



January 10, 2024

The Honorable Elizabeth Warren
309 Hart Senate Office Building
Washington, DC 20510

The Honorable Pramila Jayapal
2346 Rayburn House Office Building
Washington DC, 20515

Re: December 13, 2023 Correspondence Regarding Patent Listings

Dear Senator Warren and Representative Jayapal:

I write on behalf of Amneal Pharmaceuticals LLC (Amneal), a New Jersey-headquartered pharmaceutical company providing millions of American patients with accessible, essential medicines, powered by a robust U.S. generic medicines business and growing biosimilar and specialty businesses. We are the leading U.S.-domiciled company that manufactures accessible, essential medicines, with approximately 2,400 U.S.-based employees, and more than 270 FDA-approved generic products to date.

We appreciate your attention to the matters raised in your December 13, 2023 correspondence referencing the U.S. Federal Trade Commission (FTC) November 7, 2023 letter to Impax Laboratories LLC (Impax), a wholly owned subsidiary of Amneal Pharmaceuticals LLC. The FTC's letter concerned two patents associated with Adrenaclick® (epinephrine injection). Consistent with our mission to introduce competition to markets where it is otherwise lacking, Adrenaclick® was developed as an alternative to the EpiPen® autoinjector and has been available to American patients since 2003,¹ 15 years prior to FDA approval of generic versions of EpiPen® (epinephrine injection).

As you note, this product is approved under a new drug application (NDA), and is subject to the "patent listing" provisions under section 505(b) of the Federal Food, Drug, and Cosmetic Act that require NDA applicants to submit "the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or (II) claims a method of using such drug for which approval is sought or has been granted in the application."²

¹ The product was approved in 2003 as Twinject®. Twinject® underwent labeling changes, which the U.S. Food and Drug Administration (FDA) approved in 2009, and became known as Adrenaclick®.
² 21 U.S.C. § 355(b)(1)(A)(viii).

In a good faith effort to comply with this statutory requirement given the regulatory guidance at the time, we submitted for listing in FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book) Patent No. 10166334 and Patent No. 7905352, the patents identified in the FTC's November 7, 2023 letter. However, we never have asserted the patents against a generic applicant for Adrenaclick® or any other party. Amneal reasonably believed the patents were properly listed. Numerous inquiries regarding whether these types of patents should be listed in the Orange Book have been made and regulators have declined to provide an opinion.³ Upon receipt of the FTC's letter, we voluntarily requested delisting of both patents on November 21, 2023, which delisting is reflected in the Orange Book.⁴ We also conducted a review of our portfolio of patent listings in the Orange Book and voluntarily delisted two additional patents listed for Twinject® (a discontinued version of our epinephrine auto-injector).⁵ As with our patents covering Adrenaclick®, we never asserted these Twinject® patents against any third party. Thus, we have never triggered a 30-month stay in connection with the Adrenaclick® or Twinject® patents.

We share your concerns about the potential misuse of the patent system to stifle competition and inflate drug prices. In fact, we are currently involved in a litigation brought by Teva Branded Pharmaceutical Products R & D, Inc. (Teva) over our abbreviated new drug application filing for a generic version of Teva's ProAir® HFA (albuterol sulfate) inhalation aerosol product.⁶ All of the patents asserted against us were listed in FTC's November 7, 2023 letter to Teva,⁷ and the filing of this complaint by Teva triggered a 30-month stay of FDA final approval of our generic version until the litigation is resolved or the stay period expires. We recently informed FTC of this pending litigation along with our assertion of several antitrust and patent delisting counterclaims against Teva.

³ See e.g., Letter from the Centers for Drug Evaluation and Research, Food and Drug Administration, to GlaxoSmithKline, Wilmer Cutler Pickering Hale and Dorr LLP, Ropes & Gray LLP, Novo Nordisk Inc. and Finnegan, Henderson, Farabow, Garrett & Dunner LLP (June 1, 2020), available at <https://www.regulations.gov/document/FDA-2005-A-0476-0006> (last accessed on Jan. 10, 2024). See also *Listing of Patent Information in the Orange Book; Establishment of a Public Docket*, Docket No. FDA-2020-N-1127, 85 FR 33169 (June 1, 2020), available at <https://www.federalregister.gov/documents/2020/06/01/2020-11684/listing-of-patent-information-in-the-orange-book-establishment-of-a-public-docket-request-for>, (last accessed on Jan. 10, 2024).

⁴ See Orange Book Delisted Patents, available at https://www.accessdata.fda.gov/scripts/cder/ob/search_patent.cfm?listed=delisted (last accessed on Jan. 10, 2024).

⁵ See Orange Book Patent Listing Disputes, available at <https://www.fda.gov/media/105080/download?attachment> (last accessed on January 10, 2024).

⁶ *Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Limited, and Teva Pharmaceuticals USA, Inc. v. Amneal Pharmaceuticals of New York, LLC; Amneal Ireland Limited; Amneal Pharmaceuticals LLC, and Amneal Pharmaceuticals Inc.*, U.S. District Court for the District of New Jersey, Case No. 2:23-cv-20964.

⁷ Letter to Teva Counsel, Teva Branded Pharmaceutical Products R&D Inc. fr. R. Rao, Dep. Dir., FTC Bureau of Competition re Improper Orange Book-Listed Patents for QVAR 40, ProAir HFA, ProAir DigiHaler (Nov. 7, 2023), available at www.ftc.gov/system/files/ftc_gov/pdf/teva-branded-pharma-orange-book.pdf (last accessed on Jan. 10, 2024).

Thank you for your attention to this critical issue and the opportunity to provide a response. Please contact me with any questions or requests for additional information. It is Amneal's steadfast commitment to conduct our operations with the highest standards of ethical conduct and transparency, consistent with all applicable law. Amneal remains dedicated to its mission, and we look forward to bringing more accessible, essential medicines to the market and positively impacting patient lives.

Sincerely,

Maryll W. Toufanian

Digitally signed by Maryll W.
Toufanian
Date: 2024.01.10 11:27:55 -05'00'

Maryll W. Toufanian, J.D.
Senior Vice President - Regulatory Strategy and
Government Affairs
Amneal Pharmaceuticals LLC



February 7, 2024

The Honorable Elizabeth Warren
United States Senator
309 Hart Senate Office Building
Washington, DC 20510

The Honorable Pramila Jayapal
United States Representative
1510 Longworth House Office Building
Washington, DC 20515

Dear Senator Warren and Representative Jayapal:

Thank you for your December 13, 2023, letter in which you requested that AstraZeneca voluntarily delist five Symbicort patents from the Food and Drug Administration's (FDA) Orange Book that were identified in a Federal Trade Commission (FTC) letter¹ dated November 7, 2023. In your letter, you also requested responses to several questions related to the five listed patents, which we have responded to in the attachment to this letter.

As an initial matter, we believe that it is important to emphasize the reasons why we have confirmed that these patent listings are accurate. This confirmation was based on our good faith understanding of the statutory patent listing requirements, FDA regulations and guidance, relevant case law,² and the statutory intent of the bipartisan Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman)³.

First, AstraZeneca understands that one important way that Hatch-Waxman facilitates market competition is to provide generic drug manufacturers with public notice of the patents that could be infringed by the manufacture, use and sale of a generic copy of a branded drug product and to permit timely resolution of patent challenges before marketing begins.⁴ Importantly, listing a patent in the Orange Book provides public notice and enables generic manufacturers to assess a potential patent dispute.

