May 7, 2025

Submitted Electronically

Mr. Eric Longnecker
Deputy Assistant Secretary for Technology Security
Bureau of Industry and Security
Office of Strategic Industries and Economic Security
U.S. Department of Commerce
1401 Constitution Avenue NW
Washington, DC 20230

Re: BIS-2025-0022 and XRIN 0694-XC120, the Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

Dear Deputy Assistant Secretary Longnecker:

AstraZeneca appreciates the opportunity to submit comments in response to the Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients.

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialization of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Alexion, AstraZeneca Rare Disease is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development, and delivery of life-changing medicines. Our innovative medicines are sold in more than 125 countries and used by millions of patients worldwide.

We share the Department of Commerce's goal to ensure the security of the U.S. pharmaceutical supply chain. Efforts to restrict pharmaceutical imports – through tariffs or other trade actions – and without a corresponding investment to build up needed U.S. manufacturing capacity may be counterproductive to the Administration's goals. We ask the Department to consider instead how global and regional integration strengthens the U.S. pharmaceutical supply chain and how U.S. tax and industrial policies to boost manufacturing can achieve similar outcomes.

Our comments are as follows:

1. **AstraZeneca has more manufacturing sites in the U.S. than anywhere else in the world; and a robust, resilient global supply chain which supports our domestic manufacturing base.** The United States is AstraZeneca's largest market, and we have had a U.S. presence since before the Astra AB and Zeneca PLC merger formed AstraZeneca PLC in 1999. AstraZeneca helps treat tens of thousands of U.S. patients with cancer, cardiovascular, respiratory, and rare diseases. Our company contributes $2.4 billion in U.S. federal and state taxes, invests $12 billion annually in our U.S. operations (including $5 billion for research and development (R&D)) and proudly employs more than 18,000 people in the United States. Studies have demonstrated that a direct job in our industry typically supports six external jobs in the overall workforce[1] (i.e. upstream suppliers, construction, distribution, and other service providers), so we

[1] National Association of Manufacturers (September 2021), Ensuring a Healthy Future: The Impact and Importance of Pharmaceutical Manufacturing, https://nam.org/wp-content/uploads/2021/09/ENSURING-A-HEALTHY-FUTURE.pdf

estimate that our company supports 126,000 direct and indirect jobs in the United States. The value of AstraZeneca's U.S. exports to the rest of world is $2.2 billion and supports nearly 4,000 U.S. manufacturing operations jobs.

Additionally, we are committed to expanding our U.S. footprint. On November 12, 2024, AstraZeneca announced a further $3.5 billion investment[2] to expand our R&D and manufacturing in the U.S., including: specialty manufacturing in Texas, expanded cell therapy capacities on the West and East Coasts, a state-of-the-art R&D center in Massachusetts, and a next generation manufacturing facility for biologics in Maryland. We incidentally held the ribbon cutting ceremony for this new facility on May 5, 2025, in the presence of several Maryland government leaders. These investments will create 1,000 highly skilled jobs and strengthen our ability to bring life-changing medicines to market – most often launching new treatments in the United States before anywhere else in the world. We are working on more, much larger investments to be implemented in the near future.

Our supply networks are designed to be resilient, flexible, and operationally efficient to grow and respond to patient demands and support a robust pipeline of new medicines. AstraZeneca has strategically diversified supply chains to meet differing regulatory and market needs for the U.S., Europe, China, and other countries. This helps mitigate risks of shortages, enhances health security, and ensures a more stable supply of AstraZeneca's innovative medicines to the United States.

2. **Imposing tariffs will impact innovation and stifle broader economic goals.** Tariffs could be counterproductive to shared goals listed in President Trump's April 15, 2025, Executive Order "Lowering Drug Prices by Once Again Putting Americans First"[3]. A recent survey of Biotechnology Innovation Organization (BIO) members[4] found that tariffs could disrupt innovation and affordability:
   - **Stall Medical Innovation:** Tariffs on a major trading partner like the European Union (EU) would force 50% of biotechnology companies to identify new research and manufacturing partners. Half of those surveyed say they would have to rework or potentially delay regulatory filings, jeopardizing the pace of innovation. Further, 80% of companies report needing time to find alternative suppliers, leading to delays that could disrupt the pipeline of breakthrough treatments.
   - **Reduce Access to Affordable Medicines:** 94% of biotechnology companies anticipate surging manufacturing costs if tariffs are placed on a major trading partner like the EU.

