IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JANSSEN BIOTECH, INC., Plaintiff, v. AMGEN INC., Defendant.	C.A. No. 22-1549-MN [redacted]

FIRST AMENDED COMPLAINT

INTRODUCTION

1. Janssen's scientists and clinicians spent decades developing STELARA® (ustekinumab), a complex biological product and a first-in-kind anti-IL-12/IL-23 fully human antibody medicine. Janssen invested many millions of dollars and countless research hours, and sponsored over 100 clinical trials to expand STELARA®'s use into a variety of diseases and patient populations. Currently, STELARA® is prescribed in the United States to treat plaque psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis ("UC"). Hundreds of thousands of patients have benefited from Janssen's innovative work to date.

2. Janssen's scientists were at the forefront, working to develop a fully human antibody manufactured in living cells and identifying a novel target for that antibody. The antibody Janssen's scientists invented, STELARA®, helps in the removal of IL-12 and IL-23, proteins made by the body as part of the immune response. The mechanisms by which IL-12 and IL-23 affect the body are complex and not completely understood (even today). As a result of its innovative work, Janssen was awarded a patent directed to its novel anti-IL-12 antibody, U.S. Patent No. 6,902,734 ("the '734 patent"), covering the active compound in STELARA®.

3. But the antibody's invention was just the beginning. Janssen's scientists conducted dozens of clinical trials, leading to FDA approvals for the use of STELARA® for multiple conditions. Despite approvals for treatment of plaque psoriasis, psoriatic arthritis, and Crohn's disease, Janssen pressed ahead with large-scale clinical studies for the treatment of UC. The result of this investment was a new treatment option, allowing patients to avoid life-altering surgery and, in many cases, achieve remission of their disease. Fort this discovery, Janssen was awarded U.S. Patent No. 10,961,307 ("the '307 patent") covering methods of treating UC with STELARA®.

4. Janssen also made significant investments in research and development concerning the processes for generating and manufacturing antibodies for therapeutic use. Those efforts included Janssen's October 1, 2020 acquisition of Momenta Pharmaceuticals, Inc. ("Momenta") for $6.5 billion, which provided Janssen with access to new technologies for antibody manufacturing. Momenta was a highly skilled biosimilar manufacturer: its research and development focused on manufacturing antibodies, including enabling biosimilars to more effectively match the reference product. These R&D efforts and technologies are important in Janssen's continuing efforts to manufacture antibody-based therapeutics.

5. Janssen owns U.S. Patent Nos. 9,475,858 ("the '858 patent"), 8,852,889 ("the '889 patent"), 9,217,168 ("the '168 patent"), and 9,663,810 ("the '810 patent") (collectively, "the Manufacturing Patents"). Each of these Manufacturing Patents is directed to methods of using cell culturing processes to target and control features of biosimilar antibodies to assure equivalence to a reference product.

6. As reflected by the grant of the Manufacturing Patents, these covered methodologies are valuable manufacturing techniques. The Biosimilar Price Competition and

Innovation Act of 2009 ("BPCIA") established an abbreviated regulatory pathway for biosimilar manufacturers to seek approval from The U.S. Food & Drug Administration ("FDA") to market products that are "biosimilar" to an approved "biologic" or "referenced" product. 42 U.S.C. § 262 *et seq*. To obtain approval, biosimilar manufacturers need not conduct the expensive and lengthy clinical trials that reference product manufacturers are required to conduct. Instead, a biosimilar manufacturer need only show "biosimilarity" between the proposed biosimilar and the reference product. Further, to obtain the status of an "interchangeable" biosimilar—which allows a biosimilar to be substituted for the reference product without the intervention of the prescribing health care provider—a manufacturer must show the proposed biosimilar can be expected to produce the same clinical result as the reference product. The inventions covered by the Manufacturing Patents further and facilitate the production of biosimilar and interchangeable products by specifying methodologies to derive biosimilars that have the same chemical structure and clinical performance as the reference product.

7. The biosimilars arm of Amgen Inc. ("Amgen" or "Defendant") used and is using these patented methodologies to prepare to commercialize ABP 654, a biosimilar copy of STELARA®—designed to have the same amino acid sequence as the active ingredient (ustekinumab) and highly similar physical and biological properties, so it can be sold as a substitute for STELARA®.[1]

8. On November 7, 2022, Amgen informed Janssen of its intention, pursuant to 42 U.S.C. § 262(l)(8)(A), to begin marketing its biosimilar version of STELARA® after 180 days

[1] *See* Ex. O, https://www.amgenbiosimilars.com/products/our-pipeline ("ABP 654 is an investigational biosimilar to STELARA® (ustekinumab).")

(or upon receiving FDA approval thereafter). Ex. A. REDACTED REDACTED *Id.*

9. Because the launch of ABP 654 would constitute infringement of the STELARA® compound patent (the '734 patent) and UC patent (the '307 patent), Janssen filed its initial Complaint in this matter on November 30, 2022, for infringement of these two patents. Janssen also requested that Amgen disclose its manufacturing process, to allow Janssen to assess whether Amgen infringed the Manufacturing Patents. Amgen initially refused to disclose its manufacturing processes. The reason for its delay is now apparent: following Amgen's belated disclosure on December 5, 2022, Janssen discovered that Amgen's processes infringe the Manufacturing Patents.

10. Thereafter, REDACTED

REDACTED

REDACTED

11. Consequently, Janssen hereby amends its pleading to address Amgen's further infringement of Janssen's patents. Specifically, if Amgen carries through with its stated plan to market ABP 654 REDACTED "for all indications for which STELARA® is approved",

REDACTED

Amgen will infringe at least five Janssen patents: the '307 patent, and each of the four Manufacturing Patents (the '858, '889, '168, and '810 patents). Once ABP 654 hits the market, it will trigger renegotiation of a complex web of contracts between Janssen and Pharmacy Benefit Managers (PBMs) that ultimately control whether and how insurance companies and other payors actually pay for STELARA® (and other drugs encompassed in those contracts). These renegotiations resulting from Amgen's infringing launch will cause irreparable economic harm to Janssen in the form of, among other things, price erosion, damage to Janssen's research and development, loss of goodwill, and harm to Janssen's ongoing relationships with payors and customers. On information and belief, Amgen has already begun communications with PBMs and/or other Janssen customers concerning availability of ABP 654.

12. Janssen files this action seeking a declaratory judgment of infringement of Janssen's patents, and to preliminarily and permanently enjoin Amgen from infringing at least the '307, '858, '889, '168, and '810 patents.

NATURE OF THE ACTION

13. Janssen Biotech, Inc. ("Janssen" or "Plaintiff"), for its Complaint against Amgen, further alleges as follows.

14. This civil action arises under the Patent Laws of the United States, 35 U.S.C. §§ 1, *et seq.*, including 35 U.S.C. § 271(a)-(c), (e) & (g), the BPCIA, including 42 U.S.C. § 262(*l*), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202.

15. This lawsuit results from Amgen's planned and/or ongoing manufacture, use, offer to sell, sale, and import/export of its biosimilar to STELARA® (ustekinumab), called ABP 654—which will infringe Janssen's patents concerning its innovative biologic drug, STELARA®, including at least the '734, '307, '858, '889, '168, and '810 patents.

PARTIES

16. Janssen is a Pennsylvania corporation with its principal place of business at 800 Ridgeview Road, Horsham, Pennsylvania, 19044.

17. Upon information and belief, Amgen is a Delaware corporation with a principal place of business at One Amgen Center Drive, Thousand Oaks, California, 91320.

18. Upon information and belief, Amgen is a biopharmaceutical company in the business of developing, manufacturing, marketing, and selling both biologic and biosimilar drugs, including the proposed biosimilar version of Janssen's STELARA® (ustekinumab) product, ABP 654.

JURISDICTION AND VENUE

19. This is an action for patent infringement under the Patent Laws of the United States, 35 U.S.C. §§ 1, *et seq.*, including 35 U.S.C. § 271(a) *et seq.*, the BPCIA, including 42 U.S.C. § 262(*l*), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201(a), and 2202.