AstraZeneca's commitment to listing patents openly and in compliance with the law enables potential generic entrants to understand the intellectual property landscape they will need to

¹ The five Symbicort patents identified in the FTC November 7, 2023, letter: U.S. Patent Nos. 7,587,988; 8,387,615; 8,528,545; 8,616,196; and 8,875,699.

² 21 U.S.C. § 355(c)(2); 21 C.F.R. § 314.53(b); 68 Fed. Reg. 36,676, 36,680 (June 18, 2003); *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756, 761 (Fed. Cir. 1997), *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, 60 F.4th 1373, 1379 (Fed. Cir. 2023); *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1345 (Fed. Cir. 2002).

³ Pub. Law 98-417

⁴ See, e.g., 68 Fed. Reg. at 36684.

navigate before they launch. Additionally, a failure to list an eligible patent in the Orange Book may expose the reference drug sponsor to legal risks. Indeed, at least one generic applicant has argued that a failure to do so constitutes a violation of the antitrust laws by depriving the applicant of information that would have affected its decision whether to develop a generic product.⁵

Second, our legally compliant listing of the aforementioned patents in the Orange Book has not prevented generic competition from entering the market and AstraZeneca never intended the listing to have an unfair exclusionary effect. In particular, AstraZeneca has not taken action to enforce the five patents identified in the FTC's letter and, as such, those patents have never triggered a statutory 30-month stay under Hatch-Waxman that postpones the FDA approval of a generic application until related infringement litigation resolves or the stay period expires. In fact, to date, at least one generic competitor to Symbicort has already entered the US market.

With respect to generic competition more generally, it is important to recognize that inhaled respiratory products are complex drug-device combinations that are costly and complicated for both branded and generic products to develop, gain FDA approval, and manufacture consistently.⁶

According to senior FDA officials, "...developing an orally inhaled drug-device combination product can be a costly and time-consuming venture that requires overcoming many challenges, including the complexity associated with developing products such as these that have reliable lung delivery across patient populations and challenges with effective patient use. The complexity of this challenge is compounded when considering generic orally inhaled drug-device combination products, where the development of such a product must not only be capable of delivering the medication to the lungs but must also accomplish this through performance equivalent to the reference listed drug (RLD)."⁷

As such, focusing narrowly on Orange Book patent listings as a potential barrier to generic competition not only misconstrues its purpose under Hatch-Waxman, but also fundamentally underestimates the technical complexity of development and manufacture of these important medicines.

⁵ Complaint, *Mut. Pharm. Co. v. Hoechst Marion Roussel, Inc.*, No. 96-CV-01409-CG, ECF 1, ¶¶ 37, 91 (E.D. Pa. 1996) ("Mutual, to its detriment, relied upon the patents listed in the Orange Book in effect at the time in considering whether to file and in filing its ANDA. Had the '129 patent been listed in the Orange Book, Mutual would not have expended over \$500,000.00 to develop its generic terfenadine product and file its terfenadine ANDA.").

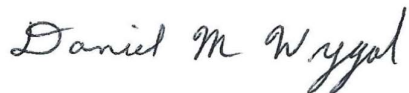
⁶ See FDA Approves First Generic of Symbicort to Treat Asthma and COPD (March 15, 2022), <https://www.fda.gov/news-events/press-announcements/fda-approves-first-generic-symbicort-treat-asthma-and-copd>. FDA recognized that Symbicort is a "complex drug-device combination product," and notes that "[s]ince drug-device combination products can be more challenging to develop, fewer exist, resulting in less market competition. Addressing the challenges related to complex generics, and promoting more generic competition to these medicines, is a key part of the [FDA's Drug Competition Action Plan](#), and the agency's efforts to promote patient access and more affordable medicines."

⁷ Newman B, Babiskin A, Bielski E, et al. "Scientific and regulatory activities initiated by the U.S. Food and Drug Administration to foster approvals of generic dry powder inhalers: Bioequivalence perspective." *Advanced Drug Delivery Reviews*. 2022;190:114526. doi:10.1016/j.addr.2022.114526

Finally, we support your bipartisan, bicameral work in Congress to question and rein in the practices of pharmacy benefit managers (PBMs) demanding high rebates that drive up the price of prescription medicines. These rebates account for most of the Medicare Part D program spending in this class of medicines. The Government Accountability Office (GAO) recently reported that three therapeutic drug classes accounted for 73 percent of rebates in the Medicare Part D program⁸, including anti-asthma drugs such as Symbicort. As a case in point, your letter referenced a Medicare spend of \$2 billion for Symbicort in 2021, but only a fraction of that amount was invoiced by AstraZeneca while the rest is extremely large rebates to intermediaries.

AstraZeneca appreciates your commitment to identifying and highlighting antitrust concerns and acknowledges the effort to help ensure patents are properly listed in the Orange Book. We also want you to know that following receipt of the FTC letter, AstraZeneca also received a letter from the FDA regarding a challenge to the listing of five Symbicort patents under 21 C.F.R. § 314.53(f).⁹ We take seriously these inquiries and responded timely to that request, confirming the five patents listed in the Orange Book for Symbicort are properly listed.

Sincerely,

A handwritten signature in cursive script that reads "Daniel M. Wygal".

Daniel M. Wygal
Vice President, US Corporate & Government Affairs

Attachment

⁸ Dicken, John E. "MEDICARE PART D CMS Should Monitor Effects of Rebates on Drug Coverage and Spending." United States Government Accountability Office. Testimony before the Subcommittee on Health, Committee on Energy and Commerce. September 19, 2023.

⁹ AstraZeneca received the FDA 314.53(f) Patent Listing Dispute letter on November 16, 2023.

Answers to specific questions raised in the December 13 letter

1. FTC identified five patents for Symbicort that have been improperly or inaccurately listed in the Orange Book.

a. Has AstraZeneca ever taken action to enforce any of these patents against any other drug manufacturer? If so, please list all such actions, and their outcome.

AstraZeneca has not taken action to enforce the five patents identified in the FTC's letter dated November 7, 2023.

b. During the time period in which you were challenging these patents, or in the ensuing 30-month period in which you were granted a stay that delayed approval of a generic competitor to one of these drugs, what were total sales (in dollars) of these drugs? What were total sales to Medicare and Medicaid?

AstraZeneca has not taken action to enforce the five patents identified in the FTC's letter dated November 7, 2023. Accordingly, there was no 30-month stay in connection with the enforcement of these patents. Additionally, at least one generic competitor has already entered the US market.

2. Has AstraZeneca voluntarily de-listed the ten patents listed in the Orange Book with regard to the Symbicort product that the FTC has disputed as being improperly or inaccurately listed?

AstraZeneca has not voluntarily delisted the five patents identified in the FTC's letter dated November 7, 2023. Rather, AstraZeneca confirmed the correctness of the listing of these five patents in a letter to FDA dated December 14, 2023, in response to the FDA 314.53(f) Patent Listing Dispute letter sent to AstraZeneca on November 16, 2023.

a. Please specify which ones you have de-listed.

Please see our response to question 2.

b. Please specify when you will de-list them if you have not done so yet.

AstraZeneca does not plan to delist the five identified patents. AstraZeneca believes these patents are appropriately listed in the Orange Book for Symbicort under the patent listing provisions of the Federal Food, Drug, and Cosmetic Act and FDA's regulations.