   Patients served by Alexion's rare disease medicines would be disproportionately impacted by shortages and disruptions due to the lack of alternative treatment options for their conditions. If rare disease treatment was pushed outside the U.S. or launched in other markets before the U.S., it could disrupt medically necessary treatments and force U.S. families to seek care abroad.

   Targeted flexibilities should be prioritized for such patients as there are fewer options for reshoring or shifting supply chains for specialized and rare disease medicines owing to high barriers for conducting R&D, clinical trials, and small-batch manufacturing. Disruptions, shortages or increased costs for patients with such conditions could worsen health outcomes, disease progression, and would be met with strong concern and opposition by the U.S. public.

[2] AstraZeneca (12 November 2024), AstraZeneca invests $3.5 billion in R&D and manufacturing in the United States, https://www.astrazeneca.com/media-centre/press-releases/2024/astrazeneca-invests-3bn-500mn-in-us.html
[3] The White House (15 April 2025), Lowering drug prices by once again putting Americans first, https://www.whitehouse.gov/presidential-actions/2025/04/lowering-drug-prices-by-once-again-putting-americans-first/
[4] Biotechnology Innovation Organization (BIO) (26 March 2025), New survey: U.S. biotechs warn tariffs could impeded access to cures, stifle innovation, https://www.bio.org/press-release/new-survey-us-biotechs-warn-tariffs-could-impede-access-cures-stifle-innovation

A 2025 Ernst & Young study[5] found that a 25 percent tariff rate would have a $50.8 billion impact on medicines in the U.S., with $35.7 billion impacting finished medicines intended for health providers and patients, and $15.1 billion increasing costs for intermediate inputs used in U.S. manufacturing. It estimated that if tariff burdens were passed onto domestic sales, prices could rise by 12.9 percent.

Increasing costs would have a counterproductive impact on U.S. exports. EY found that a significant share of U.S. production activity was related to export sales, with $101 billion of medicines exported from the United States in 2023. If tariffs raised U.S. production costs higher, it could reduce export demand and worsen trade imbalances.

A February 2025 survey of health professionals conducted by Black Book Research[6] said tariffs could drive up the cost of providing care at hospitals and health systems by at least 15 percent. Ninety percent of surveyed hospital finance executives said they would have to shift costs to insurers and patients, meaning tariffs would lead to higher health care costs across the health ecosystem from manufacturers to health plans (including commercial and government health benefit plans such as Medicare). As Medicare costs grow, it would put further pressure on the program's trust fund that the 2024 Medicare Trustees report projected would become insolvent by 2036[7], potentially forcing cuts to promised benefits for millions of American seniors and taxpayers. Higher costs to patients could also lead to delays or inability to seek care, and impact health outcomes and workforce productivity.

In summary, tariffs on innovative biopharmaceuticals would increase costs across supply chains, impact medical innovation, and could particularly severely impact vulnerable patients with life-threatening conditions, such as people living with a rare disease.

3. **Strategic supply chains strengthen security for innovative medicines amid generic drug challenges.** Pharmaceutical and Research Manufacturers of America (PhRMA) estimates that almost two thirds of the value of medicines consumed in the United States are made in the United States. AstraZeneca's supply chains for innovative medicines are geographically subdivided to ensure supply chain resilience and access for U.S. patients. AstraZeneca does not import medicines from China, Mexico or Canada, only from Europe. On the other hand, our U.S. exports to other markets are substantial.

   As the U.S. pharmaceutical trade deficit and drug shortages are predominantly caused by generic medicines, it could be more effective to target trade policies related to those medicines to address the investigation's security concerns.

   Even during the global disruptions that all industries experienced during the pandemic, AstraZeneca's supply chains met our commitments to U.S. patients and no AstraZeneca product appeared on the FDA's Drug Shortage database between 2021 and 2024[8]. That's because innovative biopharmaceutical supply chains build in important safeguards to protect against major disruptions, track anticipated demand, and continuously monitor supply and distribution lines. Companies like ours invest in these safeguards and strengthen our manufacturing base through regionally integrated networks to ensure we can meet the needs of our U.S. patients.