20. The Court has personal jurisdiction over Amgen because Amgen is a corporation organized and existing under the laws of Delaware, and has availed itself of the rights and benefits of Delaware law, including by engaging in patent litigation in this District. *See, e.g.*, *Amgen Inc. v. USV Private Ltd.*, No. 22-387-MN (D. Del.); *Amgen Inc. v. Aurobindo Pharm. Ltd.*, No. 22-227-MN (D. Del.); *Amgen Inc. v. MSN Lab'ys Private Ltd.*, 21-662-MN (D. Del.); *Amgen Inc. v. Alembic Pharm. Ltd.*, No. 21-61-CFC (D. Del.); *Amgen Inc. v. Hospira*, Inc., No. 20-561-CFC (D. Del.). Furthermore, on information and belief, Amgen has regularly and systematically transacted business in Delaware, has engaged in substantial and continuing contacts with Delaware, and through its intended launch will commit acts of patent infringement in Delaware.

21. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391(b)-(c) and 28 U.S.C. § 1400 because Amgen, a Delaware corporation subject to personal jurisdiction in the judicial district of Delaware, resides in the District. Furthermore, on information and belief, Amgen has regularly and systematically transacted business in Delaware and through its intended launch will commit acts of patent infringement in Delaware.

STELARA®

22. STELARA® is a fully human antibody biologic medicine. Its active ingredient is ustekinumab, a fully human isolated anti-IL-12 antibody.[3]

23. FDA first approved STELARA® in September 2009, for the treatment of adults with moderate to severe plaque psoriasis. Today, STELARA® is approved to treat a number of different conditions and patient populations: both adult patients and pediatric patients six years and older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy; both adult patients and pediatric patients six years and older with active psoriatic arthritis; adult patients with moderately to severely active Crohn's disease; and adult patients with moderately to severely active UC.

24. FDA approved STELARA®'s use to treat UC, the most recent indication, in October 2019. For this indication, STELARA® is prescribed, recommended, or suggested in its label for administration to subjects with moderately to severely active UC as a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of ustekinumab.

[3] Ustekinumab, the antibody that is the active ingredient in STELARA®, binds both IL-12 and IL-23 in the body; it can thus be characterized as an anti-IL-12 antibody, as well as an anti-IL-12/IL-23 antibody.

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JANSSEN'S MANUFACTURING OF THERAPEUTIC ANTIBODIES

25. Alongside Janssen's development of STELARA® and other biologic products, Janssen has made significant investments in research and development concerning the processes for generating and manufacturing antibodies for therapeutic use. The intellectual property derived from that research and development has facilitated Janssen's ability to manufacture STELARA® and other products safely and consistently to deliver therapies to patients.

26. Janssen's efforts have also included the acquisition of technologies developed by others in the antibody manufacturing industry. In particular, on October 1, 2020, Janssen acquired Momenta. Momenta's research and development included a substantial focus on methods of manufacturing biosimilar antibodies, including cell culturing processes that impact attributes of recombinant antibodies. These patents are directed to enabling biosimilar manufacturers to use these processes to control attributes of the antibodies produced, thereby more precisely targeting the characteristics of the reference product—and ultimately, producing a better copy than would otherwise be produced. Janssen now owns the '858, '889, '168, and '810 patents.

ABP 654, THE AMGEN BIOSIMILAR PRODUCT

27. Amgen has developed a proposed biosimilar to Janssen's STELARA® product, called ABP 654. Amgen has publicly announced that "ABP 654 is being developed as a biosimilar candidate to STELARA," and further that "ABP 654 has the same pharmaceutical form, dosage strength, route of administration and dosing regimen as" STELARA®. Ex. B at 2-3.

28. In developing ABP 654, Amgen set out to create a copy of STELARA® (ustekinumab). *See* Ex. A; Ex. R, Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab)."). Pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), to be biosimilar ABP 654 must be highly similar to STELARA® with only minor differences in

clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency.

29. On November 11, 2020, Amgen initiated a Phase 3 study evaluating the efficacy and safety of ABP 654 compared with STELARA®. *See* Ex. C. Amgen has publicly stated that this Phase 3 study "evaluating the efficacy and safety of ABP 654 compared to STELARA® . . . demonstrat[ed] no clinically meaningful differences between ABP 654 and STELARA." *See* Ex. B at 1; *see also* Ex. D at 41 ("Preliminary results from a Phase 3 study evaluating the efficacy and safety compared to STELARA® in adult patients with moderate to severe plaque psoriasis met the primary efficacy endpoint.").

30. On information and belief, Amgen also intends to seek approval of ABP 654 as an interchangeable product with respect to STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(k)(4), to be interchangeable, ABP 654 must be biosimilar, and further meet the criteria that it be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

31. Thus, Amgen set out to create a biosimilar version of ustekinumab matching STELARA®'s structural and functional characteristics, such that the ustekinumab antibody in Amgen's ABP 654 product would have no major differences from the ustekinumab antibody in STELARA®, and there would be no clinically meaningful differences between ABP 654 and STELARA® in terms of safety, purity, or potency. This goal informed both Amgen's development process for ABP 654 and the final parameters of Amgen's manufacturing process for ABP 654 and selected characteristics of ABP 654.

32. According to Amgen's aBLA, REDACTED

33. For example, REDACTED

34. REDACTED

35. Moreover, REDACTED

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REDACTED

36. Furthermore, REDACTED

37. REDACTED

38. Amgen has made public statements regarding the development of ABP 654 scientific and healthcare investor conferences, touting it as "analytically similar" to the reference product, STELARA®. *See, e.g.*, Exs. G-I.

39. On information and belief, FDA has not yet approved Amgen's proposed ABP 654 biosimilar product.

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AMGEN'S NOTICE OF COMMERCIAL MARKETING AND THIS INFRINGEMENT ACTION

40. On REDACTED , Amgen submitted an aBLA to FDA seeking approval to market in the United States a biosimilar version of Janssen's STELARA® product. On November 3, 2022, Amgen publicly announced that Phase 3 data had been "submitted to FDA to support U.S. approval" of its biosimilar copy of STELARA® (ustekinumab). *See* Ex. J at 42. Amgen's aBLA submission to FDA[4] constitutes an act of infringement under the BPCIA. *See* 42 U.S.C. § 271(e)(2)(C).

41. On November 7, 2022, Amgen provided its 180-day notice of commercial marketing to Janssen, stating:

> Pursuant to 42 U.S.C. § 262(*l*)(8)(A), Amgen hereby provides this notice of commercial marketing not later than 180 days before the date of the first commercial marketing of Amgen's ABP 654 drug products that are biosimilar candidates to the drug products covered by Biologics License Application Nos. 125261 and 761044 ("Stelara® drug products"). Amgen intends to commercially market its ABP 654 drug products with a full label that includes all the FDA approved indications for the Stelara® drug products. Amgen will decide on a specific date to commence U.S. commercial marketing of its ABP 654 drug products and intends to be ready to commence commercial marketing upon receiving FDA approval.

Ex. A.

42. This notice signals Amgen's stated intent to begin selling its infringing biosimilar product prior to expiration of Janssen's Patents. Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"). Amgen informed Janssen it intends to

[4] Amgen's Notice of Commercial Marketing further supports that Amgen has already submitted its aBLA, since Amgen informed Janssen that it provided that notice "[p]ursuant to 42 U.S.C. § 262(l)(8)(A)." Ex. A. The cited statutory section, 42 U.S.C. § 262(*l*)(8)(A), provides that "[t]he *subsection (k) applicant shall provide notice* to the reference product sponsor not later than 180 days before the date of the first commercial marketing . . . ." (emphasis added). By providing notice "pursuant to" § 262(*l*)(8)(A), Amgen confirms it is a "subsection (k) applicant"—an aBLA submitter under 42 U.S.C. § 262(k).

market ABP 654 for all indications and patient groups for which STELARA® is approved. Ex. A ("Amgen intends to commercially market its ABP 654 drug products with a full label that includes all FDA approved indications for the Stelara® drug products.").

43. On November 11, 2022, counsel for Janssen asked Amgen's counsel whether Amgen had filed its aBLA with FDA, whether and when FDA had accepted Amgen's aBLA application, whether Amgen intended to participate in the BPCIA "patent dance," and whether Amgen would provide its aBLA to Janssen. *See* Ex. K. Amgen did not disclose when it filed its aBLA, whether FDA had accepted it, or whether Amgen intended to participate in the BPCIA "patent dance."

44. Given Amgen's initial refusal to provide its aBLA, Janssen identified patents that "could be identified pursuant to section 351(l)(3)(A)(i)." 35 U.S.C. § 271(e)(2)(C); *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1674–75 (2017) (failure to provide aBLA "does not define the act of artificial infringement itself" but "merely assists in identifying which patents will be the subject of the artificial infringement suit").