3. Will AstraZeneca voluntarily review and de-list additional patents the company has listed in the Orange Book that are improperly or inaccurately listed?

We believe we have appropriately considered whether a patent is subject to the patent listing requirements under the Federal Food, Drug, and Cosmetic Act and FDA's regulations before submitting patent information to FDA for listing in the Orange Book. As part of its routine

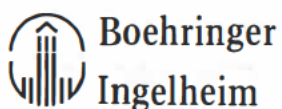
practice, AstraZeneca will incorporate any change in the applicable FDA guidance, or new legislation or case law on patent listing into its review of whether patent listings or delistings are appropriate.

a. Please specify which ones you will de-list.

AstraZeneca does not plan to delist any patents.

b. What is your specific timeline for doing so?

AstraZeneca does not plan to delist any patents.



January 15, 2024

The Hon. Elizabeth Warren
United States Senate
Washington, DC 20510

The Hon. Pramila Jayapal
United States House of Representatives
Washington, DC 20515

**Boehringer Ingelheim
USA Corporation**
900 Ridgebury Road
Ridgefield, CT 06877

Jean-Michel Boers
US Country Managing Director/
President and CEO



Dear Senator Warren and Representative Jayapal:

Thank you for your December 13, 2023, letter. Boehringer Ingelheim Pharmaceuticals, Inc. ("BIPI") welcomes the opportunity to share information about our patent listings related to our respiratory products referenced in the FTC's November 7, 2023, letters to multiple pharmaceutical companies, including BIPI. For over 135 years, Boehringer Ingelheim has been focused on innovating and developing breakthrough therapies for patients in areas of unmet medical need to improve the lives of patients in the United States and throughout the world. BIPI's commitment to developing innovative medicines spans a wide range of challenging diseases, including the invention of groundbreaking and life-changing treatments for respiratory illnesses. The company is, first and foremost, a research-driven pharmaceutical company.

As discussed in greater detail below, BIPI follows statutory and regulatory requirements with regard to all of its patents listed in the Orange Book. BIPI is confident that all of its patents identified in the FTC's November 7, 2023, letter are properly listed under FDA regulations governing the Orange Book requirements. To the extent these requirements change in the future, BIPI remains committed to complying with the regulations relating to patent listings in the Orange Book. On December 15, 2023, BIPI confirmed to FDA that the patents are listable in response to the agency's November 18, 2023, notice of the FTC's listing dispute. We believe transparency surrounding patents is of paramount importance to allow for the innovation and development of therapies for patients.

The Inhalation Market and BIPI's Innovative Inhalation Products

Boehringer Ingelheim has a long history of developing innovative therapies. Indeed, the company's heritage in developing medicines for respiratory diseases spans almost 100 years – almost since the company was founded.

Life forward

Treatments for chronic obstructive pulmonary disease (“COPD”), asthma, idiopathic pulmonary fibrosis, lung cancer, allergic rhinitis and infantile respiratory distress syndrome have originated from our research facilities around the world and improved the lives of countless Americans ranging from children to the elderly. For instance, the company was responsible for launching the first commercially available metered-dose inhaler (MDI) in the United States and Europe. We are proud of our history of innovation – for people of all ages with COPD and asthma.

How these therapies are delivered to their site of action in the lungs is hugely important for COPD and asthma patients and makes a very real difference in the effectiveness of their treatments. Indeed, the method of medicine delivery is critically important, and the design and ease of use of the device is essential to the effective use of these respiratory therapies by patients (again, ranging from children to the elderly). At the same time, the development of these important and novel drug delivery technologies for COPD and asthma medicines is particularly complex. For example, to achieve direct delivery to lungs, the active pharmaceutical ingredient is administered through the device in nebulized form that is dispersed in the lungs in the form of tiny droplets, measured in micrograms, or via a fine powder (Spiriva HandiHaler).

FDA Patent Listing Requirements

The patent listing requirements are dictated by the Federal Food, Drug, and Cosmetic Act (“FDCA”) and its implementing regulations. The holder of a New Drug Application (“NDA”) must submit certain patent information to FDA.¹ These patents fall into three buckets, those covering the active pharmaceutical ingredient, the drug product, and a method of using the drug. As relevant here, FDA specified that for drug product patents, the patent listing requirement applies to patents that claim the “finished dosage form.”² In turn, “dosage form” is defined to mean the “physical manifestation of containing the active and inactive ingredients that delivers a dose of the drug product,” including factors such as the way the product is administered and design features that affect frequency of dosing, among others.³ It is therefore unsurprising that, in the context of patent listing, FDA has recognized both drug delivery systems and metered aerosols and sprays – like Atrovent HFA, Combivent Respimat, Spiriva HandiHaler, and Spiriva Respimat – as examples of dosage forms.⁴

Your August 28, 2023, letter to Dr. Califf asserted that FDA has not declared what types of patents should be listed in the Orange Book, and it asked that the agency clearly articulate those guidelines.⁵ Respectfully and to the contrary, however, FDA has provided

¹ 21 U.S.C. § 355(b)(1)(A)(viii).

² *Applications for FDA Approval to Market a New Drug; Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed*, 68 Fed. Reg. 36,676, 36,680 (June 18, 2003); 21 C.F.R. § 314.53(b). Under the listing regulations, an NDA holder submitting information on a drug product patent must certify “[w]hether the patent claims the drug product for which approval is being sought, as defined in § 314.3.” 21 C.F.R. § 314.53(c)(2)(i)(N)(1).

³ *Id.*

⁴ 68 Fed. Reg. 36,676, 36,680 (June 18, 2003) (In the preamble to the final rule, FDA recognized dosage forms include, among other things, “metered aerosols, capsules, metered sprays, gels, and pre-filled drug delivery systems.”)

⁵ Senator Warren, Representative Jayapal, Letter to Dr. Califf (Aug. 28, 2023), available at <https://www.warren.senate.gov/imo/media/doc/2023.08.28%20Letter%20to%20FDA%20re%20drug%20patents.pdf> (last visited Jan. 3, 2023).

guidance with regard to the listing of patents in the Orange Book and made clear that patents claiming the approved drug product should be submitted for listing. Moreover, although the agency has had multiple opportunities to provide further guidance, the agency has not done so to date. Between 2005 and 2012, pharmaceutical manufacturers submitted five (5) requests for advisory opinions asking FDA to clarify its approach to patent listing for drug delivery devices. These requests sought guidance from FDA on, among other issues, whether patents directed to drug delivery devices must be listed in the Orange Book if those patents do not claim or disclose the active ingredient or formulation. Instead of providing a determination on the substance of the requests, FDA instead, published a Federal Register notice on June 1, 2020, announcing the opening of a docket to solicit comments on patent listing issues, including listing device-related patents. Although multiple comments have been submitted to the docket, the agency has yet to provide further guidance.

Current regulations continue to require the holder of an approved NDA to submit information for patents claiming the drug product, which includes the device that delivers the medicine to the patient. BIPI's inhaler medicines referenced in the FTC letter, thus, include the device that delivers the active pharmaceutical ingredient to the patient.

