May 7, 2025

Mr. Stephen Astle
Director, Defense Industrial Base Division
Office of Strategic Industries and Economic Security
Bureau of Industry and Security
US Department of Commerce

Submitted Electronically

RE: XRIN 0694-XC120 - Notice of Request for Public Comment on Section 232 National Security Investigation of Imports of Pharmaceutical Products and Their Derivatives

Dear Director Astle,

Ardelyx, Inc. appreciates the opportunity to provide input on the Administration's initiative to strengthen U.S. pharmaceutical manufacturing and ensure consistent access to life-saving therapies. Founded in 2007 and headquartered in Waltham, Massachusetts, Ardelyx is a biopharmaceutical company focused on innovative treatments for gastrointestinal and cardiorenal diseases. Our lead products include IBSRELA®, a prescription medicine used in adults to treat irritable bowel syndrome with constipation (IBS-C), and XPHOZAH®, a prescription medicine used to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy when phosphate binders do not work well, or when phosphate binders cannot be tolerated.

We support the Administration's objective to secure domestic supply chains for critical medications. However, we believe it is important to highlight key regulatory barriers that impede efforts to reduce reliance on foreign sources for essential raw materials. A specific case is dioctadecylamine (DODA)—a critical material used in the production of both IBSRELA® and XPHOZAH®. At present, a stable, sustainable domestic production of DODA does not exist, leaving only bespoke chemical solutions that severely limit our ability to localize production.

The current U.S. regulatory framework has, in practice, diminished the commercial incentive to manufacture specialty chemicals like DODA domestically. This constraint represents the primary obstacle to Ardelyx's alignment with reshoring goals. We urge the Administration to focus its reshoring strategy on modernizing regulations that would encourage domestic production of foundational chemical inputs essential to biopharmaceutical manufacturing.

Additionally, we recommend the establishment of a "run-in" period for manufacturers actively working to reshore their supply chains. This would provide companies like Ardelyx the time and flexibility needed to establish a reliable U.S.-based source of all components necessary for manufacturing, including raw materials, regulatory starting materials (RSMs), and active pharmaceutical ingredients

(APIs). Conversely, the imposition of new ad valorem duties on critical inputs during this transitional period would significantly hinder progress and limit our ability to meet patient demand.

We encourage a balanced, strategic approach that addresses both the immediate need for patient access to treatment and the long-term benefits of strengthening U.S. pharmaceutical manufacturing. Ardelyx remains committed to supporting these national objectives and looks forward to continued engagement with federal policymakers.

IBSRELA® AND XPHOZAH® Supply Chains

As mentioned, our ability to produce our medications is heavily reliant on foreign procurement due to the lack of domestic access to critical inputs. Currently, we rely on foreign markets that provide adequate and reliant supply, for some of our raw materials, our RSMs and our API. The manufacturing and packaging of our finished products, however, are already fully based in the United States. This grants Ardelyx a unique opportunity to continue onshoring the remaining components of our supply chain—provided the Administration incentivizes both new and existing U.S. competition in raw material, RSM and API production and processing.

We have a strong desire to maintain a secure supply of our medication to ensure that patient access is upheld. However, trade policy in this space must recognize that U.S. producers are faced with a regulatory environment that slows production, leading to output that is entirely untenable for pharmaceutical manufactures to meet our demand.

Chemical Manufacturing: Regulatory Relief

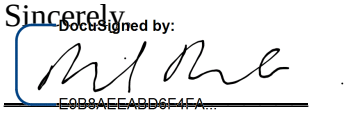
A more flexible regulatory environment—achieved not by weakening core environmental protections, but through selective relief within existing statutory frameworks—could significantly expand domestic production of raw materials, RSMs and APIs. The Clean Water Act (CWA) imposes stringent discharge requirements that often necessitate costly wastewater treatment infrastructure, driving up production costs. Similarly, the Resource Conservation and Recovery Act (RCRA) mandates complex handling and disposal protocols for regulated byproducts, requiring substantial compliance investments. The Toxic Substances Control Act (TSCA) adds further constraints through extensive chemical testing and approval requirements, which can delay innovation.

However, the Environmental Protection Agency (EPA) retains discretion under current law to ease certain burdens through pragmatic measures—such as streamlining permitting processes, expanding conditional exemptions, and issuing clearer guidance or waivers for low-risk activities. These actions, consistent with statutory authority, would reduce operational barriers for domestic chemical manufacturers and improve the economic feasibility of producing raw materials, RSMs and APIs in the United States. In turn, this would enhance the resilience of the U.S. pharmaceutical supply chain. Beyond environmental policy, targeted adjustments under the Occupational Safety and Health Administration's (OSHA) existing authorities could further incentivize domestic production. OSHA regulations are essential for workplace safety, but some requirements—such as extensive documentation, chemical exposure monitoring, and process safety management—can disproportionately burden small and mid-sized manufacturers. Providing more flexible compliance pathways, updated guidance reflecting modern chemical manufacturing processes, and expanded access to technical assistance would reduce administrative overhead without compromising safety. For example, simplified

hazard communication standards for well-characterized substances, or alternative safety protocols for low-risk operations, could facilitate facility expansion and lower costs.

Taken together, these targeted reforms would create a more enabling regulatory environment to support the reshoring of raw materials, RSMs and API manufacturing and reduce dependence on foreign supply chains. Ardelyx is committed to partnering with the Administration in advancing this agenda. We welcome continued dialogue with federal agencies to ensure that patients across the country have reliable access to essential medicines.

Sincerely,

DocuSigned by:

E0B8AEEABD6F4FA...

Mike Raab
CEO
Ardelyx, Inc.