45. Based on Amgen's failure to disclose its aBLA, the BPCIA also authorized Janssen to "bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product." 42 U.S.C. § 262(l)(9)(C).

46. On November 29, 2022, Janssen filed its original complaint in this action based on Amgen's infringement of the '734 (compound) and '307 (UC) patents.

47. Amgen did not provide Janssen with a copy of its aBLA until December 5, 2022. *See* Ex. V.

48. On December 8, 2022—three days after Amgen provided Janssen access to its aBLA—Janssen requested Amgen's permission to share Amgen's confidential information with expert consultants to evaluate the several hundred thousand pages of highly technical information included in Amgen's aBLA. *See* Ex. W. Amgen refused to authorize any expert access whatsoever for several weeks. *See* Ex. X. Amgen eventually agreed to authorize three experts on January 4, 2023. As a result, Janssen's expert consultants were unable to even begin their review of Amgen's 326,977-page aBLA materials until January 4, a full month after Amgen first provided it to Janssen.

49. On January 23, 2023, after weeks of negotiations with Janssen, Amgen stipulated to an order that, REDACTED

50. On February 2, 2023, Janssen served on Amgen a list of patents, which included the '734, '307, '858, '889, '168, and '810 patents, for which Janssen believes a claim of patent infringement could reasonably be asserted. *See* 42 U.S.C. § 262(l)(3)(A). Janssen served this list of patents out of an abundance of caution. To date, Amgen has not complied with the patent dance—instead providing its aBLA before, not "after," FDA acceptance of its aBLA for review. *See* 42 U.S.C. § 262(l)(2). And despite numerous requests from Janssen, Amgen also failed to

clearly confirm that it intends to comply with the patent dance. Ex. Y. Instead, Amgen stated that it only provided its aBLA to Janssen "voluntarily." Ex. V.

51. REDACTED

Janssen has not yet obtained discovery concerning any past infringement of the '734 patent or current activities Amgen contends fall under the § 271(e) safe harbor. Furthermore, Amgen continues to take action in Ireland in preparation for importation of ABP 654 into the United States. Ex. Z.

52. Amgen intends to launch ABP 654 prior to expiration of the '307, '858, '889, '168, and '810 patents. Ex. A. Thus, there exists between the parties a controversy of sufficient immediacy to support and maintain a declaratory judgment of patent infringement under 35 U.S.C. § 271(a) *et seq*.

53. On information and belief, FDA's approval of Amgen's aBLA is imminent.[5] FDA has expressed its intention to "[r]eview and act on 90 percent of original biosimilar biological product application submissions within 10 months of the 60 day filing date." Ex. L at 4.

54. As set forth below, Amgen's commercial manufacture, use, sale, offers for sale, and/or importation of its ABP 654 biosimilar product will infringe Janssen's patents, either literally or under the doctrine of equivalents. See 35 U.S.C. §§ 271(a)-(c), (e) & (g).

[5] Unlike the Hatch-Waxman Act, filing a lawsuit under the BPCIA does not trigger an automatic 30-month stay of FDA approval for the biosimilar. Instead, the FDA approval process continues regardless of any patent infringement.

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JANSSEN'S ASSERTED PATENTS

55. In the course of developing STELARA®, Janssen obtained patents related to ustekinumab (the fully human monoclonal anti-IL-12 antibody that is the active compound in STELARA®), including its administration to treat UC and methods of manufacturing of therapeutic antibodies, such as ustekinumab.

56. Janssen asserts the '734, '307, '858, '889, '168, and '810 patents in this suit.

The '734 Patent

57. The '734 patent is titled "Anti-IL-12 antibodies and compositions thereof," and was duly and legally issued on June 7, 2005. A true and correct copy of the '734 patent is attached hereto as Ex. M. Janssen is the owner by assignment of the '734 patent. Broadly speaking, the '734 patent is directed to and claims compositions of ustekinumab, the antibody that is the active ingredient in STELARA®. The '734 patent includes four claims, two of which are independent. Claim 1 recites:

> 1. An isolated anti-IL-12 antibody, comprising a heavy chain variable region (V_H) of the amino acid sequence set forth in SEQ ID NO:7 and a light chain variable region (V_L) of the amino acid sequence set forth in SEQ ID NO:8.

The '307 Patent

58. The '307 patent is titled "Methods of Treating Moderately to Severely Active Ulcerative Colitis by Administering an Anti-IL12/IL23 Antibody," and was duly and legally issued on March 30, 2021. A true and correct copy of the '307 patent is attached hereto as Ex. N. Janssen is the owner by assignment of the '307 patent. In general, the '307 patent is directed to and claims methods of treating UC with ustekinumab, the antibody that is the active ingredient in STELARA®. The '307 patent includes 34 claims, four of which are independent.

59. Claim 3 (which depends from claim 1) recites:

> 1. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of an anti-IL-12/IL-23p40 antibody, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6, wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤2 points with no individual subscore >1 and the US definition of clinical remission with absolute stool number ≤3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore, (iv) improvements from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) score, (v) mucosal healing, (vi) decrease from baseline in Mayo score, and (vii) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.
>
> 3. The method of claim 1, wherein the antibody comprises a heavy chain of the amino acid sequence of SEQ ID NO:10 and a light chain of the amino acid sequence of SEQ ID NO:11.

60. Claim 11 (which depends from claims 1, 2 or 3 and 4, 6, 7, and 9) recites:

> 4. The method of any one of claims 1-3[6], wherein the antibody is in a pharmaceutical composition for intravenous administration comprising a solution comprising 10 mM L-histidine, 8.5% (w/v) sucrose, 0.04% (w/v) polysorbate 80, 0.4 mg/mL L-methionine, and 20 µg/mL EDTA disodium salt, dehydrate, at pH 6.0.

[6] The language of claims 1 and 3 are recited in paragraph 59.

> 6. The method of claim 4, wherein the antibody is administered intravenously to the subject at week 0 of the treatment, at a dosage of about 6.0 mg/kg body weight of the subject or 130 mg per administration.
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> 7. The method of claim 6, wherein the antibody is further administered subcutaneously to the subject at week 8 of the treatment, at a dosage of about 90 mg per administration.
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> 9. The method of claim 7, wherein the antibody is administered in a maintenance dose every 8 weeks after the treatment at week 8 or every 12 weeks after the treatment at week 8.
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> 11. The method of claim 9, wherein the subject is in corticosteroid-free clinical remission at least 44 weeks after week 0.

The '858 Patent

61. The '858 patent is titled "Cell Culture Process" and was duly and legally issued on October 25, 2016. A true and correct copy of the '858 patent is attached hereto as Ex. AA. Janssen is the owner by assignment of the '858 patent. In general, the '858 patent is directed to and claims methods of manufacturing a preparation of a recombinant antibody, such as ustekinumab, targeting a reference standard, including, among other things, culturing a cell in a medium comprising a recited amount of lysine or arginine to achieve that standard. The '858 patent includes 38 claims, two of which are independent.

62. Claim 14 (which depends from claim 1) recites:

> 1. A method of manufacturing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium comprising 2 g/L lysine to 8 g/L lysine under conditions in which the cell expresses a recombinant antibody;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody; and
>
> formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.
>
> 14. The method of claim 1, wherein the cell is a CHO cell.

63. Claim 33 (which depends from claim 20) recites:

> 20. A method of manufacturing a preparation of a recombinant antibody, comprising:
> culturing a cell in a medium comprising 2 g/L arginine to 8 g/L arginine under conditions in which the cell expresses a recombinant antibody;
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;
> and formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.
>
> 33. The method of claim 20, wherein the cell is a CHO cell.

The '889 Patent

64. The '889 patent is titled "Cell Culture Process" and was duly and legally issued on October 7, 2014. A true and correct copy of the '889 patent is attached hereto as Ex. BB. Janssen is the owner by assignment of the '889 patent. In general, the '889 patent is directed to and claims methods of producing a preparation of a recombinant antibody, such as ustekinumab, targeting a reference standard, including, among other things, culturing a cell in a medium comprising a recited amount of lysine or arginine to achieve that standard. The '889 patent includes 30 claims, three of which are independent.

65. Claim 6 (which depends from claim 1) recites:

> 1. A method of producing a preparation of a recombinant antibody, comprising:
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L lysine to less than 20 g/L lysine; and
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody.
>
> 6. The method of claim 1, wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini, and the method further comprises measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.

