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# Ardelyx Inc. (ARDX - OUTPERFORM): Tenapanor Meets Primary Endpoint in ESRD Trial, Diarrhea Rates a Concern, but likely Manageable, in our View, Reiterate OP rating and $31 PT

**Price: $19.69** **12-Month Price Target: $31**

- **Primary endpoint is met in Ph 2b study of tenapanor in treating hyperphosphatemia in ESRD.** Compared to placebo, tenapanor demonstrated a statistically significant (p=0.012) dose-related decrease in serum phosphate levels from baseline in ESRD patients with hyperphosphatemia. The double-blind, dose-finding study evaluated 3 and 30mg qd and 1, 3, 10 and 30mg bid dose levels of tenapanor for four weeks in dialysis patients who have elevated serum phosphate levels. ARDX noted that the bid dosing schedule had superior PD activity. We expect full data to be presented at a medical conference later this year, likely the American Society of Nephrology annual meeting November 3-8.

- **Diarrhea rates were higher than expected, but without higher-than-expected discontinuation rates, it was likely manageable.** ARDX noted that diarrhea rates were higher than that previously observed with tenapanor. A specific rate was not provided, and data from earlier clinical studies of tenapanor in renal disease remain unpublished, making it impossible to ascertain how significant the increase was in this study. The fact that ARDX felt it was materially relevant to mention potentially raises concerns about the magnitude of the increase, and how this affects the future development plans of tenapanor remain to be seen. However, we note that no mention was made of higher discontinuation rates, and we believe that indicates that the diarrhea was likely manageable. We note that diarrhea was observed in 11% of patients receiving the 50mg dose in the Ph 2b IBS-C study, although rates in the ESRD study are likely to be higher, given the underlying pathophysiology associated with IBS-C.

- **We believe investor reaction may be overblown, and we note other approved drugs in this space have significant GI side effects.** Given the critical need to control phosphorus levels in ESRD patients, an elevated risk of diarrhea may be an acceptable trade-off. Recall that hyperphosphatemia is a condition that develops in a majority of patients with kidney failure and is associated with a variety of cardiovascular complications. Dialysis does not readily remove phosphorus, and currently-approved phosphate binders (the only approved treatments for hyperphosphatemia) are associated with a high pill burden and their own specific safety concerns (including hypercalcemia in calcium-based binders and metal toxicity in Fosrenol and other metal-based binders). A 24% rate of diarrhea has also been observed with Fosrenol and other standardly used phosphate binders, along with high rates of nausea (29% to 37%) and vomiting (22% to 27%) (Finn WF. Clinical Nephrology, 2006). Given that nausea and vomiting were not specifically mentioned as safety concerns with tenapanor, the small molecule NHE3 inhibitor may be a more tolerable option than currently available therapies.

- **We anticipate the release of the full dataset from the Ph 2b study later this year, which should provide greater clarity on the dose relationship on safety and efficacy.** We continue to believe that a safe, minimally effective tenapanor dose can be identified for future development in ESRD. We also expect data in Q2:15 from the Ph 2 tenapanor study (evaluating 5 to 60mg bid for 12 weeks) in CKD patients to provide additional insight into the safety of tenapanor. We note that we value the IBS-C program alone at $15/share; given where the stock is trading now, investors have essentially a near-free call option on the ESRD and CKD indications.

- **Reiterate OUTPERFORM rating and $31 price target.** Our price target of $31 is derived by applying a 6 multiple to ARDX's share of 2022 tenapanor sales in the US, added to a 15 multiple of the royalty ARDX is expected to receive in 2022 for ex-US sales of tenapanor.

- Risks to the achievement of our price target include clinical or regulatory failure for tenapanor and failure to achieve sales or earnings estimates.

**Milestones:**
Q2:15 Results from Ph2a study of tenapanor in Stage 3 CKD patients with Type 2 diabetes and albuminuria.

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| Company | Disclosure |
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| Ardelyx Inc. | 1,3,4,5 |

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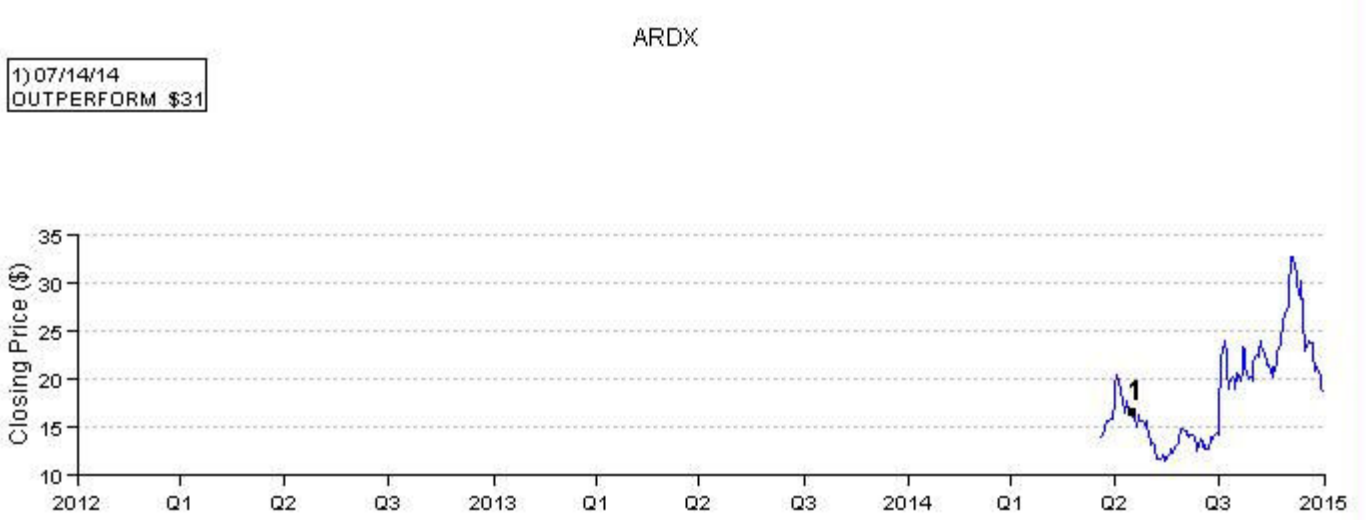


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