[5] Ernst & Young (22 April 2025), Impacts of potential tariffs on the US pharmaceuticals industry, Prepared for PhRMA
[6] Black Book Market Research (2 February 2025), Double-digit tariffs disrupt U.S. Healthcare costs and supply chain instability, industry leaders warn in Black Book poll, https://blackbookmarketresearch.newswire.com/news/double-digit-tariffs-disrupt-u-s-healthcare-costs-and-supply-chain-22513308
[7] Centers for Medicare & Medicaid Services (6 May 2024), 2024 Annual Report of the Boards of Trustees of the Federal Hospital Insurance Fund and Federal Supplemental Medical Insurance Trust Funds, https://www.cms.gov/oact/tr/2024
[8] AstraZeneca, Internal data (2021-2024)

That cannot be said for all medicines. An April 2025 study from the National Security Commission on Emerging Biotechnology[9] and the congressional American-Made Medicines Caucus[10] share concerns about the risks associated with the production of raw starting materials and APIs that are typically used in generic drug production. The congressional caucus notes that the United States is highly reliant on imports for 90% of all generic drugs, which therefore contributes significantly in volume to the $127 billion trade deficit in pharmaceuticals in 2024.

Further, a June 4, 2024, study from U.S. Pharmacopeia (USP), an independent, scientific nonprofit organization, found that more drug shortages in the United States over the previous decade can be attributed to generic medicines[11]. A significant portion of these shortages are for generic sterile injectable medicines, representing about 53% of new shortages. There were more than twice as many generic drug shortages that began in the previous decade than brand drug shortages. This data shows there are more targeted ways to address supply chain risks, trade imbalances, and drug shortages that contribute more heavily to U.S. national and health security concerns.

4. **Increasing U.S. domestic pharmaceutical capacity will take significant time, investment, and strategic collaboration with the U.S. government to address economic and operational challenges.** Consider that it can take five to ten years to build and make operational a new pharmaceutical manufacturing facility. This includes the time and costs of receiving the necessary governmental approvals required in our highly regulated industry, and streamlining processes will take time to fully implement.

   For example, the U.S. Food and Drug Administration (FDA) mandates strict adherence to Current Good Manufacturing Practices (CGMP), which requires companies to develop, document, and receive approvals for quality management systems, quality control for raw materials, written operating procedures, processes for identifying and investigating quality issues, and certification of testing laboratories. Even changing a source for an input must be reported to the FDA and can potentially require approval or an inspection from U.S. or international regulatory authorities. As multiple companies work to expand capacity and reshore simultaneously, there could be delays and backlogs at FDA that impact our ability to get medicines into the U.S. health system and to patients.

   Shifting production for innovative biologic medicines in AstraZeneca's portfolio can be even more complex than shifting manufacturing for some small molecule generics. It could take potentially years to transfer production to a new site and receive necessary government approvals. The inputs that go into biologics tend to be unique and difficult to procure without appropriate lead time. This could add to the overall timeline of five to ten years cited above.

   To meet these challenges, AstraZeneca is seeking the opportunity to collaborate with the Department and policymakers to establish pragmatic and robust solutions to boost U.S. manufacturing and secure more of America's pharmaceutical supply.

   Ideas include targeted flexibilities to ensure tariffs do not expose U.S. patients to shortages or disrupt ongoing treatments. The patients most at risk would be those with critical or life-threatening conditions, patients who lack viable treatment alternatives, and those who rely on medicines administered through highly complex delivery devices (such as inhaled respiratory therapies).

[9] National Security Commission on Emerging Biotechnology (April 2025), Charting the future of biotechnology: An action plan for American security and prosperity, https://www.biotech.senate.gov/final-report/chapters/
[10] Office of Representative Buddy Carter (R-GA) (24 April 2025), Carter launches American-Made Medicines Caucus, https://buddycarter.house.gov/news/documentsingle.aspx?DocumentID=15591
[11] U.S. Pharmacopeia (4 June 2024), USP Annual Drug Shortages Report: Economic factors underpin 2023 shortages, https://go.usp.org/l/323321/2024-05-31/92zsjg/323321/1717187146zgOpt4vW/GEA_GC_056R_MSM_Report_2024_05_FINAL.pdf

There are also ongoing efforts in Congress and the Executive branch to strengthen tax and manufacturing incentives to boost reshoring efforts and increase the competitiveness of U.S. exports. This includes discussions in Congress to ensure R&D incentives and credits in the U.S. are not outmatched by R&D efforts in other nations. Efforts to enhance the work of initiatives like the U.S. Administration for Strategic Preparedness and Response (ASPR)'s Industrial Base Expansion project[12], to encourage public-private partnerships in advanced technology (such as AI-enabled development models), and to strengthen our manufacturing workforce would make the nation's industrial base more resilient and secure. But we also acknowledge that actions in the U.S. alone cannot address all the Administration's concerns.

That is why we support the Administration's continued efforts to negotiate new bilateral and sectoral trade agreements with foreign governments to address America's goals of increasing patient access to new medicines, eliminating unfair trade barriers, and further developing new medicines by ensuring all trading partners are contributing to innovation. AstraZeneca stands ready as a partner in finding and building on smart solutions that would support the Administration's broader economic, health, and national security goals.