66. Claim 26 (which depends from claim 16) recites:

> 16. A method of producing a preparation of a recombinant antibody, comprising:
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L arginine to less than 20 g/L arginine, and wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini;
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;
> and measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.
>
> 26. The method of claim 16, wherein the host cell is a CHO cell.

The '168 Patent

67. The '168 patent is titled "Methods of Cell Culture" and was duly and legally issued on December 22, 2015. A true and correct copy of the '168 patent is attached hereto as Ex. CC. Janssen is the owner by assignment of the '168 patent. In general, the '168 patent is directed to and claims methods of producing a preparation of a recombinant antibody, such as ustekinumab, targeting a reference standard, including, among other things, culturing a cell in a culture medium comprising a recited amount of putrescine to achieve that standard. The '168 patent includes 28 claims, four of which are independent. Claim 23 (which depends from claim 1, 10, 13, or 16) recites:

> 1. A method of producing a recombinant protein preparation having a target value of one or more of galactosylated glycans, high mannose glycans, and sialylated glycans, the method comprising:
> (a) providing a cell genetically engineered to express a recombinant protein;
> (b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and
> (c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the one or more of galactosylated glycans, high mannose glycans, and sialylated glycans,

wherein the target value of galactosylated glycans, or sialylated glycans is a level at least 10% higher than a level of galactosylated glycans, or sialylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine; or

wherein the target value of high mannose glycans is a level at least 10% lower than a level of high mannose glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.

23. The method of any one of claim 1, 10, 13, or 16, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

The '810 Patent

68. The '810 patent is titled "Methods of Cell Culture" and was duly and legally issued on May 30, 2017. A true and correct copy of the '810 patent is attached hereto as Ex. DD. Janssen is the owner by assignment of the '810 patent. In general, the '810 patent is directed to and claims methods of producing a preparation of a recombinant antibody, such as ustekinumab, targeting a reference standard, including, among other things, culturing a cell in a culture medium comprising a recited amount of putrescine to achieve that standard. The '810 patent includes 24 claims, three of which are independent. Claim 22 (which depends from claim 1, 10, or 14) recites:

1. A method of producing a recombinant protein preparation having a target value of fucosylated glycans, the method comprising:

(a) providing a cell genetically engineered to express a recombinant protein;

(b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and

(c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the fucosylated glycans

wherein the target value of fucosylated glycans is a level at least 10% higher than a level of fucosylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.

22. The method of any one of claims 1, 10, or 14, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

COUNT I
Infringement of the '734 Patent Under 35 U.S.C. § 271(e)(2)(C)

69. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 68 as though fully set forth herein.

70. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

71. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

72. The active ingredient in ABP 654 is an isolated anti-IL-12 antibody having an amino acid sequence identical to ustekinumab. Such an antibody meets multiple claims of the '734 patent. For example, Claim 1 recites:

> 1. An isolated anti-IL-12 antibody, comprising a heavy chain variable region (V_H) of the amino acid sequence set forth in SEQ ID NO:7 and a light chain variable region (V_L) of the amino acid sequence set forth in SEQ ID NO:8.

73. As a biosimilar to STELARA®, the active ingredient in ABP 654 is an isolated anti-IL-12 antibody.

74. REDACTED

75. Moreover, pursuant to 42 U.S.C. § 262(k)(2)(A)(i), the active ingredient in ABP 654 and ustekinumab must utilize the same mechanism or mechanisms of action for the condition or conditions of use. Amgen has publicly stated that its Phase 3 study "evaluating the efficacy and safety of ABP 654 compared to STELARA® . . . demonstrat[ed] no clinically meaningful differences between ABP 654 and STELARA." *See* Ex. B at 1.

76. After the filing of the original complaint, Janssen included the '734 patent on a list of patents served, in an abundance of caution, pursuant to 42 U.S.C. 262(l)(3)(A) ("3A list"). Ex. II.

77. Thus, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '734 patent is an act of infringement of one or more of the claims of the '734 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

78. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '734 patent, either literally or under the doctrine of equivalents. Ex. K, Ex. JJ.

79. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '734 patent, either literally or under the doctrine of equivalents. Ex. K, Ex. JJ.

80. Amgen has knowledge of and is aware of the '734 patent, including due to both Janssen's counsel's November 11, 2022 email, *see* Ex. K, and the filing of Janssen's original complaint, and on information and belief, has been aware of the '734 patent for months, if not years, before then. Janssen provided notice of the '734 patent to Amgen by marking Stelara® to associate it with U.S. Pat. No. 6,902,734. *See* 35 U.S.C. § 287(a); Ex. KK, https://janssenpatents.com/products-patents?key=stelara.

81. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '734 patent.

82. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT II
Declaratory Judgment of Infringement of the '734 Patent

83. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 82 as though fully set forth herein.

84. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(C); 35 U.S.C. § 271(a)-(c), (e); 28 U.S.C. §§ 2201, 2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

85. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar

version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

86. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

87. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 after 180 days, as early as REDACTED (or upon receiving FDA approval thereafter). Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"), Ex. P. Amgen informed Janssen it intends to market ABP 654 for all indications and patient groups for which STELARA® is approved. Ex. A ("Amgen intends to commercially market its ABP 654 drug products with a full label that includes all FDA approved indications for the Stelara® drug products."). Amgen's stated intention to launch its ABP 654 biosimilar product as soon as possible presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(a)-(c) and (e).

88. On information and belief, Amgen has already begun manufacture in preparation for that imminent launch of ABP 654. REDACTED

89. Amgen's submission of its aBLA, along with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or importation of ABP 654 prior to the expiration of the '734 patent (i.e., immediately upon FDA

approval), creates an actual, immediate, and real controversy within the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '734 patent, literally or under the doctrine of equivalents.

90. Amgen did not provide Janssen a copy of its aBLA prior to the time Janssen filed its original complaint in this action. But to be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

91. Indeed REDACTED REDACTED REDACTED REDACTED For example, Claim 1 recites:

> 1. An isolated anti-IL-12 antibody, comprising a heavy chain variable region (V_H) of the amino acid sequence set forth in SEQ ID NO:7 and a light chain variable region (V_L) of the amino acid sequence set forth in SEQ ID NO:8.

92. As a biosimilar to STELARA®, the active ingredient in ABP 654 is an isolated anti-IL-12 antibody. Ex. HH, Amgen_ABP654_000034947 at 34947.

93. REDACTED

94. Moreover, pursuant to 42 U.S.C. § 262(k)(2)(A)(i), the active ingredient in ABP 654 and ustekinumab must utilize the same mechanism or mechanisms of action for the condition or conditions of use. Amgen has publicly stated that its Phase 3 study "evaluating the efficacy and safety of ABP 654 compared to STELARA® … demonstrat[ed] no clinically meaningful differences between ABP 654 and STELARA." *See* Ex. B at 1.

95. After the filing of the original complaint, Janssen included the '734 patent on a list of patents served, in an abundance of caution, pursuant to 42 U.S.C. 262(l)(3)(A) ("3A list"). Ex. II.

96. Amgen has directly infringed or will directly infringe at least one claim of the '734 patent by making, using, offering for sale, selling within and/or importing into the United States ABP 654, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a).

97. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '734 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c).

98. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '734 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

99. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '734 patent, either literally or under the doctrine of equivalents.

100. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '734 patent, either literally or under the doctrine of equivalents.

101. Amgen has knowledge of and is aware of the '734 patent, including due to both Janssen's counsel's November 11, 2022 email, *see* Ex. K, and the filing of Janssen's original complaint, and on information and belief, has been aware of the '734 patent for months, if not years, before then. Janssen provided notice of the '734 patent to Amgen by marking Stelara® to associate it with U.S. Pat. No. 6,902,734. *See* 35 U.S.C. § 287(a); https://janssenpatents.com/products-patents?key=stelara.

102. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '734 patent.

COUNT III
Infringement of the '307 Patent Under 35 U.S.C. § 271(e)(2)(C)

103. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 102 as though fully set forth herein.

104. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

105. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

106. Moreover, pursuant to 42 U.S.C. § 262(k)(2)(A)(i), the active ingredient in ABP 654 and ustekinumab must utilize the same mechanism or mechanisms of action for the condition or conditions of use. Amgen has publicly stated that its Phase 3 study "evaluating the efficacy and safety of ABP 654 compared to STELARA® . . . demonstrat[ed] no clinically meaningful differences between ABP 654 and STELARA." *See* Ex. B at 1.

