The individual CSBM responder rate from the six of 12 week analysis was the one secondary endpoint not met and those data are not consistent with the results from our previous clinical studies. We plan to assess these data alongside the results from T3MPO-2, our six-month Phase 3 study, to evaluate the total benefit that tenapanor may provide to patients with this extremely challenging condition."

T3MPO-1 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 treated with tenapanor, as compared with placebo, were diarrhea (14.6% vs 1.7%) and nausea (2.6% vs 1.7%). Discontinuations due to diarrhea were 5.9 percent for the tenapanor-treated patients, compared to 0.6 percent for the placebo group, based on the preliminary results.

T3MPO-2 and T3MPO-3

A second Phase 3 trial, T3MPO-2, a 26-week study evaluating tenapanor for the treatment of patients with IBS-C is ongoing with data expected early in the fourth quarter of 2017. 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 expected to conclude in late 2017.

T3MPO-1 Primary and Key Secondary Endpoint Definitions

- 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.
- 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 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.
- 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 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, May 12, 2017 at 8:30 a.m. ET to discuss the T3MPO-1 findings. To participate in the conference call, please call (855)-296-9612 (toll-free) or (920)- 663-6277 (toll) and reference call ID number 23050169. A webcast of the call can also 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 for IBS-C

Tenapanor, invented and developed internally by scientists at Ardelyx, is a first-in-class, proprietary, oral, experimental medication that works primarily in the gut and is 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 GI tract to reduce the absorption of dietary sodium into the blood stream. 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, which loosens stool, helping to relieve constipation. We have also seen a desired benefit in the abdominal pain component of IBS-C in our studies to-date. The mechanism of abdominal pain is currently

under investigation to be detailed in future manuscripts.

About IBS-C
Irritable bowel syndrome with constipation, or IBS-C, is a gastrointestinal disorder characterized by significant abdominal pain and constipation (when a bowel movement is difficult due to insufficient/decreased amount of fluid in the GI, or happens less often than normal). 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, and there are currently no specific diagnostic tests or biomarkers for detection. Therefore, IBS-C is diagnosed by symptoms and by eliminating other disorders. IBS-C is similar to chronic constipation but is clinically distinct as a result of the significant abdominal pain component.

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, a TGR5 agonist approaching Phase 1 development. Leveraging the company's platform and unique gut-restriction chemistry, Ardelyx intends to build a fully integrated, revenue-generating biopharmaceutical company with leading cardiorenal and GI business portfolios. For more information, please visit 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 IBS-C patients; Ardelyx's future development plans for tenapanor and its other product candidates and the expected timing thereof; Ardelyx's expected timing for the receipt of results from the T3MPO-2 and T3MPO-3 clinical trials evaluating tenapanor in IBS-C; 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 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 and the uncertainties in the manufacture of clinical trial material, including process development, including the regulatory approval , the uncertainties in the manufacture of clinical trial material, including process development, and uncertainties in the drug commercialization 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 May 5, 2017, and its future current and periodic reports to be filed with the Securities and Exchange Commission.