Service to those affected by chronic kidney disease

Date August 17, 2021

To: Joyce Yu, PharmD
Designated Federal Officer (DFO)
Division of Advisory Committee and Consultant Management
Office of Executive Programs
FDA Cardiovascular and Renal Drugs Advisory Committee
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From: Lori Hartwell
Founder/President of Renal Support Network

Re: The FDA's Complete Response Letter to Ardelyx, Inc.'s New Drug Application for tenapanor for the control of serum phosphorus in adult patients with chronic kidney disease on dialysis.

Renal Support Network exists to empower people who have kidney disease to become proactive in their care, and to work with healthcare professionals, regulatory agencies, and legislative leaders to get the best care and health outcomes possible. RSN strongly supports the Food and Drug Administration (FDA) policy of fostering innovation in treating kidney diseases. We are writing with concern about the FDA's recent Complete Response Letter (CRL) to Ardelyx, Inc., denying approval of its New Drug Application (NDA) for tenapanor. We are confused by this decision as it is contrary to the FDA's stated commitment to innovate to improve kidney care. Innovative therapies with novel mechanisms of action that have the potential to lower phosphorus with less treatment burden for people that have chronic kidney disease (CKD) are desperately needed.

The FDA is a partner in the Kidney Health Initiative, founded in 2012 to address the need for innovation in treating kidney disease and to accelerate innovation while ensuring patient safety. RSN agrees with Harris and Cahill, writing in the Clinical Journal of the American Society of Nephrology, on how this partnership should approach development of novel therapies: "Innovative drug and device development will only be successful if it is built around the needs of people with kidney disease and focused on improving their quality of life."

The CRL acknowledged tenapanor's efficacy, stating "the submitted data provide substantial evidence that tenapanor is effective in reducing serum phosphorus in CKD patients on dialysis." Tenapanor met the primary and key secondary endpoints in all three Phase 3 pivotal trials. In the long-term Phase 3 trial, tenapanor also demonstrated comparable safety to an active control.

We currently have only one class of therapy available for hyperphosphatemia – phosphate binders – which often place a significant treatment pill burden on people who have kidney failure. Large pills can be difficult to swallow. It is often necessary to take pills with every meal and snack, while at the same time monitoring and limiting liquid intake. Tenapanor has the potential to significantly reduce the current pill burden on patients. That could lead to better quality of life, better patient compliance with the treatment regimen, and subsequently better outcomes.

Phosphorus levels and their impact on bone and mineral management are critical to people who have kidney disease. They will suffer and become debilitated if phosphorus is not managed appropriately. Quality of life

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considerations should prompt an open approach to novel treatment therapies. As the FDA acknowledges that tenapanor trial results indicate safety and efficacy, why not allow doctors and patients to have the choice?

If innovation is a goal, and success is determined by addressing patient needs and improving quality of life, the decision in this CRL is not inspiring as it constrains options for doctors and patients by imposing a subjective assessment of treatment efficacy.

For existing approved therapies, data shows that in any given month, 42% of patients are unable to achieve target phosphorus levels, and over a 6-month period 77% of patients are unable to maintain target phosphorus levels. For patients dealing with hyperphosphatemia, existing approved therapies aren't achieving great results. Drug treatments don't work for all patients in the same way. Patients need treatment options.

RSN asks the FDA to reconsider innovative therapies that benefit patients by reducing phosphorus that can improve lab results. Phosphorus management is one of the most difficult elements a patient has to manage, especially with all the preservatives that are in food options today.

In RSN's opinion, the FDA's decision is not in the best interest of patients, the physicians who treat them, and the nephrology community focused on innovation that addresses patient needs and improves quality of life. Please reconsider this decision and help patients have treatment options and inspire other companies to burn the midnight oil to improve our care.

Please let me know if you have any questions or need additional information.

Warmest Regards,

Lori Hartwell, President & Founder

About RSN:

The Renal Support Network (RSN) serves the kidney community by empowering people who have kidney disease to become knowledgeable about their illness, proactive in their care and hopeful about their future. RSN reaches hundreds of thousands of people who have kidney disease and their families through our many patient programs, all of which are offered at no charge. RSN is the leader in engaging people who have kidney disease. RSN was founded by Lori Hartwell who has been a kidney disease survivor since the age of two and founded RSN in 1993 to help her peers have hope and have access to the best care.