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We also appreciate the opportunity to provide a response to the Department's request for information regarding domestic and foreign supply chains:

I. **What is the role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients:**

Globally and regionally integrated supply chains create efficiencies by allowing companies like ours to focus on high-value activities rather than diverting resources to create redundant production lines for starting materials, chemicals, and APIs that can be created more affordably and at-scale in other markets.

AstraZeneca's U.S. supply chain is made more efficient and resilient by combining our strong U.S. manufacturing base with globally integrated processes. These efficiencies are particularly important to Alexion therapies that serve small global patient populations. Rare disease medicines use a global central manufacturing model to leverage supply chains and specialization in different countries to optimize costs and efficiencies. For example, one of our medicines that treats certain rare and serious blood and nerve disorders manufactures its pharmaceutical ingredients in Europe, formulates those substances into a drug product at multiple European and U.S. sites, and then moves to another location for final steps before distribution. Each step in the production process is complex, required building up specialized workforce and expertise, and would be difficult to shift entirely to the U.S. without increasing disruption risks that would have significant health implications for patients.

II. **To what extent can domestic production of pharmaceuticals and pharmaceutical ingredients meet or not meet domestic demand:**

Pharmaceutical products are delivered across complex supply chains crossing multiple borders. Some raw materials essential for pharmaceutical production must be imported because they are not available domestically or cannot be produced as efficiently or in sufficient quantities to meet U.S. needs. This makes localizing entire production processes within the U.S. a significant challenge.

AstraZeneca's strategically subdivided supply chains are designed to meet the needs of different therapeutic areas and the patients we serve in the United States. This can include some critical manufacturing steps located in the United States. For example, the AstraZeneca facility in Redwood City, California processes

[12] Administration for Strategic Preparedness & Response (ASPR), Industrial Base Expansion, https://aspr.hhs.gov/ibx/Pages/default.aspx

porous particles for use in our respiratory therapies. But while a strong U.S. manufacturing base is important, concentrating too much of the supply chain in the United States can have unintended consequences.

Consider the severe IV shortages last year when a natural disaster struck key facilities in North Carolina. After the hurricane in September 2024, global sources helped bring some supply stability until production was finally able to reach pre-disaster levels in February 2025[13], underscoring the safety net that globally integrated supply chains can provide. This regional and global strategy has minimized our exposure to supply shortages, maximized efficiencies, and protected our U.S. consumers, which would be more difficult with domestic suppliers alone.

III. **What is the feasibility of increasing domestic capacity for pharmaceuticals and pharmaceutical ingredients to reduce import reliance:**

An orderly transition with targeted flexibilities, paired with manufacturing incentive policies, would allow AstraZeneca to better identify needs that could be met domestically and where additional capacity in the U.S. will be more challenging to develop, especially with regards to APIs and key starting materials. Even potential options such as partnering with Contract Manufacturing Organizations (CMOs) to expand capacity would grow constrained as more companies try to maximize existing capacity in the United States. Building new capacity would become more expensive and limited over time as manufacturers from all sectors (not just pharmaceuticals) seek to reshore. With increased costs across the U.S. health system caused by tariffs, CMOs may be incentivized to shift uptake in orders outside of the U.S. to maintain profitability margins.

IV. **Conclusion and potential solutions:**

As the Department weighs its recommendations to the President, we ask for targeted flexibilities for key inputs that do not currently exist (in sufficient quantity and quality) in the United States, protections for medicines treating critical and life-threatening conditions (including for rare diseases), and a transition period to address the feasibility and timeline for building new U.S. manufacturing capacities. A balanced approach with targeted relief measures and strategic partnerships, could provide more sustainable solutions to safeguard the U.S. pharmaceutical supply chain, ensuring continued innovation and patient access.

AstraZeneca is grateful for the opportunity to submit comments regarding the Section 233 investigation into pharmaceutical and pharmaceutical ingredients. We look forward to continuing to engage with the Department as the investigation and recommendations are developed and implemented.

Sincerely,

Daniel M. Wygal

Daniel M. Wygal
Vice President
US Corporate & Government Affairs

[13] U.S. Food & Drug Administration (FDA) (21 February 2025), Hurricane Helene: Baxter's manufacturing recovery in North Carolina, https://www.fda.gov/drugs/updates-2024-hurricane-season/hurricane-helene-baxters-manufacturing-recovery-north-carolina