107. Furthermore, ABP 654 must be prescribed, recommended, or suggested for the condition or conditions previously approved for STELARA® with the same route of administration, dosage form, and strength as STELARA®. STELARA® is approved for treatment of, among other things, moderately to severely active UC, with recommended dosing comprising: (1) a single intravenous infusion using weight-based dosing of 260 mg for patients up to 55 kg, 390 mg for patients greater than 55 kg to 85 kg, and 520 mg for patients greater than 85 kg, followed by (2) a subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, and every 8 weeks thereafter. Accordingly, on information and belief, ABP 654 will be prescribed, recommended, or suggested in its labeling for treatment of moderately to severely active UC, with recommended dosing the same as STELARA®.

108. Use of ABP 654 as directed on its label for the treatment of moderately to severely active UC meets each limitation of at least Claim 3 of the '307 patent, which depends from Claim 1 and recites:

> 1. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of an anti-IL-12/IL-23p40 antibody, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6, wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤2 points with no individual subscore >1 and the US definition of clinical remission with absolute stool number ≤3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore, (iv) improvements from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) score, (v) mucosal healing, (vi) decrease from baseline in Mayo score, and (vii) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.
>
> 3. The method of claim 1, wherein the antibody comprises a heavy chain of the amino acid sequence of SEQ ID NO:10 and a light chain of the amino acid sequence of SEQ ID NO:11.

109. As a biosimilar to STELARA®, the active ingredient in ABP 654 is an anti-IL-12/IL-23p40 antibody. REDACTED

110. As a biosimilar to STELARA®, ABP 654 will be prescribed, recommended, or suggested in its label for administration to subjects with moderately to severely active UC as a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of a biosimilar to ustekinumab. Ex. LL, Amgen_ABP654_000038495 at 38495-38498, 38523-38527.

111. As a biosimilar to STELARA®, ABP 654 will be prescribed, recommended, or suggested in its label that UC patients receiving ABP 654 will be responders achieving the same or highly similar clinical responses as those for STELARA®. *Id.*

112. The STELARA® label indicates that UC patients receiving STELARA® include patients that achieved clinical remission defined as a Mayo stool frequency subscore of 0 or 1, Mayo rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1 (modified so that 1 does not include friability; endoscopic improvement defined as a Mayo endoscopy subscore of 0 or 1 (modified so that 1 does not include friability); clinical response defined as a decrease from baseline in the modified Mayo score by >30% and > 2 points, with either a decrease from bassline in the rectal bleeding subscore >1 or a rectal bleeding subscore of 0 or 1; and/or mucosal improvement defined as a combined endoscopic improvement (Mayo endoscopy subscore of 0 or 1) and histologic improvement of the colon tissue (neutrophil infiltration of <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulations of tissue). Accordingly, UC patients receiving STELARA® include responders that at least demonstrate "(i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤2 points with no individual subscore >1 and the US definition of clinical remission with absolute stool number ≤3,

rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1," "(ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore," "(v) mucosal healing," or "(vi) decrease from baseline in Mayo score."

113. Amgen provided Janssen with a copy of Amgen's aBLA for ABP 654 on December 5, 2022, including Amgen's proposed label for ABP 654. REDACTED

REDACTED

114. After the filing of the original complaint, Janssen included the '307 patent on its 3A list.

115. Thus, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '307 patent is an act of infringement of one or more of the claims of the '307 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

116. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the prescription, recommendation, or suggestion of ABP 654 to subjects with moderately to severely active UC directly infringes at least one claim of the '307 patent, either literally or under the doctrine of equivalents. Ex. K; Ex. JJ.

117. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '307 patent, either literally or under the doctrine of equivalents. Ex. K; Ex. JJ.

118. Amgen has knowledge of and is aware of the '307 patent, including due to both Janssen's counsel's November 11, 2022 email, *see* Ex. K, and the filing of Janssen's original complaint, and on information and belief, has been aware of the '307 patent for months, if not years, before then. Janssen provided notice of the '307 patent to Amgen by marking Stelara® to associate it with U.S. Pat. No. 10,961,307. *See* 35 U.S.C. § 287(a); https://janssenpatents.com/products-patents?key=stelara.

119. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '307 patent.

120. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT IV
Declaratory Judgment of Infringement of the '307 Patent

121. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 120 as though fully set forth herein.

122. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(A); 35 U.S.C. § 271(a)-(c) and (e); 28 U.S.C. §§ 2201, 2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

123. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

124. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

125. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '307 patent. Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"); Ex. P.

REDACTED

REDACTED

[redacted]. Amgen's stated intention to launch its ABP 654 biosimilar product as early as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '307 patent presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(b)-(c) and (e).

126. Amgen's submission of its aBLA, combined with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '307 patent, creates an actual, immediate, and real controversy within the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '307 patent, literally or under the doctrine of equivalents.

127. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

128. Moreover, pursuant to 42 U.S.C. § 262(k)(2)(A)(i), the active ingredient in ABP 654 and ustekinumab must utilize the same mechanism or mechanisms of action for the condition or conditions of use. Amgen has publicly stated that its Phase 3 study "evaluating the efficacy and safety of ABP 654 compared to STELARA® . . . demonstrat[ed] no clinically meaningful differences between ABP 654 and STELARA." *See* Ex. B at 1.

129. Furthermore, ABP 654 must be prescribed, recommended, or suggested for the condition or conditions previously approved for STELARA® with the same route of administration, dosage form, and strength as STELARA®. STELARA® is approved for treatment of, among other things, moderately to severely active UC, with recommended dosing comprising: (1) a single intravenous infusion using weight-based dosing of 260 mg for patients up to 55 kg, 390 mg for patients greater than 55 kg to 85 kg, and 520 mg for patients greater than 85 kg, followed by (2) a subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, and every 8 weeks thereafter. Accordingly, on information and belief, ABP 654 will be prescribed, recommended, or suggested in its labeling for treatment of moderately to severely active UC, with recommended dosing the same as STELARA®.

130. REDACTED REDACTED meets each limitation of at least Claim 3 of the '307 patent, which depends from Claim 1 and recites:

> 1. A method of treating moderately to severely active ulcerative colitis (UC) in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of an anti-IL-12/IL-23p40 antibody, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising: a complementarity determining region heavy chain 1 (CDRH1) amino acid sequence of SEQ ID NO:1; a CDRH2 amino acid sequence of SEQ ID NO:2; and a CDRH3 amino acid sequence of SEQ ID NO:3; and the light chain variable region comprising: a complementarity determining region light chain 1 (CDRL1) amino acid sequence of SEQ ID NO:4; a CDRL2 amino acid sequence of SEQ ID NO:5; and a CDRL3 amino acid sequence of SEQ ID NO:6, wherein after treating with the antibody, the subject is a responder to treatment by at least one measure of response to treatment selected from the group consisting of: (i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤2 points with no individual subscore >1 and the US definition of clinical remission with absolute stool number ≤3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1, (ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo

> endoscopy subscore, (iv) improvements from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) score, (v) mucosal healing, (vi) decrease from baseline in Mayo score, and (vii) clinical response as determined by a decrease from baseline in the Mayo score by ≥30% and ≥3 points and a decrease from baseline in the rectal bleeding subscore ≥1 points or a rectal bleeding subscore of 0 or 1.
>
> 3. The method of claim 1, wherein the antibody comprises a heavy chain of the amino acid sequence of SEQ ID NO:10 and a light chain of the amino acid sequence of SEQ ID NO:11.

131. Amgen provided Janssen with a copy of Amgen's aBLA for ABP 654 on December 5, 2022. REDACTED

132. REDACTED as a biosimilar to STELARA®, ABP 654 will be prescribed, recommended, or suggested in its label for administration to subjects with moderately to severely active UC as a pharmaceutical composition comprising a clinically proven safe and clinically proven effective amount of a biosimilar to ustekinumab. Ex. LL, Amgen_ABP654_000038495 at 38495-38498, 38523-38527.

133. REDACTED as a biosimilar to STELARA®, ABP 654 will be prescribed, recommended, or suggested in its label that UC patients receiving ABP 654 will be responders achieving the same or highly similar clinical responses as those for STELARA®. *Id.*

134. The STELARA® label indicates that UC patients receiving STELARA® include patients that achieved clinical remission defined as a Mayo stool frequency subscore of 0 or 1, Mayo rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1 (modified so that 1 does not include friability; endoscopic improvement defined as a Mayo endoscopy subscore of 0 or 1 (modified so that 1 does not include friability); clinical response defined as a decrease from baseline in the modified Mayo score by >30% and > 2 points, with either a decrease from bassline in the rectal bleeding subscore >1 or a rectal bleeding subscore of 0 or 1; and/or mucosal improvement defined as a combined endoscopic improvement (Mayo endoscopy subscore of 0 or 1) and histologic improvement of the colon tissue (neutrophil infiltration of <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulations of tissue). Accordingly, UC patients receiving STELARA® include responders that at least demonstrate "(i) clinical remission based on at least one of the global definition of clinical remission with Mayo score ≤2 points with no individual subscore >1 and the US definition of clinical remission with absolute stool number ≤3, rectal bleeding subscore of 0 and Mayo endoscopy subscore of 0 or 1," "(ii) endoscopic healing with a Mayo endoscopy subscore of 0 or 1, (iii) clinical response based on the Mayo endoscopy subscore," "(v) mucosal healing," or "(vi) decrease from baseline in Mayo score."

135. Amgen provided Janssen with a copy of Amgen's aBLA for ABP 654 on December 5, 2022, including Amgen's proposed label for ABP 654. REDACTED

136. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '307 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c).

137. After the filing of the original complaint, Janssen included the '307 patent on its 3A list.

138. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '307 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

139. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the prescription, recommendation, or suggestion of ABP 654 to subjects with moderately to severely

active UC directly infringes at least one claim of the '307 patent, either literally or under the doctrine of equivalents. Ex. K; Ex. JJ.

140. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '307 patent, either literally or under the doctrine of equivalents. Ex. K; Ex. JJ.

141. Amgen has knowledge of and is aware of the '307 patent, including due to both Janssen's counsel's November 11, 2022 email, *see* Ex. K, and the filing of Janssen's original complaint, and on information and belief, has been aware of the '307 patent for months, if not years, before then. Janssen provided notice of the '307 patent to Amgen by marking Stelara® to associate it with U.S. Pat. No. 10,961,307. *See* 35 U.S.C. § 287(a); Ex. KK, https://janssenpatents.com/products-patents?key=stelara.

142. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '307 patent.

143. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '307 patent.

144. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT V
Infringement of the '858 Patent Under 35 U.S.C. § 271(e)(2)(C)

145. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 144 as though fully set forth herein.

146. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF,

Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

147. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

148. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '858 patent. For example, Claim 14 (which depends from claim 1) recites:

> 1. A method of manufacturing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium comprising 2 g/L lysine to 8 g/L lysine under conditions in which the cell expresses a recombinant antibody;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody; and
>
> formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.
>
> 14. The method of claim 1, wherein the cell is a CHO cell.

149. REDACTED

150. REDACTED

151. REDACTED

152. REDACTED

153. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R

Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

154. REDACTED

155. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

156. REDACTED

157. REDACTED

REDACTED

158. REDACTED

159. REDACTED

160. As another example, Claim 33 (which depends from claim 20) recites:

> 20. A method of manufacturing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium comprising 2 g/L arginine to 8 g/L arginine under conditions in which the cell expresses a recombinant antibody;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;

and formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.

33. The method of claim 20, wherein the cell is a CHO cell.

161. REDACTED

162. REDACTED

163. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

164. REDACTED

165. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

166. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

167. REDACTED

168. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

169. REDACTED

170. REDACTED

171. REDACTED

172. Thus, on information and belief, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '858 patent is an act of infringement of one or more of the claims of the '858 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

173. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '858 patent, either literally or under the doctrine of equivalents. Ex. JJ.

174. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '858 patent, either literally or under the doctrine of equivalents. Ex. J.

175. Amgen has knowledge of and is aware of the '858 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '858 patent for months, if not years, before then.

176. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '858 patent.

177. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT VI
Declaratory Judgment of Infringement of the '858 Patent

178. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 177 as though fully set forth herein.

179. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(A); 35 U.S.C. § 271(a)-(c), (e), (g); 28 U.S.C. §§ 2201, 2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

180. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

181. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

182. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '858 patent. Ex. P; Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"). Amgen's stated intention to launch its ABP 654 biosimilar product as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '858

patent presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(a)-(c), (e), and (g).

183. Amgen's submission of its aBLA, combined with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '858 patent, creates an actual, immediate, and real controversy within the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '858 patent, literally or under the doctrine of equivalents.

184. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

185. Based on confidential information in Amgen's aBLA Amgen makes ABP 654 using a process that meets multiple claims of the '858 patent. For example, Claim 14 (which depends from claim 1) recites:

> 1. A method of manufacturing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium comprising 2 g/L lysine to 8 g/L lysine under conditions in which the cell expresses a recombinant antibody;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody; and
>
> formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.

14. The method of claim 1, wherein the cell is a CHO cell.

186. REDACTED

187. REDACTED

188. REDACTED

REDACTED

189. REDACTED

190. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab). Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone. REDACTED

191. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

192. REDACTED

193. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

194. REDACTED

195. REDACTED

196. REDACTED

197. As another example, Claim 33 (which depends from claim 20) recites:

> 20. A method of manufacturing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium comprising 2 g/L arginine to 8 g/L arginine under conditions in which the cell expresses a recombinant antibody;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;
>
> and formulating the preparation into a drug product if the preparation meets a target value of C-terminal variants of the recombinant antibody, wherein the C-terminal variants differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini.
>
> 33. . . . wherein the cell is a CHO cell.

198. REDACTED

199. REDACTED

REDACTED

200. REDACTED

201. REDACTED

202. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same

clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

203. REDACTED

204. REDACTED

205. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

206. REDACTED

207. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

208. REDACTED

209. Thus, on information and belief, Amgen has directly infringed or will directly infringe at least one claim of the '858 patent by using the patented method in the manufacture of ABP 654 in the United States, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a).

210. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '858 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c) and (g).

211. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '858 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

212. On information and belief, Amgen, without authority, has imported or will import into the United States or has offered to sell, sold, or used or will offer to sell, sell, or use within

the United States ABP 654 and/or the active ingredient in ABP 654, which are made by a process claimed in at least one claim of the '858 patent, during the term of the '858 patent, under 35 U.S.C. § 271(g). On information and belief, ABP 654 and the active ingredient in ABP 654 are not materially changed by subsequent processes and are not a trivial and nonessential component of another product.

213. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '858 patent, either literally or under the doctrine of equivalents. Ex. JJ.

214. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '858 patent, either literally or under the doctrine of equivalents. Ex. JJ.

215. Amgen has knowledge of and is aware of the '858 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '858 patent for months, if not years, before then.

216. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '858 patent.

217. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '858 patent.

218. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT VII
Infringement of the '889 Patent Under 35 U.S.C. § 271(e)(2)(C)

219. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 218 as though fully set forth herein.

220. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

221. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

222. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '889 patent. For example, Claim 6 (which depends from claim 1) recites:

> 1. A method of producing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L lysine to less than 20 g/L lysine; and
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody.

6. The method of claim 1, wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini, and the method further comprises measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.

223. REDACTED

224. REDACTED

225. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

226. REDACTED

227. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or

diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

228. REDACTED

229. REDACTED

230. REDACTED

REDACTED

231. As another example, Claim 26 (which depends from claim 16) recites:

> 16. A method of producing a preparation of a recombinant antibody, comprising:
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L arginine to less than 20 g/L arginine, and wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini;
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;
> and measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.
>
> 26. . . . wherein the host cell is a CHO cell.

232. REDACTED

233. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

234. REDACTED

235. REDACTED

REDACTED

236. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

237. REDACTED

238. REDACTED

239. REDACTED

240. REDACTED

241. Thus, on information and belief, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '889 patent is an act of infringement of one or more of the claims of the '889 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

242. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '889 patent, either literally or under the doctrine of equivalents. Ex. JJ.

243. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '889 patent, either literally or under the doctrine of equivalents. Ex. JJ.

244. Amgen has knowledge of and is aware of the '889 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '889 patent for months, if not years, before then.

245. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '889 patent.

246. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT VIII
Declaratory Judgment of Infringement of the '889 Patent

247. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 246 as though fully set forth herein.

248. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(A); 35 U.S.C. § 271(a)-(c), (e), (g); 28 U.S.C. §§ 2201, 2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

249. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

250. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

251. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '889 patent. Ex. P; Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"). Amgen's stated intention to launch its ABP 654 biosimilar product as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '889 patent presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(a)-(c), (e), and (g).

252. Amgen's submission of its aBLA, combined with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or

importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '889 patent, creates an actual, immediate, and real controversy within the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '889 patent, literally or under the doctrine of equivalents.

253. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

254. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '889 patent. For example, Claim 6 (which depends from claim 1) recites:

> 1. A method of producing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L lysine to less than 20 g/L lysine; and
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody.
>
> 6. The method of claim 1, wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini, and the method further comprises measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.

255. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

256. REDACTED

257. REDACTED

258. REDACTED

REDACTED

259. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

260. REDACTED

REDACTED

261. REDACTED

262. REDACTED

REDACTED

263. As another example, Claim 26 (which depends from claim 16) recites:

> 16. A method of producing a preparation of a recombinant antibody, comprising:
>
> culturing a cell in a medium under conditions in which the cell expresses a recombinant antibody, wherein the medium comprises 1.5 g/L arginine to less than 20 g/L arginine, and wherein the culturing produces C-terminal variants of the recombinant antibody that differ in amino acid sequence only by the presence or absence of a lysine at their carboxyl termini;
>
> isolating the recombinant antibody, thereby producing a preparation of the recombinant antibody;
>
> and measuring a level of one or more C-terminal variants of the recombinant antibody in the preparation.
>
> 26. . . . wherein the host cell is a CHO cell.

264. REDACTED

265. REDACTED

REDACTED

266. REDACTED

267. REDACTED

268. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).")

Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

269. REDACTED

270. REDACTED

REDACTED

271. REDACTED

272. REDACTED

273. Thus, on information and belief, Amgen has directly infringed or will directly infringe at least one claim of the '889 patent by using the patented method in the manufacture of ABP 654 in the United States, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a).

274. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '889 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c) and (g).

275. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '889 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

276. On information and belief, Amgen, without authority, has imported or will import into the United States or has offered to sell, sold, or used or will offer to sell, sell, or use within the United States ABP 654 and/or the active ingredient in ABP 654, which are made by a process claimed in at least one claim of the '889 patent, during the term of the '889 patent, under 35 U.S.C. § 271(g). On information and belief, ABP 654 and the active ingredient in ABP 654 are not materially changed by subsequent processes and are not a trivial and nonessential component of another product.

277. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '889 patent, either literally or under the doctrine of equivalents. Ex. K.

278. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '889 patent, either literally or under the doctrine of equivalents. Ex. K.

279. Amgen has knowledge of and is aware of the '889 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '889 patent for months, if not years, before then.

280. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '889 patent.

281. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '889 patent.

282. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT IX
Infringement of the '168 Patent Under 35 U.S.C. § 271(e)(2)(C)

283. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 282 as though fully set forth herein.

284. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

285. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

286. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '168 patent. For example, Claim 23 (which depends from claim 1, 10, 13, or 16) recites:

> 1. A method of producing a recombinant protein preparation having a target value of one or more of galactosylated glycans, high mannose glycans, and sialylated glycans, the method comprising:
>
> (a) providing a cell genetically engineered to express a recombinant protein;
>
> (b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and
>
> (c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the one or more of galactosylated glycans, high mannose glycans, and sialylated glycans,
>
> wherein the target value of galactosylated glycans, or sialylated glycans is a level at least 10% higher than a level of galactosylated glycans, or sialylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine; or
>
> wherein the target value of high mannose glycans is a level at least 10% lower than a level of high mannose glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.
>
> 23. The method of any one of claim 1, 10, 13, or 16, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

287. REDACTED

288. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

289. REDACTED

290. REDACTED

291. REDACTED

292. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

293. REDACTED Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

294. REDACTED

295. REDACTED

296. REDACTED

297. REDACTED

298. REDACTED

299. REDACTED

300. REDACTED

301. REDACTED

302. REDACTED

303. Thus, on information and belief, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '168 patent is an act of infringement of one or more of the claims of the '168 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

304. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '168 patent, either literally or under the doctrine of equivalents. Ex. K.

305. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '168 patent, either literally or under the doctrine of equivalents. Ex. K.

306. Amgen has knowledge of and is aware of the '168 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '168 patent for months, if not years, before then.

307. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '168 patent.

308. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT X
Declaratory Judgment of Infringement of the '168 Patent

309. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 308 as though fully set forth herein.

310. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(A); 35 U.S.C. § 271(a)-(c), (e), (g); 28 U.S.C. §§ 2201, 2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

311. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

312. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

313. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '168 patent. Ex. P; Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"); Amgen's stated intention to launch its ABP 654 biosimilar product as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '168

patent presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(a)-(c), (e), and (g).

314. Amgen's submission of its aBLA, combined with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '168 patent, creates an actual, immediate, and real controversy within the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '168 patent, literally or under the doctrine of equivalents.

315. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

316. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '168 patent. For example, Claim 23 (which depends from claim 1, 10, 13, or 16) recites:

> 1. A method of producing a recombinant protein preparation having a target value of one or more of galactosylated glycans, high mannose glycans, and sialylated glycans, the method comprising:
>
> (a) providing a cell genetically engineered to express a recombinant protein;
>
> (b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and

(c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the one or more of galactosylated glycans, high mannose glycans, and sialylated glycans,

wherein the target value of galactosylated glycans, or sialylated glycans is a level at least 10% higher than a level of galactosylated glycans, or sialylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine; or

wherein the target value of high mannose glycans is a level at least 10% lower than a level of high mannose glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.

23. The method of any one of claim 1, 10, 13, or 16, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

317. REDACTED

318. REDACTED

319. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

320. REDACTED

321. REDACTED

322. REDACTED

323. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4),

ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

324. REDACTED

325. REDACTED

326. REDACTED

327. REDACTED

328. REDACTED

329. REDACTED

330. REDACTED

331. REDACTED

332. REDACTED

333. Thus, on information and belief, Amgen has directly infringed or will directly infringe at least one claim of the '168 patent by using the patented method in the manufacture ABP 654 in the United States, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a).

334. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '168 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c) and (g).

335. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '168 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

336. On information and belief, Amgen, without authority, has imported or will import into the United States or has offered to sell, sold, or used or will offer to sell, sell, or use within the United States ABP 654 and/or the active ingredient in ABP 654, which are made by a process claimed in at least one claim of the '168 patent, during the term of the '168 patent, under 35 U.S.C. § 271(g). On information and belief, ABP 654 and the active ingredient in ABP 654 are not materially changed by subsequent processes and are not a trivial and nonessential component of another product.

337. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '168 patent, either literally or under the doctrine of equivalents. Ex. K.

338. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '168 patent, either literally or under the doctrine of equivalents. Ex. K.

339. Amgen has knowledge of and is aware of the '168 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '168 patent for months, if not years, before then.

340. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '168 patent.

341. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '168 patent.

342. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT XI
Infringement of the '810 Patent Under 35 U.S.C. § 271(e)(2)(C)

343. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 342 as though fully set forth herein.

344. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

345. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

346. Based on confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '810 patent. For example, Claim 22 (which depends from claim 1, 10, or 14) recites:

> 1. A method of producing a recombinant protein preparation having a target value of fucosylated glycans, the method comprising:
> (a) providing a cell genetically engineered to express a recombinant protein;
> (b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and
> (c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the fucosylated glycans
> wherein the target value of fucosylated glycans is a level at least 10% higher than a level of fucosylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.
>
> 22. The method of any one of claims 1, 10, or 14, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

347. REDACTED

348. REDACTED

349. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

350. REDACTED

351. REDACTED

352. REDACTED

353. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).")

Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

354. REDACTED

355. REDACTED

REDACTED

356. REDACTED

357. REDACTED

358. REDACTED

359. Thus, on information and belief, Amgen's submission of its aBLA to obtain approval to engage in the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 prior to the expiration of the '810 patent is an act of infringement of one or more of the

claims of the '810 patent under 35 U.S.C. § 271(e)(2)(C), either literally or under the doctrine of equivalents.

360. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '810 patent, either literally or under the doctrine of equivalents. Ex. K.

361. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '810 patent, either literally or under the doctrine of equivalents. Ex. K.

362. Amgen has knowledge of and is aware of the '810 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. JJ, and the filing of this amended complaint, and on information and belief, has been aware of the '810 patent for months, if not years, before then.

363. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '810 patent.

364. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

COUNT XII
Declaratory Judgment of Infringement of the '810 Patent

365. Janssen incorporates by reference the allegations set forth in paragraphs 1 through 364 as though fully set forth herein.

366. This declaratory judgment action is authorized by, *inter alia*, the BPCIA due to Amgen's provision of a notice of commercial marketing, and by the Declaratory Judgment Act. *See* 42 U.S.C. §§ 262(*l*)(8)(A-B), 262(*l*)(9)(A); 35 U.S.C. § 271(a)-(c), (e), (g); 28 U.S.C. §§ 2201,

2202. A judicial determination of infringement is necessary and appropriate to resolve this controversy.

367. On REDACTED , Amgen submitted an aBLA to FDA seeking approval for the commercial manufacture, use, offer for sale, sale, and/or importation of ABP 654, its biosimilar version of STELARA® (ustekinumab). Ex. EE, Amgen_ABP654_000000136 at 136-139; Ex. FF, Amgen_ABP654_000037798 at 37798-377800; Ex. J at 42. The reference products for ustekinumab are BLA Nos. 125261 and 761044. Janssen is the holder of BLA Nos. 125261 and 761044.

368. On November 7, 2022, Amgen provided Janssen a notice of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A). Ex. A.

369. Amgen has made substantial preparations and intends to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '810 patent. Ex. P; Ex. A (Amgen "intends to be ready to commence commercial marketing upon receiving FDA approval"). Amgen's stated intention to launch its ABP 654 biosimilar product as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '810 patent presents a controversy of sufficient immediacy to support declaratory judgment of patent infringement under 35 U.S.C. § 271(a)-(c), (e), and (g).

370. Amgen's submission of its aBLA, combined with its stated intention in its Notice of Commercial Marketing to begin commercial manufacture, use, sale, offers for sale, and/or importation of ABP 654 as early as REDACTED (or upon receiving FDA approval thereafter) prior to the expiration of the '810 patent, creates an actual, immediate, and real controversy within

the Declaratory Judgment Act that Amgen will infringe one or more of the claims of the '810 patent, literally or under the doctrine of equivalents.

371. To be marketed as biosimilar to STELARA® pursuant to 42 U.S.C. § 262(i)(2) & (k)(2)(A)(i), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency. Ustekinumab is the active ingredient in STELARA®. Accordingly, ABP 654 must contain either ustekinumab or a human monoclonal antibody identical or highly similar in amino acid sequence to ustekinumab, and also highly similar in other characteristics (*e.g.*, post-translational modifications, carbohydrate profile, etc.).

372. Based on the confidential information in Amgen's aBLA, Amgen makes ABP 654 using a process that meets multiple claims of the '810 patent. For example, Claim 22 (which depends from claim 1, 10, or 14) recites:

> 1. A method of producing a recombinant protein preparation having a target value of fucosylated glycans, the method comprising:
> (a) providing a cell genetically engineered to express a recombinant protein;
> (b) culturing the cell in a culture medium comprising 0.1 mg/L to 10 mg/L putrescine under conditions in which the cell expresses the recombinant protein; and
> (c) harvesting a preparation of the recombinant protein produced by the cell that meets the target value of the fucosylated glycans
> wherein the target value of fucosylated glycans is a level at least 10% higher than a level of fucosylated glycans in a preparation produced by culturing the cell in the medium not comprising 0.1 mg/L to 10 mg/L putrescine.
>
> 22. The method of any one of claims 1, 10, or 14, wherein the cell is a Chinese Hamster Ovary (CHO) cell.

373. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

374. REDACTED

375. REDACTED

376. REDACTED

377. REDACTED

378. REDACTED

379. Amgen's commercial manufacturing of ABP 654 is intended to produce a preparation of ustekinumab that is biosimilar to STELARA®. *See* Ex. A; Ex. R Amgen_ABP654_000038766 at 38769 ("ABP 654 is a biosimilar to Stelara® (ustekinumab).") Amgen is also conducting a Phase 3 clinical study to investigate interchangeability of ABP 654 for STELARA®. *See* Ex. E; *see also* Ex. F at 40 ("A Phase 3 study to support an interchangeability designation in the U.S. is ongoing."). Pursuant to 42 U.S.C. § 262(i)(2), (k)(2)(A)(i), & (k)(4), ABP 654 must be highly similar to STELARA® with only minor differences in clinically inactive components, and with no clinically meaningful difference between ABP 654 and STELARA® in terms of safety, purity, and potency, and if interchangeable, must be expected to produce the same clinical result as STELARA® in any given patient, and have no increased risk in terms of safety or diminished efficacy of alternating or switching between the use of ABP 654 and STELARA® compared to using STELARA® alone.

380. REDACTED

CONTAINS PLAINTIFF'S & DEFENDANT'S CONFIDENTIAL INFORMATION

REDACTED

381. REDACTED

382. REDACTED

383. REDACTED

384. Thus, on information and belief, Amgen has directly infringed or will directly infringe at least one claim of the '810 patent by using the patented method in the manufacture ABP 654 in the United States, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a).

385. On information and belief, Amgen has an affirmative intent to actively induce or contribute to infringement by others of at least one claim of the '810 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b)-(c) and (g).

386. Through submitting its aBLA to FDA, Amgen has infringed or will infringe at least one claim of the '810 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e).

387. On information and belief, Amgen, without authority, has imported or will import into the United States or has offered to sell, sold, or used or will offer to sell, sell, or use within the United States ABP 654 and/or the active ingredient in ABP 654, which are made by a process claimed in at least one claim of the '810 patent, during the term of the '810 patent, under 35 U.S.C. § 271(g). On information and belief, ABP 654 and the active ingredient in ABP 654 are not materially changed by subsequent processes and are not a trivial and nonessential component of another product.

388. Amgen is aware, has knowledge, and/or is willfully blind to the fact that the commercial manufacture, use, sale, offer to sell, and/or importation of ABP 654 directly infringes at least one claim of the '810 patent, either literally or under the doctrine of equivalents. Ex. K.

389. Amgen will knowingly or with willful blindness induce or contribute to another's direct infringement of at least one claim of the '810 patent, either literally or under the doctrine of equivalents. Ex. K.

390. Amgen has knowledge of and is aware of the '810 patent, including due to both Janssen's counsel's November 28, 2022 letter, *see* Ex. K, and the filing of this amended complaint, and on information and belief, has been aware of the '810 patent for months, if not years, before then.

391. Janssen will suffer irreparable injury for which damages are an inadequate remedy unless Amgen is enjoined from infringing the claims of the '810 patent.

392. Janssen seeks a declaratory judgment that future commercial manufacture, use, sale, offer for sale, and/or importation of ABP 654 will infringe the '810 patent.

393. Janssen seeks an injunction preventing Amgen from the commercial manufacture, use, sale, offer for sale within and/or importation into the United States of ABP 654.

PRAYER FOR RELIEF

WHEREFORE, Janssen respectfully requests that this Court enter judgment in its favor against Amgen and grant the following relief:

A. a judgment and declaration that Amgen has or will infringe or has or will induce or contribute to infringement of one or more claims of the Asserted Patents by engaging in the manufacture, import, offer for sale, sale, or use within the United States of the Amgen aBLA Product before the expirations of the '734, '307, '858, '889, '168, and/or '810 patents;

B. preliminary and permanent equitable relief, including but not limited to a preliminary and permanent injunction that enjoins Amgen, its officers, partners, agents, servants, employees, parents, subsidiaries, affiliate corporations, other related business entities, and all other persons acting in concert, participation, or in privity with them and/or their successors or assigns from infringing the '734, '307, '858, '889, '168, and/or '810 patents, or inducing or contributing to anyone to do the same, by acts including the manufacture, use, offer to sell, sale, or distribution within the United States, or importation into the United States, of any current or future versions of the Amgen aBLA Product, the use or manufacturing of which infringes the '734, '307, '858, '889, '168, and/or '810 patents;

C. a declaration that this is an exceptional case and an award to Plaintiff of its attorneys' fees, costs, and expenses pursuant to 35 U.S.C. § 271(e)(4) and 35 U.S.C. § 285;

D. any available damages pursuant to 35 U.S.C. § 284; and

E. such other relief as this Court may deem just and proper.

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