BIPI's Response to FTC's November 7, 2023, Letter

BIPI takes seriously its legal obligations under all applicable statutory and regulatory requirements, including requirements with regard to patents listed in the Orange Book. Consistent with that commitment and in response to FTC's November 7, 2023, letter, we engaged in a careful review of the nine unique patents⁶ referenced in the letter regarding the following BIPI inhalation products: Atrovent HFA (NDA 21527)⁷; Spiriva HandiHaler (NDA 21395)⁸; Combivent Respimat (NDA 21747)⁹; and Spiriva Respimat (NDA 21936).¹⁰ After closely reexamining these patents, along with the regulatory framework and case law, we determined that the patent listing information in the Orange Book does not require modification. As specified by FDA, the drug product is the finished dosage form. Thus, importantly, the approved drug product for each of the BIPI inhaler products referenced in FTC's letter includes the device that delivers the medicine to the patient.

BIPI files patents to protect the company's investment in innovations that benefit patients and improve their lives, and those patents enable the company to continue to invest in research and development for new and better medicines. Both the active pharmaceutical ingredient and the device are critical for the safe and effective use of inhalation products by patients, and the complexities of developing and manufacturing inhalation drug-and-device combination products requires substantial investments in research and development. When a patent embodying these investments is infringed and the company determines action is

⁶ Boehringer notes that your December 13, 2023, letter stated that the FTC referenced 22 Boehringer patents. There are six patents listed for both Spiriva Respimat and Combivent Respimat, two patents listed for Spiriva HandiHaler, and one patent listed for Atrovent HFA.

⁷ U.S. Patent No. 8,474,447.

⁸ U.S. Patent Nos. 7,694,676 and 9,010,323.

⁹ U.S. Patent Nos. 7,284,474; 7,396,341; 7,837,235; 7,896,264; 8,733,341; and 9,027,967.

¹⁰ U.S. Patent Nos. 7,284,474, 7,396,341, 7,837,235, 7,896,264, 8,733,341, and 9,027,967.

appropriate, BIPI takes actions to enforce its patents to provide the company the opportunity to protect its innovations and to continue to innovate.

Moreover, doctors and patients have a significant number of choices in monotherapy and combination therapy intended to treat respiratory diseases, available in a variety of inhaler devices. These treatment options mean that physicians and patients can choose therapies appropriate to patients' disease severity and in a delivery device that works best for the patient. Generic inhalers are also available for many products. For instance, in June 2023, the FDA approved Lupin's generic version of BIPI's Spiriva HandiHaler to treat COPD, and Lupin announced the launch of this product on August 18, 2023. In addition, generics are also available, for example, for both GSK's Advair product and AstraZeneca's Symbicort product to treat both asthma and COPD.

In addition to choice, patient access to affordable medicine is also very important to BIPI. Many inhaler products on the market are covered by commercial insurance, Medicare, and Medicaid. While coverage and cost-sharing obligations will always vary by product, the payor, and the specific plan associated with said payor, BIPI significantly discounts its products, including its respiratory products, such that they are widely available to patients and works to make sure they are most preferred on insurers' formularies. In addition to discounting its products, BIPI also offers certain products free of charge to eligible patients through its Patient Assistance Program.

BIPI is proud of its innovations to improve the lives of patients, including drug products that incorporate inhaler devices, and remains committed to developing innovative medicines across a wide range of challenging diseases. BIPI has followed and will continue to follow the statutory and regulatory requirements regarding the listing of patents in the Orange Book, and we are confident that all of our patents noted in the FTC's November 7, 2023, letter are properly listed under FDA regulations.

Thank you for the opportunity to respond to your December 13, 2023, inquiry.

Sincerely,



Jean-Michel Boers
U.S. Country Managing Director and
Chief Executive Officer
Boehringer Ingelheim US Corporation



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January 12, 2024

Senator Elizabeth Warren
United States Senate
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Representative Pramila Jayapal
United States House of Representatives
2346 Rayburn House Office Building
Washington, DC 20515

RE: December 13, 2023 Letter Concerning GlaxoSmithKline’s Orange Book Patent Listing

Dear Senator Warren and Representative Jayapal:

We write in response to your December 13, 2023, letter (the “Letter”) to GlaxoSmithKline (“GSK”) regarding GSK’s listing of certain patents in the Food and Drug Administration’s (“FDA”) *List of Approved Drug Products with Therapeutic Equivalence* (the “Orange Book”).

The United States’ patent system is an important driver of pharmaceutical innovation, promoting investment from companies like GSK in the development of life-saving, life-sustaining, and life-improving medications for patients. As a company with a strong legacy in respiratory and other products, GSK stands behind our intellectual property, which reflects innovation in drug and drug-device combination products that have saved and substantially improved millions of lives.

Certain pharmaceutical patents—including those covering an approved drug product—are required by statute, regulation, and FDA guidance to be listed in the FDA’s Orange Book. The listing of such patents is mandatory and furthers policy goals that promote generic drug development, such as providing notice to generic pharmaceutical companies regarding which patents their products may infringe, and incentivizing generic companies to challenge patents they believe are invalid or not infringed through the potential for 180-day exclusivity, a feature available only if patents are listed in the Orange Book.

GSK takes its obligations regarding Orange Book patent listing seriously and follows a careful and deliberate process before listing patents in the FDA’s Orange Book. GSK only lists patents in the FDA’s Orange Book that it concludes legitimately cover the approved drug product. The application, however, of the listing criteria to patents related to drug-device combinations has historically raised unique questions.

GSK and others in the industry have requested that the FDA provide specific guidance to help them make listing decisions regarding such patents. Although the FDA explained that the term “Drug Product” means the finished dosage form, expressly including inhalers and other drug-device combinations, it has failed to provide more specific guidance related to, for example, patents covering only the approved device or components integral to the use of the approved device. GSK has therefore been left to work through application of the listing criteria to such patents based on the existing guidance, the policy goals of the listing regime, and developing industry practice as reflected in the Orange Book itself.

As you note in your Letter, on November 7, 2023, the FTC challenged the listing of certain GSK patents in the Orange Book. This was undertaken pursuant to an FDA process for challenging listings that is open to anyone, without cost to the challenger. Specifically, the FTC challenged the listing of five¹ patents. These patents cover a subset of GSK’s proprietary innovations related to four of GSK’s respiratory drug products: Arnuity Ellipta, Ventolin HFA, Advair HFA, and Flovent HFA. The patents identified by the FTC (and their associated Pediatric Exclusivity) are listed below:

<u>Patent Number</u>	<u>Product(s) Covered</u>
8,113,199 (and 8,113,199*PED)	Arnuity Ellipta
8,161,968 (and 8,161,968*PED)	Arnuity Ellipta
8,534,281 (and 8,534,281*PED)	Arnuity Ellipta
8,746,242 (and 8,746,242*PED)	Arnuity Ellipta
7,500,444 (and 7,500,444*PED)	Advair HFA, Ventolin HFA, Flovent HFA

GSK carefully considered the information provided regarding the basis for the FTC’s challenge, along with other information GSK had already been considering, including the patents’ claims, the statutory and regulatory criteria governing the listing of patents in the Orange Book, changes in the law, and evolving

¹ Your December 13, 2023, letter indicates that the FTC identified seven or, later, fourteen patents as improperly or inaccurately listed in the FDA Orange Book. However, the FTC only identified five distinct patents. It is our understanding that the difference in the patent counts results from double/triple-counting of patents due to the fact that one of five patents was listed for three GSK products and each of the patents identified by the FTC had a corresponding “PED” number because of Pediatric Exclusivity. Thus, our response addresses the five distinct patents identified by the FTC and their corresponding Pediatric Exclusivity.

views regarding application of those criteria to patents covering drug-device combinations. While GSK believes that all five identified patents were properly listed consistent with the applicable statutes, regulations, and FDA guidance, GSK recognizes the recent shift in policy, and the existence of potentially applicable case law in recent years, regarding the application of Orange Book listing criteria to patents covering drug-device combinations. Accordingly, GSK ultimately delisted four of the five patents identified by the FTC, maintaining the listing of U.S. Patent No. 8,746,242 (and 8,746,242*PED) for Arnuity Ellipta (NDA 205625). The '242 patent specifically covers the approved Drug Product, i.e., the finished dosage form of the Arnuity Ellipta device, even taking into account the changes in the law and evolving views mentioned above. Accordingly, the continued Orange Book listing of the '242 patent upholds key policies underpinning the listing requirement, i.e., (i) providing notice of the potential applicability of the patent to potential generic competitors and (ii) allowing for the 180-day exclusivity incentive. With respect to the four delisted patents, each remains valid and enforceable, even though they are no longer listed in the Orange Book.

Your letter poses certain specific questions to GSK regarding the above-listed challenged patents, which are addressed below:

- 1. FTC identified seven² patents for GlaxoSmithKline's products that have been improperly or inaccurately listed in the Orange Book.**
 - a. Has GlaxoSmithKline ever taken action to enforce any of the patents against any other drug manufacturer? If so, please list all such actions, and their outcome.**

As noted above, GSK does not believe that any of the patent listings challenged by the FTC were "improper" or "inaccurate." Regardless, with one exception, none of the patents subject to the FTC's listing challenges has been enforced against a generic manufacturer. The one exception occurred in December 2016, when TEVA Pharmaceuticals USA, Inc. ("Teva") sent GSK a Paragraph IV notice with respect to Flovent HFA (0.11 mg), certifying U.S. Patent No. 7,500,444 (as well as other patents not identified by the FTC). In response to the Paragraph IV certification, GSK filed suit on March 31, 2017, stating in its complaint for patent infringement that the technical information in Teva's Paragraph IV certification and Teva's ANDA was "insufficient to conclusively determine" whether Teva was infringing U.S. Patent No.

² See footnote 1.

7,500,444. Complaint, ECF No. 1, *Glaxo Group Ltd. v. Teva Pharmaceuticals USA, Inc.*, No. 1:17-cv-00357-UNA (D. Del. Mar. 31, 2017). After carefully considering the facts regarding Teva's proposed ANDA, which were available to GSK (through its counsel) only by virtue of the ANDA litigation, GSK determined that Teva's device did not infringe the '444 and GSK voluntarily dismissed the complaint on June 20, 2017. In GSK's view, the legal process required by the Hatch-Waxman Act worked both to incentivize Teva's ANDA filing and to protect the legitimate interests of GSK as patent holder. Teva ultimately voluntarily withdrew its ANDA for Flovent HFA (0.11 mg), for reasons unknown to GSK. Considering the various reasons described above, GSK's actions relating to the '444 patent had no impact on Teva's generic product entry.

- b. During the time period in which you were challenging these patents, or in the ensuing 30-month period in which you were granted a stay that delayed approval of a generic competitor to one of these drugs, what were total sales (in dollars) of these drugs? What were the total sales to Medicare and Medicaid?**

The lawsuit identified above had no effect on generic competition; it was voluntarily dismissed prior to Teva receiving tentative approval for its generic Flovent HFA product, and therefore there was no period of generic delay.

- 2. Has GlaxoSmithKline voluntarily de-listed the 14³ patents listed in the Orange Book with regard to the inhaler-related products that the FTC has disputed as being improperly or inaccurately listed?**

- a. Please specify which ones you have de-listed.**
- b. Please specify when you will de-list them if you have not already done so.**

As explained above, in light of evolving policies and developments in the law regarding the listing of drug-device combinations, on December 15, 2023, GSK requested the withdrawal and removal of the following patents and the Pediatric Exclusivity attached to those patents from the FDA Orange Book under 21 CFR 314.53(f)(2)(iv):

U.S. Patent No. 8,113,199 (and 8,113,199*PED) for NDA 205625

U.S. Patent No. 8,161,968 (and 8,161,968*PED) for NDA 205625

³ See footnote 1.

U.S. Patent No. 8,534,281 (and 8,534,281*PED) for NDA 205625

U.S. Patent No. 7,500,444 (and 7,500,444*PED) for NDAs N021254, N020983, and N021433

GSK has maintained the listing of the '242 patent because it covers the drug product for which approval was granted, i.e., the inhaler containing a medicament in powdered form. Accordingly, we are obliged by law to maintain the listing of the '242 in order to provide notice to a generic applicant that this is a patent it will need to address in connection with its launch of its generic product.

3. Will GlaxoSmithKline voluntarily review and de-list additional patents the company has listed in the Orange Book that are improperly or inaccurately listed?

a. Please specify which ones you will de-list.

b. What is your specific timeline for doing so?

As noted above, GSK does not believe that any of its patent listings were “improper” or “inaccurate.” Regardless, GSK responds that it is de-listing the following patents for the same reason it de-listed the four patents identified above:

U.S. Patent No. 8,113,199 (and 8,113,199*PED) for Anoro Ellipta (NDA 203975)

U.S. Patent No. 8,113,199 (and 8,113,199*PED) for Breo Ellipta (NDA 204275)

U.S. Patent No. 8,113,199 (and 8,113,199*PED) for Trelegy Ellipta (NDA 209482)

U.S. Patent No. 8,113,199 for Incruse Ellipta (NDA 205382)

U.S. Patent No. 8,161,968 for Incruse Ellipta (NDA 205382)

U.S. Patent No. 8,534,281 for Incruse Ellipta (NDA 205382)

Sincerely,



Amy Chevalier Efantis

Vice President, Government Affairs & Public Policy

GSK

January 15, 2024

The Honorable Elizabeth Warren
309 Hart Senate Office Building
Washington, DC 20510

The Honorable Pramila Jayapal
2346 Rayburn House Office Building
Washington, DC 20515

Dear Senator Warren and Representative Jayapal,

This responds to your December 13, 2023 letter, which follows on from the Federal Trade Commission's November 7, 2023 letter to AbbVie regarding the propriety of certain patents for AbbVie's Restasis Multidose[®] product being listed in the Orange Book. The FTC's letter stated its belief that "certain patents have been improperly or inaccurately listed in the Orange Book with regard to AbbVie Inc.'s Restasis Multidose product" and that it has initiated "the FDA's regulatory process and submitted patent listing dispute communications to the FDA" regarding U.S. Patent Nos. 8,292,129, 8,561,859, 9,669,974, and 9,676,525.¹ While your letter refers to "sham" patents and concerns about "abusing the patent system,"² the FTC's letter makes no assertions that these patents were ill-gotten or are otherwise illegitimate. Rather, the FTC questioned whether these patents meet the statutory and regulatory criteria for listing in the Orange Book. In fact, federal law and regulation appear to **require** AbbVie to list these patents.

The Federal Food, Drug, and Cosmetic Act mandates which patents must be listed in the Orange Book. It requires that holders of approved drug applications "**shall**" file with the FDA information regarding:

each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and **that—**

- (I) **claims** the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or **a drug product** (formulation or composition) patent; or
- (II) claims a method of using such drug for which approval is sought or has been granted in the application.³

In 2003, the FDA set forth in rulemaking that the "drug product" for purposes of patent listing refers to the "finished dosage form," which the FDA stated includes "metered aerosols, capsules, metered sprays, gels, and **pre-filled drug delivery systems**."⁴

The four Restasis Multidose product patents identified in the FTC's letter cover the Restasis Multidose pre-filled drug delivery system. That pre-filled drug delivery system claimed in these four patents is directly involved in "[t]he way the product is administered."⁵ And the patents claim that "finished dosage form" (as opposed to claiming mere container packaging or only a component of the drug product) and thus are appropriately listed. This is evidenced by, among other things, the fact that the FDA-approved labeling for Restasis Multidose contains detailed instructions for preparing the delivery device for first-time and subsequent uses to administer the precisely approved "one drop" dose via the delivery device.⁶ Each patent identified in the FTC's letter claims a pre-filled drug delivery system and reads upon AbbVie's Restasis Multidose product. The applicable federal statutes and FDA regulations provide that AbbVie "shall" list in the Orange Book all patents claiming the Restasis Multidose drug product (i.e., the pre-filled drug delivery system), including the four patents at issue here.⁷

¹ Letter from U.S. Federal Trade Commission to AbbVie Inc., November 7, 2023, at 1.

² Letter from Senator Warren and Representative Jayapal to AbbVie Inc., December 13, 2023, at 1, 3.

³ 35 U.S.C. § 355(c)(2), (b)(1)(A)(viii) (emphasis added).

⁴ 21 C.F.R. § 314.53(b); *Applications for FDA Approval to Market a New Drug; Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed*, 68 Fed. Reg. 36,676, 36,680 (June 18, 2003) (emphasis added).

⁵ 21 C.F.R. § 314.3(b).

⁶ Restasis Multidose Prescribing Information §§ 2-2.2.

⁷ Since the FDA's 2003 regulations establishing that pre-filled drug delivery systems are "drug products," for which patents shall be listed in the Orange Book, there have been five separate requests for "clarification regarding what constitutes an approved pre-filled drug delivery system for the purposes of determining whether patent relating to that system should be listed in the Orange Book." See Novo Nordisk Inc., Request for Advisory Opinion, Docket No. FDA-2012-A-1169 (Nov. 26, 2012); Finnegan, Henderson, Farabow, Garrett & Dunner, LLP on behalf of Forest Labs., Inc., Request for Advisory Opinion, Docket No. FDA-2011-A-0363 (May 12, 2011); Ropes & Gray LLP on behalf of AstraZeneca, Request for Advisory Opinion, Docket No. FDA-2007-A-0099 (June 21, 2007); Ropes & Gray LLP on behalf of AstraZeneca, Request for Advisory Opinion, Docket No. FDA-2006-A-0063 (Aug. 10, 2006); GlaxoSmithKline, Request for

AbbVie has not used any of these four patents for Restasis Multidose to “unfairly block competition” or to “employ anticompetitive tactics to extend [its] government-granted monopolies, insulate [itself] from generic and biosimilar competition, and keep prices artificially high.”⁸ AbbVie has received three notices (in September 2020, December 2021, and April 2023) that generic applicants had filed Abbreviated New Drug Applications with the FDA referencing Restasis Multidose. After reviewing each generic’s notice letter, AbbVie **did not** assert infringement of any of these four patents. No 30-month stay of FDA approval was ever imposed in connection with these generic applications. AbbVie has no visibility into the status of these generic companies’ efforts to obtain regulatory approval, which presumably remain pending at the FDA.

While your letter states that the “Medicare Part D program spent more than \$1.6 billion on a *single formulation* of Restasis in 2021 alone, making it the 19th costliest drug in overall Medicare spending that year,”⁹ that single formulation does not appear to be Restasis Multidose, which is listed in the CMS database separately.¹⁰ Rather, the single formulation of Restasis that you reference in your letter appears to be Restasis Unit Dose[®], and the four patents at issue here have never been listed in the Orange Book with reference to the Restasis Unit Dose product. Three generic versions of Restasis Unit Dose have been approved by the FDA.

AbbVie further provides the following responses to the specific questions in your letter.

1. FTC identified four patents for Restasis that have been improperly or inaccurately listed in the Orange Book.

a. Has AbbVie ever taken action to enforce any of these patents against any other drug manufacturer? If so, please list all such actions, and their outcome.

RESPONSE: AbbVie has not taken action to enforce the four patents identified in the FTC’s letter with reference to Restasis Multidose against any other drug manufacturer.

b. During the time period in which you were [enforcing] these patents, or in the ensuing 30-month period in which you were granted a stay that delayed approval of a generic competitor to one of these drugs, what were total sales (in dollars) of these drugs? What were total sales to Medicare and Medicaid?

RESPONSE: This question is not applicable. There was no time period in which AbbVie was enforcing these patents. Accordingly, there was no ensuing 30-month stay of approval for any generic version of Restasis Multidose.

2. Has AbbVie voluntarily de-listed the four patents listed in the Orange Book with regard to the Restasis Multidose product that the FTC has disputed as being improperly or inaccurately listed?

RESPONSE: AbbVie has not de-listed from the Orange Book the four patents identified in the FTC’s letter because, for the reasons explained above, the applicable federal law and regulations appear to require them to be listed.

a. Please specify which ones you have de-listed.

RESPONSE: This question is not applicable. For the reasons explained above, AbbVie has not de-listed from the Orange Book the four patents identified in the FTC’s letter.

Advisory Opinion, Docket No. FDA-2005-A-0476 (Jan. 10, 2005). The FDA denied all five of these requests for clarification and instead issued a Federal Register notice in June 2020 soliciting public comment on patent listing issues. No further clarification on the patent listing requirements beyond the 2003 regulations has been issued by the FDA.

⁸ Letter from Senator Warren and Representative Jayapal to AbbVie Inc., December 13, 2023, at 2.

⁹ *Id.* at 2 (emphasis added).

¹⁰ Centers for Medicare & Medicaid Services, “Medicare Part D Spending by Drug,” 2021, <https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicare-spending-by-drug/medicare-part-d-spending-by-drug//data>

b. Please specify when you will de-list them if you have not done so yet.

RESPONSE: Under the present Orange Book listing requirements imposed by federal law and regulation, the four patents identified in the FTC's letter appear to be required to be listed in the Orange Book with regard to the Restasis Multidose product. If the FDA engages in further rulemaking or provides new guidance on those requirements, then AbbVie will implement the new rules or guidance appropriately.

3. Will AbbVie voluntarily review and de-list additional patents the company has listed in the Orange Book that are improperly or inaccurately listed?

RESPONSE: AbbVie carefully monitors developments in the Orange Book listing requirements imposed by statute and FDA regulations. Should the FDA engage in further rulemaking or provide new guidance on Orange Book listing requirements, then AbbVie will incorporate such new rules or guidance when reviewing Orange Book listings, including, if appropriate, by de-listing patents.

In October 2019, Allergan (which owned the Restasis Multidose product before being acquired by AbbVie in 2020) submitted a request to the FDA to de-list U.S. Patent Nos. 8,629,111, 8,633,162, 8,642,556, 8,648,048, 8,685,930, and 9,248,191 with reference to both Restasis Unit Dose and Restasis Multidose. In 2022, the FDA de-listed these patents with respect to Restasis Unit Dose but has not yet acted on AbbVie's de-listing request for these patents with respect to Restasis Multidose. AbbVie understands that there are certain circumstances in which the FDA will delay amending or removing patent information after receiving a de-listing request by the NDA holder.¹¹ Under the current federal statutory and regulatory requirements for Orange Book patent listing, AbbVie is not presently aware of any other patents for which a de-listing request would be appropriate.

a. Please specify which ones you will de-list.

RESPONSE: In October 2019, a request was made to the FDA to de-list U.S. Patent Nos. 8,629,111, 8,633,162, 8,642,556, 8,648,048, 8,685,930, and 9,248,191 with reference to Restasis Multidose, on which the FDA has not yet taken action.

b. What is your specific timeline for doing so?

RESPONSE: In October 2019, a request was made to the FDA to de-list U.S. Patent Nos. 8,629,111, 8,633,162, 8,642,556, 8,648,048, 8,685,930, and 9,248,191 with reference to Restasis Multidose, on which the FDA has not yet taken action.

Thank you for your inquiry and the opportunity to provide this information.

Sincerely,



Daniel J. Bachner
Vice President, Federal Government Affairs

¹¹ See, e.g., 21 U.S.C. § 355(j)(7)(D)(iii).



1000 Mylan Boulevard
Canonsburg, PA 15317

January 12, 2024

The Honorable Elizabeth Warren
United States Senate

The Honorable Pramila Jayapal
United States House of Representatives

Dear Senator Warren and Representative Jayapal:

We write in response to your letter of December 13, 2023, concerning the Federal Trade Commission's ("FTC") correspondence regarding certain patents listed for EpiPen® and EpiPen Jr® (collectively, "EpiPen") Auto-Injectors in the Orange Book maintained by the Food and Drug Administration ("FDA").

Mylan, together with its affiliated companies as Viatriis Inc., works to enhance access to high-quality, affordable medicines for patients worldwide. With that in mind, we welcome efforts to promote compliance with laws and regulations governing patent listings, as well as other aspects of regulation affecting competition between branded and generic pharmaceuticals. In the case of EpiPen products, for instance, there has been substantial competition for years, with four approved epinephrine auto-injector products currently on the market, as well as a pre-filled syringe.

As to the EpiPen-related patents at issue in the FTC's letter, applicable law and regulations require these patents to be listed in the Orange Book. The FDA has long held that "[t]he key factor" as to whether a patent must be listed "is whether the patent being submitted claims the finished dosage form of the approved drug product," 68 Fed. Reg. 36676, at 36680 (June 18, 2003), and has specifically identified "pre-filled drug delivery systems" as an example of a dosage form. *Id.* The four EpiPen patents meet this definition, because each patent claims a pre-filled drug delivery system and therefore the finished dosage form of the product.

In addition, the four referenced patents are part of the same patent family and expire on the same September 11, 2025 date as U.S. Patent No. 8,870,827, which is also listed in the Orange Book for EpiPen products but is not mentioned in the FTC's letter. There is no dispute that the '827 patent is properly listed, and the U.S. Patent and Trademark Office has determined that the four referenced patents are "patentably indistinct" from the '827 patent.

* * *

Mylan lists and maintains patents in the Orange Book that it believes in good faith are required by law to be listed. Consistent with that approach, we believe the applicable statute and regulations here require listing the four referenced EpiPen patents in the Orange Book.

As you are also likely aware, the FDA reported to Congress in 2022 that it is forming a working group to address issues regarding what patents must be listed in the Orange Book. We look forward to the results of the FDA effort.

Thank you for your interest in this matter and the opportunity to respond.

Sincerely,



Brian S. Roman
Global General Counsel, Viatrix



111 Virginia Street, Ste 300
Richmond, Va 23219
(804) 545-6360

Via Email to [REDACTED]

January 8, 2024

The Honorable Elizabeth Warren
United States Senate
309 Hart Senate Office Building
Washington, DC 20510

The Honorable Pramila Jayapal
United States House of Representatives
2346 Rayburn House Office Building
Washington, DC 20515

Dear Senator Warren and Congresswoman Jayapal:

We are in receipt of your letter dated December 13, 2023.

Please note that with respect to the eight patents the FTC asserted were not properly listed in the Orange Book covering AUVI-Q, we believe that the decision to list each of these patents was proper, consistent, and required by the applicable statutes, regulations, and FDA guidance available at the time of listing. Nevertheless, not conceding that FTC's latest interpretation of the law is accurate, we have delisted all eight patents in question.

With respect to your specific questions as set forth below in italics:

- 1. FTC identified eight patents for AUVI-Q that have been improperly or inaccurately listed in the Orange Book.***
 - a. Has Kaléo ever taken action to enforce any of these patents against any other drug manufacturer? If so, please list all such actions, and their outcome.***
 - b. During the time period in which you were challenging these patents, or in the ensuing 30-month period in which you were granted a stay that delayed approval of a generic competitor to one of these drugs, what were total sales (in dollars) of these drugs? What were total sales to Medicare and Medicaid?***

No, Kaléo has not taken any action against any pharmaceutical manufacturer to enforce these identified patents. Further, Kaléo has not received a paragraph IV certification letter from another manufacturer challenging any of these patents. To our knowledge, none of the patents challenged by the FTC has delayed or affected in any way the development or entry of a generic version of AUVI-Q.

- 2. Has Kaléo voluntarily de-listed the eight patents listed in the Orange Book with regard to the AUVI-Q product that the FTC has disputed as being improperly or inaccurately listed?***
 - a. Please specify which ones you have de-listed.***



111 Virginia Street, Ste 300
Richmond, Va 23219
(804) 545-6360

b. Please specify when you will de-list them if you have not done so yet.

As set forth above, Kaléo believes that the decision to list each of these patents was proper, consistent, and required by the applicable statutes, regulations and FDA guidance available at the time of listing. Nonetheless, Kaléo voluntarily delisted all eight identified patents by letter to FDA dated December 6, 2023.

3. Will Kaléo voluntarily review and de-list additional patents the company has listed in the Orange Book that are improperly or inaccurately listed?

a. Please specify which ones you will de-list.

b. What is your specific timeline for doing so?

By letter to FDA dated December 13, 2023, Kaléo delisted the following FTC-identified patents covering a different product, Naloxone Hydrochloride Injection Auto-injector, NDA 215457:

- Patent No. 7731690
- Patent No. 8016788
- Patent No. 9238108

We further investigated all the other patents listed in the Orange Book that cover our products and determined that three additional patents covering AUVI-Q could be delisted based on the FTC's latest interpretation of the applicable law. Accordingly, by letter to FDA dated December 21, 2023, we delisted the following additional patents covering AUVI-Q:

- Patent No. 9149579
- Patent No. 9724471
- Patent No. 9278182

Should you have any further questions, feel free to contact me via phone at [REDACTED] or via email at [REDACTED]

Sincerely,

Ned Ruffin

Chief Legal & Compliance Officer



January 15, 2024

Sen. Elizabeth Warren
309 Hart Senate Office Building
Washington, D.C. 20510

Rep. Pramila Jayapal
2346 Rayburn House Office Building
Washington, DC 20515

Dear Sen. Warren and Rep. Jayapal:

I am writing in response to your December 13, 2023 letter regarding the Federal Trade Commission's (FTC) recent statements disputing the "accuracy or relevance" of certain patent listings in the Food and Drug Administration (FDA) publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) for four Teva products—ProAir[®] HFA, ProAir DigiHaler[®], QVAR[®] 40, and QVAR RediHaler[®]. On December 15, 2023, Teva notified FDA that the patents identified by the FTC are properly listed in the Orange Book under Orange Book listing statutes and regulations. In that statement, Teva confirmed the correctness of listing those identified patents for these four products, and thus confirmed that it does not intend to delist these identified patents in the future. We also confirm that at this time Teva does not intend to voluntarily delist any other patents the company currently has listed in FDA's Orange Book.

Our decision to maintain our patent listing comes following serious and thoughtful consideration of the FTC's contentions and our concern for Teva's strict compliance with law. Indeed, as one of the industry's only remaining "blended" companies that has both (1) an innovative product portfolio and pipeline, and (2) a global and U.S. critical portfolio of generic and biosimilar medicines, we understand the need to balance innovation with access to medicines for a wide cross section of U.S. and global patients. As such, Teva diligently reviewed all the patents identified against applicable laws and regulations, as well as the First Circuit's ruling in *In re Lantus Direct Purchaser Antitrust Litig.*, 950 F.3d 1 (1st Cir. 2020). After careful review, Teva confirmed its belief that the underlying statute and regulatory guidance support the appropriateness of listing the challenged patents.

At no time did Teva use these patent listings to stifle competition, prolong a monopoly, or price gouge patients, as your letter contends. To the contrary, robust patent listings are inherently pro-competitive as they provide (1) notice to our competitors about the patents that apply to our products, and (2) a mechanism under the Hatch-Waxman framework to litigate patent infringement and validity in parallel with FDA review. This system benefits everyone – especially patients – since it can provide certainty on when generic competition will occur and, in some instances, actually accelerate generic entry. Hatch-Waxman litigation allows for early determination of patent infringement; if a generic developer is found not to have infringed valid patents, the generic is able to receive such a determination early and launch a competitive product. Conversely, if the generic is found to infringe valid patents—which, as outlined below, was the case just a few months ago concerning a number of challenged QVAR[®] patents—the



innovator is able to receive that determination before any market harm has been done and before the generic has incurred any financial liability. In other cases, the innovator and the generic may decide to settle their patent litigation on terms that provide the generic with a license to enter the market before patent expiration, thus facilitating earlier generic competition. This system has created a generic drug industry that is the envy of the world; American patients rely on generics for 90% of their prescriptions, more than any other developed nation, and Teva fills nearly 10% of all generic prescriptions in the U.S.¹

It is important to note also that patent listings are mandatory, and a critical aspect of the legal and regulatory landscape described above. If a company concludes that a patent claims an approved product, the company is **required** by statute to list the patent in FDA’s Orange Book. This is particularly important since FDA has steadfastly refused to tell Teva and other pharmaceutical innovators how to list patents related to components of a drug product, despite repeated requests from industry for this information since at least 2005. Similarly, patent listings do not result in multiple 30 month stays. Indeed, since 2002, U.S. law has provided only a single 30-month stay per generic applicant, no matter how many patents an innovator lists in the Orange Book. It should also be noted that for these types of products, the FDA review and approval process often takes longer than 30 months. Thus, a 30-month stay is seldom the limiting factor in generic entry.

Teva and its affiliates have asserted certain of the Orange Book listed patents for ProAir[®] HFA and QVAR MDI in the following litigations:

PRODUCT	CASE CAPTION	PATENTS	DATE FILED	RESOLVED (Date)
ProAir [®] HFA	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Perrigo Pharmaceuticals Co., et al</i> , No. 12-CV-1101 (D. Del.)	U.S. Patent Nos. 7,105,152 and 7,566,445	9/15/2012	Settlement and License Agreement (6/20/14)
ProAir [®] HFA	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Perrigo Pharmaceuticals Co., et al</i> , No. 13-CV-1441 (D. Del.)	U.S. Patent Nos. 7,105,152; 7,566,445; 6,446,627 and 8,132,712	8/16/13 (consolidated to 12-CV-1101)	Settlement and License Agreement (6/20/14)

¹ IQVIA. (April 2023) “The Use of Medicines in the U.S. 2023: USAGE AND SPENDING TRENDS AND OUTLOOK TO 2027.” Accessible at: <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/the-use-of-medicines-in-the-us-2023/the-use-of-medicines-in-the-us-2023.pdf>.



ProAir [®] HFA	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Lupin Atlantis Holdings SA., et al</i> , No. 17-CV-307 (D. Del.)	U.S. Patent Nos. 7,105,152; 8,132,712 and 9,463,289	3/21/17	Settlement and License Agreement (11/2/17)
ProAir [®] HFA	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Amneal Pharmaceuticals of New York LLC, et al</i> , No. 23-cv-20964 (D. N.J.)	U.S. Patent Nos. 8,132,712; 9,463,289; 9,808,587; 10,561,808; 10,695,512; and 11,395,889	10/6/23	Pending
QVAR [®]	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Cipla Ltd.</i> , No. 20-CV-10172 (consolidated) (D. N.J.).	U.S. Patent Nos. 9,463,289; 9,908,587; 10,022,509; 10,022,510; 10,086,156; 10,561,808; and 10,695,512	8/7/20	Judgment that the '289, '557 and '808 patents are valid and infringed. (6/21/23) That judgment is on appeal.
QVAR [®]	<i>Teva Branded Pharmaceutical Products R&D, Inc. et al. v. Aurobindo</i> , No. 20-CV-14833(consolidated) (D. N.J.).	U.S. Patent Nos. 9,463,289; 9,908,587; 10,022,509; 10,022,510; 10,086,156; 10,561,808; and 10,695,512	10/22/20	Settlement and License Agreement (12/7/2022)

Regarding your request for sales data on these products, Teva considers such information commercially sensitive—among other things, this information is central to Teva’s strategy for competing against other manufacturers, and its public disclosure would unfairly advantage Teva’s competitors as they decide at what price to sell their own products. We can provide such information, but would need the protection of a confidentiality agreement to do so.

In light of the considerations above, we believe it is also important to point out the regulatory challenges that FDA and the Environmental Protection Agency (EPA) are creating for a



competitive asthma inhaler market. Recent communications from FDA and EPA suggest that the propellants used in some Teva inhalation products may be subject to required conversion to alternate propellants with low global warming potential. While this transition itself may be warranted from an environmental perspective, FDA's apparent decision to require clinical trials for the approval of a product with a new propellant will not only increase development time and costs for generics, but it could also diminish competition in the asthma inhaler market as new clinical studies bring new market exclusivities to innovators. Such an outcome is inconsistent with our shared goals—and those identified by FTC—of balancing innovation and access. Congressional attention to this dynamic is long overdue and we would welcome the opportunity to partner with you on it.

In conclusion, Teva remains strongly committed to promoting innovation, including through the appropriate pursuit and defense of intellectual property, and also to ensuring broad based access by all patients to safe, effective and affordable generic medicines. We welcome and embrace any opportunity to work with you for the benefit of patients and to restore much of the Hatch-Waxman framework that has eroded over the last forty years.

Sincerely,

A handwritten signature in black ink, appearing to read "Dov Bergwerk". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Dov Bergwerk
Acting Chief Legal Officer and Corporate Secretary