May 7, 2025

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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 Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

Dear Director Astle,

On behalf of Pharming Group N.V., a Netherlands-based biopharmaceutical company operating under the affiliate Pharming Healthcare, Inc. in the United States, we appreciate the opportunity to comment on the Department of Commerce's Section 232 investigation into pharmaceutical imports and their implications for US national security.

Pharming is a global, commercial stage biopharmaceutical company developing innovative protein replacement therapies and precision medicines for the treatment of patients with rare and ultra-rare diseases and unmet medical needs. Our US headquarters is located in Warren, NJ and we employ roughly 150 people across the US.

Our portfolio includes Joenja® (leniolisib), the only FDA-approved treatment for Activated PI3K Delta Syndrome (APDS) in adult and pediatric patients 12 years of age and older.[1] APDS is a rare genetic immunodeficiency affecting an estimated 1 to 2 people per million in the US.[2,3] Beginning in early childhood, patients with APDS have increased susceptibility to infections, autoimmune complications, lymphomas, and as a result suffer from premature mortality.[4,5] There is no alternative FDA-approved treatment option for these patients and access to Joenja is essential to their care.

We are also the manufacturer of Ruconest®, a biologic therapy for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE); it is the only FDA-approved recombinant human C1 esterase inhibitor (rhC1INH).[6] Hereditary angioedema is a rare, debilitating, life-threatening genetic disorder characterized by recurrent attacks of subcutaneous and/or submucosal angioedema with an estimated prevalence of 1 in 50,000 people in the US.[7] Ruconest is uniquely produced using a technology involving the purified milk of transgenic rabbits. It is a sterile, preservative-free, lyophilized powder for reconstitution via intravenous injection. Ruconest's manufacturing process is highly specialized, subject to rigorous controls, and not easily transferred or duplicated elsewhere.

Both Joenja and Ruconest received Orphan Drug Designation and Orphan Drug Approval from the FDA.[8] These therapies are manufactured exclusively in Europe using complex, state-of-the-art processes that are not replicable through simple scaling or relocation. Our supply chains for these products are carefully managed to ensure continuous, reliable availability for US patients who depend on these therapies for their health and quality of life.

The imposition of tariffs on these highly specialized, small-volume therapies risks significant disruption to patient access. Due to the rarity of these conditions, our manufacturing process does not benefit from broad economies of scale, and any additional cost burden from tariffs would directly impact our ability to supply these critical medicines to US patients. There are no alternative domestic manufacturers for these therapies, nor would it be feasible to develop such capacity in the near term given the scientific and regulatory complexity involved. An attempt to transfer the manufacturing process to the US would require lengthy validation through comparability studies for each step and ultimate approval by the FDA. The exercise from start to finish would require significant financial investment and take years to complete.

Pharming strongly supports efforts to enhance the resilience of the US pharmaceutical supply chain and agrees with the objective of reducing overreliance on imports where national security is at risk. However, we respectfully urge the Department to consider excluding from any future pharmaceutical tariffs therapies to treat rare, orphan diseases like APDS and HAE. Therapies like Joenja and Ruconest have no domestic substitutes and no reasonable potential for near-term alternative sourcing. Imposing tariffs and these products could unintentionally harm the very patients who are already most vulnerable due to the rarity and severity of their conditions.

We remain committed to working with the Department of Commerce and other US agencies to support patient access to innovative therapies while contributing to the Administration's goals of a healthier and more secure America. Thank you for your consideration of these comments.

Sincerely,

Heather Greenspan (May 6, 2025 12:51 EDT)

Heather Greenspan
President & General Manager
Pharming Healthcare, Inc.

References

1. Joenja® Prescribing Information. 2023. Pharming Technologies BV
2. Lucas CL, et al. *Nat. Immunol*. 2014;15(1):88-97
3. Begg M, et al. *Pulm. Pharmacol. Ther*. 2023 Apr;79:102201
4. Rao VK, et al. *Blood.* 2023;141(9):971-983
5. Busch K, et al. *Adv. Ther.* 2025 Feb;42(2):752-771
6. Ruconest® Prescribing Information. Pharming Healthcare, Inc. 2020
7. Busse PJ, et al. *J. Allergy Clin. Immunol. Pract.* 2021;9:132-50
8. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm